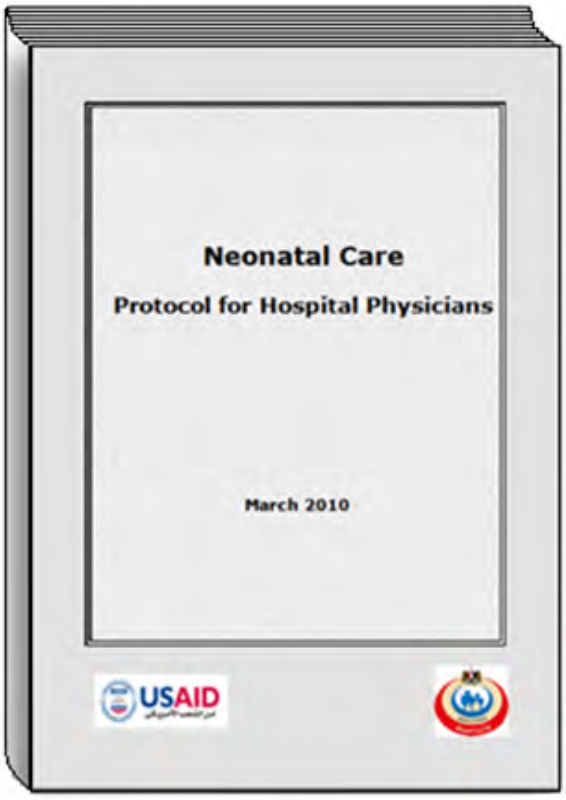
Neonatal Care
Protocol for Hospital Physicians
March 2010
USAID

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USAID
FROM THE AMERICAN PEOPLE

Ministry of Health
وزارة الصحة

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Introduction

Over the last 30 years, the Egyptian Ministry of Health (MOH) in partnership with the United States Agency for International Development (USAID) and other partners has made steady and significant strides in reducing mortality and fertility through appreciable improvements in reproductive, maternal and child health care**.** The maternal mortality ratio has decreased dramatically from 174/100,000 live births in 1993[1] to 53/100, 000 live births in 2008[2], while the total fertility rate (TFR) has decreased from 4.4 in the 1988 to 3.0 according to the 2008 Egyptian Demographic and Health Survey (EDHS). Equally impressive are the reductions in child mortality. During the ten years preceding the 2008 EDHS, infant and neonatal mortality rates dropped from 41 to 25 and 21 to 16 deaths per 1,000 live births, respectively.

In 2006, USAID awarded Pathfinder the Integrated Reproductive Health Services Project "Takamol", with the principal mandate to assist the MOH to further reduce the maternal, infant, and neonatal mortality and to reach replacement level fertility by 2017. To achieve this goal, Takamol builds upon the achievements and best practices of two previous USAID projects: Tahseen, focused on FP/RH under Pathfinder leadership, and Healthy Mother/Healthy Child (HM/HC) under the direction of John Snow, Inc. integrating the vertical interventions of the previous projects, Takamol is designed to achieve four results:

1) Increased use of quality integrated MCH/FP/RH services at the PHC level,

2) Increased use of quality integrated MCH/FP/RH services in hospitals,

3) Positive behavior change in target communities, and

4) Improved MOH capacity to sustain performance of integrated MCH/FP/RH.

The Takamol strategic approach underscores the importance of quality and integration as essential components to the implementation of sustainable MCH/FP/RH services at PHC and hospital levels.

To this end, Takamol with MOH has revised/updated the Essential Obstetric and Neonatal Care protocols previously developed under HM/HC project, integrated them with the FP/RH protocols developed by Tahseen, and provided a comprehensive and integrated package of MCH/FP/RH protocols. These protocols reflect the most recent clinical evidence-based medicine practices and have been adapted for use in district and general hospitals in Egypt. Both the accreditation process for hospitals and the National Guidelines for Infection Control were taken into consideration in their design.

The purpose of the protocols is to standardize clinical management among practitioners in providing quality integrated maternal, newborn, family planning and reproductive health services. It is planned to use them as the basis for didactic and on-the-job training for existing and new physicians and nurses. They can be used by individual providers and/or provider teams to conduct self-assessments and by their supervisors to perform routine monitoring. It is also recommended that Safe Motherhood Committees (SMC) at hospital, district, and governorate levels refer to these protocols as an additional aid in analyzing the clinical performance in the event of hospital-based maternal and/or neonatal mortalities.

The update/revision of the protocols involved the major stakeholders: service providers, hospital and governorate supervisors, trainers/coaches, MOH central departments, professors representing most of the Egyptian universities, private sector hospitals, and professional

[1] Egypt National Maternal Mortality Study, 1992-93. MOH
[2] Maternal Mortality Surveillance System, MOH

associations. A coordinating committee including one or two university professors in addition to a Takamol relevant staff member was established for each protocol to coordinate the efforts of the revision/update. It was responsible for the assessment of needed changes, distribution/collection of different chapters to/from writers and reviewers, reviewing the content and ensuring consistency, coordinating meetings and discussions with MOH counterparts, editors and formatters as well as reaching consensus on the final updated product.

This final approved product of integrated MCH/FP/RH protocols includes seven protocols:

- Integrated Obstetric and Reproductive Health Protocol for Hospital Physicians
- Integrated Obstetric and Reproductive Health Protocol for Hospital Nurses
- Neonatal Care Protocol for Hospital Physicians
- Neonatal Care Protocol for Hospital Nurses
- Obstetric-related Anesthesia Protocol for Hospital Physicians
- Obstetric/Neonatal-related Laboratory Protocol for Hospital Physicians
- Obstetric/Neonatal-related Laboratory Protocol for Hospital Technicians

The MOH and Takamol endorse the consistent and universal use of these protocols by the clinical providers and the technicians in general and district hospitals throughout Upper and Lower Egypt. It is our sincere hope that this set of protocols will contribute to improving the health and well being of women and children in our country.

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List of Abbreviations

A/C	**Assist/Control**
AAP	**American Academy of Pediatrics**
ABR	**Auditory brain stem response**
AChE	**Acetylcholinesterase**
ACOG	**American College of Obstetricians and Gynecologists**
ACTH	**Adrenocorticotropic hormone**
ADH	**Antidiuretic hormone**
AED's	**Anti-epileptic drugs**
AFP	**Alpha-fetoprotein**
AGA	**Appropriate for gestational age**
ALT	**Alanine transaminase**
AMP	**Adenosine monophosphate**
ANC	**Absolute neutrophil count**
AOP	**Anemia of prematurity**
APTT	**Activated partial thromboplastin time**
ASD	**Atrial septal defect**
AST	**Aspartate transaminase**
ATN	**Acute tubular necrosis**
AV block	**Atrioventricular block**
B/A ratio	**Bilirubin/albumin ratio**
BP	**Blood pressure**
BFHI	**Baby-Friendly Hospital Initiative**
BPD	**Bronchopulmonary dysplasia**
BSA	**Body surface area**
BUN	**Blood urea nitrogen**
CAH	**Congenital adrenal hyperplasia**
CB	**Conjugated bilirubin**
CBC	**Complete blood count**
CDC	**Centers for Disease Control**
CH	**Congenital hypothyroidism**
CHD	**Congenital heart disease**
CHF	**Congestive heart failure**
CK	**Creatine kinase**
CLD	**Chronic lung disease**

CMV	**Cytomegalovirus**
CNS	**Central nervous system**
CONS	**Coagulase-negative staphylococci**
CPAP	**Continuous positive airway pressure**
CRP	**C-reactive protein**
CRBSI	**Catheter related blood stream infection**
CSF	**Cerebrospinal fluid**
CST	**Contraction stress test**
CT	**Computed tomography**
CVP	**Central venous pressure**
CVS	**Chorionic villus sampling**
D5W	**Dextrose 5% in water**
D7.5W	**Dextrose 7.5% in water**
D10W	**Dextrose 10% in water**
dB	**Decibell**
DDH	**Developmental dislocation of the hip**
DIC	**Disseminated intravascular coagulopathy**
DNA	**Deoxyribonucleic acid**
DR	**Delivery room**
EA	**Esophageal atresia**
EBM	**Expressed breast milk**
ECF	**Extracellular fluid**
ECG	**Electrocardiogram**
ECMO	**Extracorporial membrane oxygenation**
EEG	**Electroencephalogram**
EH	**Epidural hemorrhage**
ELBW	**Extremely low birth weight**
ENNCP	**Egyptian National Neonatal Care Program**
EOS	**Early onset sepsis**
ETCOc	**End tidal carbon monoxide**
ETT	**Endotracheal tube**
FAOD	**Fatty acid oxidation defect**
FBM	**Fetal breathing movements**
FDP's	**Fibrinogen degradation products**
FE-Na	**Fractional excretion of sodium**

FFA	**Free fatty acids**
FFP	**Fresh frozen plasma**
FHR	**Fetal heart rate**
FIO_2	**Fraction of inspired oxygen**
FRC	**Functional residual capacity**
G6PD	**Glucose-6-phosphate dehydrogenase**
GA	**Gestational age**
GALT	**Galactose-1-phosphate uridyltransferase**
GBS	**Group B streptococci**
GER	**Gastro-esophageal reflux**
GERD	**Gastro-esophageal reflux disease**
GFR	**Glomerular filtration rate**
GGT	**Gamma-glutamyl transpeptidase**
GIR	**Glucose infusion rate**
GIT	**Gastrointestinal tract**
GMH	**Germinal matrix hemorrhage**
GSD	**Glycogen storage disease**
GVHD	**Graft versus host disease**
Hb	**Hemoglobin**
HBIG	**Hepatitis B immunoglobulin**
HBsAg	**Hepatitis B surface antigen**
HBV	**Hepatitis B virus**
hCG	**Human chorionic gonadotropin**
Hct	**Hematocrit**
HCV	**Hepatitis C virus**
HDN	**Hemorrhagic disease of the newborn**
HELLP	**Hemolytic anemia, elevated liver enzymes and low platelet count**
HIE	**Hypoxic-ischemic encephalopathy**
HIV	**Human immunodeficiency virus**
HMD	**Hyaline membrane disease**
HMF	**Human milk fortifier**
Hrs	**Hours**
HPA	**Human platelet antigen**
HSV	**Herpes simplex virus**
I/E ratio	**Inspiratory/expiratory ratio**

I/T ratio	**Immature to total ratio**
IAP	**Intrapartum antimicrobial prophylaxis**
ICF	**Intracellular fluid**
IDM	**Infant of a diabetic mother**
IEM	**Inborn error of metabolism**
IgG	**Immunoglobulin G**
IM	**Intramuscular**
IMV	**Intermittent mandatory ventilation**
INR	**International normalized ratio**
IPH	**Intraparenchymal hemorrhage**
IPPV	**Intermittent positive pressure ventilation**
ITP	**Immune thrombocytopenia**
IUGR	**Intrauterine growth restriction**
IV	**Intravenous**
IVH	**Intraventricular hemorrhage**
IVIG	**Intravenous immunoglobulin**
IWL	**Insensible water losses**
KMC	**Kangaroo mother care**
L/P ratio	**Lactate/pyruvate ratio**
L/S ratio	**Lecithin / sphingomyelin ratio**
LBW	**Low birth weight**
LES	**Lower esophageal sphincter**
LGA	**Large for gestational age**
LOS	**Late onset sepsis**
LP	**Lumbar puncture**
MAP	**Mean airway pressure**
MAS	**Meconium aspiration syndrome**
MCT	**Medium chain triglycerides**
MCV	**Mean corpuscular volume**
MEN	**Minimal enteral nutrition**
MRI	**Magnetic resonance imaging**
MRSA	**Methicillin resistant *Staphylococcus aureus***
MSAFP	**Maternal serum alpha-fetoprotein**
MSUD	**Maple syrup urine disease**
MV	**Mechanical ventilator**

NCPAP	**Nasal CPAP**
NEC	**Necrotizing enterocolitis**
NG tube	**Nasogastric tube**
NICU	**Neonatal intensive care unit**
NKH	**Non ketotic hyperglycinemia**
NMDA	**N-methyl D-aspactate**
NNS	**Non-nutritive sucking**
NO	**Nitric oxide**
NPO	**Nothing per os**
NRP	**Neonatal Resuscitation Program**
NS	**Normal saline**
NST	**Non-stress test**
NTD	**Neural tube defect**
NTE	**Neutral thermal environment**
OCT	**Oxytocin challenge test**
OR	**Operation room**
OTC	**Ornithine transcarbamolase**
Oz	**Ounce**
PAF	**Platelet activating factor**
$PaCO_2$	**Partial arterial carbon dioxide pressure**
PaO_2	**Partial arterial oxygen pressure**
PAPP-A	**Pregnancy-associated plasma protein A**
PC	**Pyruvate carboxylase**
PCR	**Polymerase chain reaction**
PCV	**Packed cell volume**
PDA	**Patent ductus arteriosus**
PDH	**Pyruvate dehydrogenase**
PHHI	**Persistent hyperinsulinemic hypoglycemia of infancy**
PIE	**Pulmonary interstitial emphysema**
PMA	**Postmenstrual age**
PMN	**Polymorphnuclear**
PN	**Parenteral nutrition**
PNA	**Postnatal age**
PO	**Per-oral**
PPHN	**Persistent pulmonary hypertension**

ppm	**Parts per million**
PPV	**Positive pressure ventilation**
PSV	**Pressure support ventilation**
PT	**Prothrombin time**
PTU	**Propylthiouracil**
PTV	**Patient-triggered ventilation**
PUBS	**Percutaneous umbilical blood sampling**
PUV	**Posterior urethral valve**
PVD	**Post-hemorrhagic ventricular dilatation**
PVHI	**Periventricular hemorrhagic infarction**
q	**Every (quaque)**
RBC's	**Red blood cells**
RDS	**Respiratory distress syndrome**
Rh factor	**Rhesus factor**
rh-EPO	**Recombinant human erythropoietin**
RNA	**Ribonucleic acid**
ROM	**Rupture of membranes**
ROP	**Retinopathy of prematurity**
RR	**Respiratory rate**
SAH	**Subarachnoid hemorrhage**
SaO_2	**Arterial oxygen saturation**
SC	**Subcutaneous**
SCM	**Sternocleidomastoid muscle**
SD	**Standard deviation**
SDH	**Subdural hemorrhage**
SGA	**Small for gestational age**
SGH	**Subgaleal hematoma**
SIADH	**Syndrome of inappropriate antidiuretic hormone secretion**
SIDS	**Sudden infant death syndrome**
SIMV	**Synchronized intermittent mandatory ventilation**
SIPPV	**Synchronised intermittent positive pressure ventilation**
SLE	**Systemic lupus erythematosus**
SSC	**Skin to skin contact**
SVT	**Supraventricular tachycardia**
TAR	**Thrombocytopenia with absent radii**

TB	**Tubercle bacillus**
TBW	**Total body water**
TcB	**Transcutaneous bilirubin**
Te	**Expiratory time**
TEF	**Tracheoesophageal fistula**
TGA	**Transposition of the great arteries**
Ti	**Inspiratory time**
TMS	**Tandem mass spectrometry**
TORCH	**Toxoplasmosis, other, rubella, cytomegalovirus, and herpes simplex**
TPN	**Total parenteral nutrition**
TRAb	**Thyroid receptor antibodies**
TRH	**Thyrotropin releasing hormone**
TSB	**Total serum bilirubin**
TSH	**Thyroid stimulating hormone**
TTN	**Transient tachypnea of the newborn**
UAC	**Umbilical artery catheter**
UCB	**Unconjugated bilirubin**
UCD	**Urea cycle defect**
UDPG-T	**Uridine diphosphate glucuronyl transferase**
UE_3	**Unconjugated estriols**
UNICEF	**United Nations International Children's Emergency Fund**
UVC	**Umbilical vein catheter**
V/Q	**Ventilation perfusion**
VEGF	**Vascular endothelial growth factor**
VG	**Volume guarantee**
VLBW	**Very low birth weight**
VLCFA's	**Very long chain fatty acids**
VP	**Ventriculo perotineal**
VSD	**Ventricular septal defect**
Vt	**Tidal volume**
VWD	**Von Willebrand disease**
VZIG	**Varicella zoster immune globulin**
VZV	**Varicella zoster virus**
WBC	**White blood cell**
WHO	**World Health Organization**

Chapter 1

Integration of Perinatal Care

Integration of Perinatal Care

The successful delivery of high quality care to perinatal patients requires not only excellence from physicians, nurses**,** and other health professionals but also community involvement, and an integrated system of organization that permits the health professionals to function as a cohesive team with clear linkages established between the obstetricians and the neonatologists.

Components of the Integrated Perinatal Care in Hospitals

Notification of deliveries

- Integrated perinatal service system should include a Notification Form used to inform the neonatal team as soon as the obstetric patient is admitted and evaluated, giving a potential timeline for delivery.
- Neonatologists are notified and briefed about the circumstances of the delivery, well ahead of the delivery.
- Direct telephone communications established between the neonatal unit and the operation room (OR) or the delivery room (DR) will strengthen lines of communication.

Consensus about level of risks for neonatal care in the delivery room (DR) and operation room (OR)

- All neonatologists and obstetricians should know levels of risk for neonatal care in the DR and OR, and reach consensus about which deliveries will be attended by the resident or the specialist.
- This will enable the neonatal team to focus their efforts on the high-risk cases, thus resulting in better outcomes and more efficient use of the neonatal teams' time.

Levels of risk for neonatal care in the DR and OR

- **Level 0:** Defined as "Low Risk"
- **Level 1:** Defined as "Mild to Moderate Risk"
- **Level 2:** Defined as "Severe Risk"

Table (1-1): Classification of risk for neonatal care in DR and OR

Level 0 (Low Risk)	
Identifying maternal fetal factors	• Uncomplicated pregnancy, labor**,** and delivery
Personnel	• Doctor, or nurse, or medical staff
Equipment	• Routine equipments for resuscitation • Equipped radiant warmer
Level 1 (Mild to Moderate Risk)	
Identifying maternal fetal factors	• Cesarean section • Meconium staining • Fetal distress • 32-36 weeks' fetus • >42 weeks' fetus • Intrauterine growth restriction (IUGR) • Multiple gestations • Breech delivery • Mild Rh disease* • Maternal illness • Suspected infection • Vaginal bleeding • General anesthesia • Sedative narcotics administration • Polyhydramnios • Oligohydramnios
Personnel	• Neonatal **resident**, plus a neonatal care nurse
Equipment	• Routine equipments for resuscitation • Equipped radiant warmer • Emergency cart • Cardiorespiratory and blood pressure monitor
Level 2 (Severe Risk)	
Identifying maternal fetal factors	• <32 weeks' fetus • Known anomalies affecting transition • Severe Rh disease* • Any level 1 fetus with complications
Personnel	• Neonatal **specialist**, plus a neonatal care nurse
Equipment	• Routine equipments for resuscitation • Equipped radiant warmer • Emergency cart • Cardiorespiratory and blood pressure monitor

* The severity of Rh disease during pregnancy can be identified by maternal antibody screening. Regular ultrasound of the fetus is performed to detect fetal hydrops.

Neonatal resuscitation

- The process of delivery may be long and hard, but the loud and clear cry of a newborn is an indescribable joy. The ability to keep the newborn breathing, its nose and mouth clear, and its heart beating, are life-saving skills that must be professionally practiced by the delivery attendant. In an emergency, there is no time for panic; certain emergency steps must be initiated at once. Critical interventions within the first 20 seconds can be life saving, resulting in a happy mother returning home with a healthy neonate.
- After knowing the level of risk, proper preparation of personnel and equipment is essential.

Personnel and equipment

- Every delivery should be attended by at least one person whose only responsibility is the baby, and who is capable of initiating resuscitation. Either that person or someone else who is immediately available should have the skills required to perform a complete resuscitation.
- When resuscitation is anticipated, additional personnel should be present in the delivery room before the delivery occurs.

Essential equipment and supplies

Suction equipment

- Bulb syringe
- Mechanical suction and tubing; the negative pressure should not exceed 100 mmHg
- Suction catheters (5Fr, 6Fr, 8Fr, 10Fr)
- Meconium aspirator (if available)

Bag and mask equipment

- Self-inflating bag (suitable for neonates, approximately 750 ml) with a pressure-release valve, and a reservoir. This ambubag is capable of delivering 90-100% oxygen
- Face masks; term and preterm sizes (cushioned rim masks are preferred)
- Oral airways; term and preterm sizes
- Oxygen source with flowmeter and tubing, adjusted at a flow of 5-8 L/minute

Intubation equipment

- Laryngoscope with straight blades, No. 0 (for preterm infants), and No. 1 (for term infants); make sure the laryngoscope light is bright
- Extra bulbs and batteries for laryngoscope
- Endotracheal tubes (2.5, 3.0, 3.5, 4.0 mm internal diameter)
- Stylet (if available)
- Scissors

Umbilical vessel catheterization supplies

- Scalpel or scissors
- Povidone-iodine solution

- Umbilical tape
- Umbilical catheters (3.5Fr, 5Fr)
- Three-way stopcocks

Medications

- Epinephrine (1:10,000 solutions)
- Volume expanders, one or more of these: normal saline and ringer's lactate
- Glucose 10% solution
- Sterile water
- Naloxone hydrochloride

Miscellaneous

- Radiant warmer
- Sterile gloves
- Stethoscope (with infant-sized head)
- Feeding tubes (6Fr, 8Fr)
- Adhesive tape (½ or ¾ inch)
- Syringes (1, 3, 5, 10, 20, 50 ml)
- Needles (25, 21, 18 gauge)
- T connectors and stopcocks
- Warm linens
- Clock
- Thermometer
- Cardiac monitor and electrodes or pulse oximeter and a probe (optional)

Division of responsibility

Obstetric/Gynecology nurse responsibility

- At any time around the clock, the Obstetric/Gynecology nurse responsible for maintenance of the resuscitation area should be known and supervised.
- Before delivery the Obstetric/Gynecology nurse should ensure the following:
  - The radiant warmer is clean, well functioning, and positioned perpendicular to the wall. It should be operated and preheated 10-20 minutes before delivery.
  - Enough clean linens are available.
  - There is an efficient oxygen source. In case of oxygen cylinder, it must be full, with clean tubing and available key. There must be a back up oxygen cylinder.
  - Suction apparatus tubings are clean, water changed every 24 hrs and apparatus disinfected or sterilized as indicated. This apparatus is used only for babies and not for mothers.

- Waste receptacle and safety box are available.

- After delivery the Obstetric/Gynecology nurse should ensure the following:
  - Cleaning and disinfecting radiant warmer and suction apparatus.
  - Restoring the resuscitation area.

Neonatal nurse responsibility

(Refer to Chapter 4)

- Before delivery the neonatal nurse should ensure the following:
  - Timely arrival of the nurse and/or the neonatal resident in the OR or DR.
  - Resuscitation box properly filled with all equipment and supplies.
- After delivery the neonatal nurse attending the delivery should ensure the following:
  - Disinfecting blades of laryngoscope and mask.
  - Replacing contents of the resuscitation box, whenever used. A one week supply of supplies and drugs must be available.

Routine care after stabilization of newborn

(Refer to Chapter 5)

- Umbilical cord care: fix the cord clamp, 2 inches away from the umbilicus and cut the cord 3-5 cm from the abdomen using clean and sterile scissors or scalpel.
- Vitamin K_1 injection, 0.5-1 mg IM.
- Application of antibiotic eye drops or ointment.
- Early initiation of breastfeeding within a few minutes of delivery.
- Encouraging "rooming-in" to keep mother and baby together.

Daily maternity rounds

- Neonatologists should conduct daily maternity rounds for the care of babies rooming in with their mothers.

Monthly joint morbidity and mortality meeting

- All neonatologists and obstetricians should have a monthly joint morbidity and mortality conference.

Chapter 2

Prenatal Diagnosis and Fetal Assessment

Prenatal Diagnosis and Fetal Assessment

Prenatal Diagnosis of Fetal Disease

Prenatal diagnosis involves a variety of techniques to determine the health and condition of an unborn fetus. Two types of tests are available: screening and diagnostic tests.

Screening tests

Screening tests are performed by analysis of maternal serum during pregnancy.

First-trimester screening

- Maternal serum can be analyzed for certain biochemical markers that, in combination with ultrasound measurement of the fetal nuchal translucency, can be used to calculate a risk assessment for trisomies 18 and 21.
- These serum markers are the free β-subunit of hCG and pregnancy-associated plasma protein A (PAPP-A).
- It is performed between 10 and 13 weeks' gestation.

Maternal serum alpha-fetoprotein (MSAFP)

- It is performed between 15 and 22 weeks' gestation.
- MSAFP is used to screen for neural tube defects (NTDs), in which it is elevated.

Triple panel (AFP, hCG & UE_3)/quad panel (AFP, hCG, UE_3 & inhibin A)

- Triple or quad screen is used as a screening test in the second trimester of pregnancy. It is performed, between 15 and 22 weeks' gestation, to help evaluate the risk that a fetus has certain abnormalities, including trisomy 21 and neural tube defects.
- Low levels of AFP are associated with chromosomal abnormalities.
- Altered levels of human chorionic gonadotropin (hCG), unconjugated estriols (UE_3), and inhibin A are also associated with chromosomal abnormalities **(Table 2-1)**.
- In a pregnancy of a fetus with trisomy 21, hCG levels are higher than expected and UE_3 levels are decreased.
- The usefulness of the screen test is limited by its high number of false-positive test results. Abnormal test results warrant additional testing for making a diagnosis. These include high-resolution ultrasound and possibly amniocentesis followed by chromosome analysis.

Table (2-1): Interpretation of triple screen test

AFP	UE_3	hCG	Associated conditions
Low	Low	High	Trisomy 21 (Down syndrome)
Low	Low	Low	Trisomy 18 (Edward's syndrome)
High	Normal	Normal	NTDs (such as spina bifida), gastrointestinal defects (such as omphalocele and gastroschisis) or multiple gestation

AFP: alpha-fetoprotein, UE_3: unconjugated estriols, hCG: human chorionic gonadotropin, NTDs: neural tube defects

Diagnostic tests

Diagnostic tests are considered in a woman with a positive family history of genetic disease, a positive screening test, or at risk ultrasonographic features.

Amniocentesis

- Amniotic fluid is removed from around the fetus via a needle guided by ultrasound. The removed fluid (~20 ml) is replaced by the fetus within 24 hrs.
- It can be performed as early as 10-14 weeks' gestation, but this is associated with a pregnancy loss rate of 1-2%, so it is usually performed in the 2nd trimester (16-20 weeks' gestation).
- Amniotic fluid can be analyzed for a number of compounds, including AFP, acetyl-cholinesterase (AChE), bilirubin and pulmonary surfactant.
  - Increased level of AFP with the presence of AChE identifies NTDs.
  - Increased AFP level occurs also with congenital nephrosis, abdominal wall defects, or intestinal atresia.
  - Increased bilirubin level occurs in case of isoimmune hemolytic anemia.
  - Pulmonary surfactant can detect fetal lung maturity.
- Fetal cells can be extracted from the fluid sample and analyzed for chromosomal and genetic makeup.

Chorionic villus sampling (CVS)

- A sample of placental tissue is obtained via a catheter either transcervical or trans-abdominal placed under ultrasonic guidance.
- It can be performed in the first trimester (usually between 10-12 weeks' gestation).
- It provides the earliest possible detection of a genetically abnormal fetus, and can also be used to obtain fetal karyotype in the 3rd trimester when amniotic fluid is not available.
- Complications include pregnancy loss and limb abnormalities. However, if performed after 70 days' gestation, there is no increased incidence of limb reduction defects.

Percutaneous umbilical blood sampling (PUBS)

- Under ultrasonic guidance, a needle is placed transabdominally into the umbilical vein.
- PUBS can be performed from the second trimester until term.
- Samples of fetal blood can be obtained for karyotype, viral studies, fetal blood type, and hematocrit.
- It can also provide an access for utero-transfusion in cases of fetal hydrops.
- It has a 1-2 % risk of fetal loss along with complications that can lead to a preterm delivery.

Assessment of Fetal Well-being

Antepartum tests

These tests are not used until the 3rd trimester; fetuses may not respond appropriately earlier in gestation.

Fetal movement monitoring

- It is the simplest method of fetal assessment.
- Mother lies quietly for an hour and records each perceived fetal movement.
- Fetuses normally have a sleep-wake cycle, and mothers generally perceive a diurnal variation in fetal activity.
- Active periods average 30-40 minutes. Periods of inactivity for more than one hour are unusual in a healthy fetus and should direct attention to the possibility of fetal compromise.

Non-stress test (NST)

- The non-stress test (NST) is simple and noninvasive, with neither discomfort nor risk to mother or fetus.
- It is used to detect intact fetal brainstem function.
- The test is performed by monitoring fetal heart rate (FHR) either through a Doppler ultrasonographic device or through skin-surface electrodes on the maternal abdomen, with simultaneous recording of uterine activity through a tocodynamometer, palpation by trained test personnel, or the patient's report.
- Fetal well-being is confirmed if the baseline heart rate is normal (110-160 beats/ minute), normal beat-to-beat variability (5 beats/minute), and there are periodic increases in the fetal heart rate that are often associated with fetal movement.
- Interpretation
  - Reactive NST: In a 20-minute monitoring period, there are at least 2 accelerations of the fetal heart rate 15 beats/minute above the baseline fetal heart rate; each acceleration lasts at least 15 seconds.
  - Non-reactive NST: Fetal heart rate does not meet these criteria during a prolonged period of monitoring (usually at least 1 hour).
- Other causes of non-reactive NST besides fetal compromise:
  - A fetal sleep cycle
  - Chronic maternal smoking and exposure to medications**,** such as central nervous system depressants and propranolol
- A non-reactive NST should be followed by more definitive testing, such as a bio-physical profile or a contraction stress test.

Contraction stress test (CST)

- Contraction stress test (CST) is used to assess a fetus at risk for uteroplacental insufficiency.
- A monitor is placed on the mother's abdomen to continuously record the fetal heart rate and uterine contractions.
- An adequate test consists of at least three contractions, each lasting at least 40-60 seconds, within a period of 10 minutes. If no spontaneous contractions occur, they can be induced with intravenous oxytocin [Oxytocin Challenge Test (OCT)].
- CST is contraindicated in patients with placenta previa, and those with high-risk factors for preterm delivery (e.g., premature rupture of membranes or incompetent cervix).

- Under hypoxic conditions, the FHR slows in a characteristic way relative to the contraction (type I deceleration or deceleration of uteroplacental insufficiency).
  - FHR begins to decelerate 15-30 seconds after onset of the contraction, reaches its nadir after the peak of the contraction, and does not return to baseline until after the contraction ends.
- Interpretation:
  - Negative (normal) test: No late decelerations occur during adequate uterine contraction**;** the baseline FHR is normal. This is associated with a very low perinatal mortality rate in the week after the test.
  - Positive (abnormal) test: Late decelerations occur with at least two of three contractions over a 10-minute interval. This signifies poor fetal outcome.
  - Equivocal (suspicious) test: A late deceleration occurs with one of three contractions over a 10-minute interval. Prolonged fetal monitoring is usually recommended.

Biophysical profile (Table 2-2)

- Biophysical profile is used to assess fetal well-being, often when the NST has been non-reactive. NST is performed along with an ultrasound examination to evaluate fetal breathing movements, gross body movements, tone, and amniotic fluid volume.
- Interpretation:
  - Score 8-10: Reassuring, repeated at weekly interval
  - Score 4-6: Less reassuring, repeated later the same day
  - Score 0-2: High perinatal mortality, prompt delivery

Table (2-2): Biophysical profile scoring

Variable	Normal score (score=2)	Abnormal (score=0)
Fetal breathing movements (FBM)	At least 1 episode of FBM of at least 30 seconds duration in 30 minutes observation	Absent FBM or episode < 30 seconds in 30 minutes
Gross body movement	At least 3 discrete body/limb movements in 30 minutes	2 or less
Fetal tone	At least 1 episode of active extension with return to flexion of fetal limbs or trunk	Either a slow extension with return to partial flexion or movement of limb in full extension or absent fetal movement
Reactive FHR	At least 2 episodes of FHR acceleration >15 beats/minute and at least 15 seconds duration, associated with fetal movement in 30 minutes	Less than 2 episode of acceleration of FHR or acceleration of <15 beats/minute in 30 minutes
Qualitative amniotic fluid volume	At least 1 pocket of amniotic fluid that measures at least 2 cm in 2 perpendicular planes	Either no amniotic fluid pockets or a pocket <2 cm in 2 perpendicular planes

Adapted from Creasy RK, Resnik R (eds): Maternal-Fetal Medicine: Principles and Practice, 3rd Ed. Philadelphia, WB Saunders, 1994.

Doppler ultrasonography of fetal umbilical artery blood flow

It is a non-invasive technique to assess placental resistance expressed as resistance index. Poorly functioning placentas with extensive vasospasm or infarction have an increased resistance to flow that is particularly noticeable in fetal diastole. Absent diastolic flow and lastly reversed flow is of major importance for the prognosis of intrauterine growth restriction (IUGR) and for the decision of termination of pregnancy

Intrapartum assessment

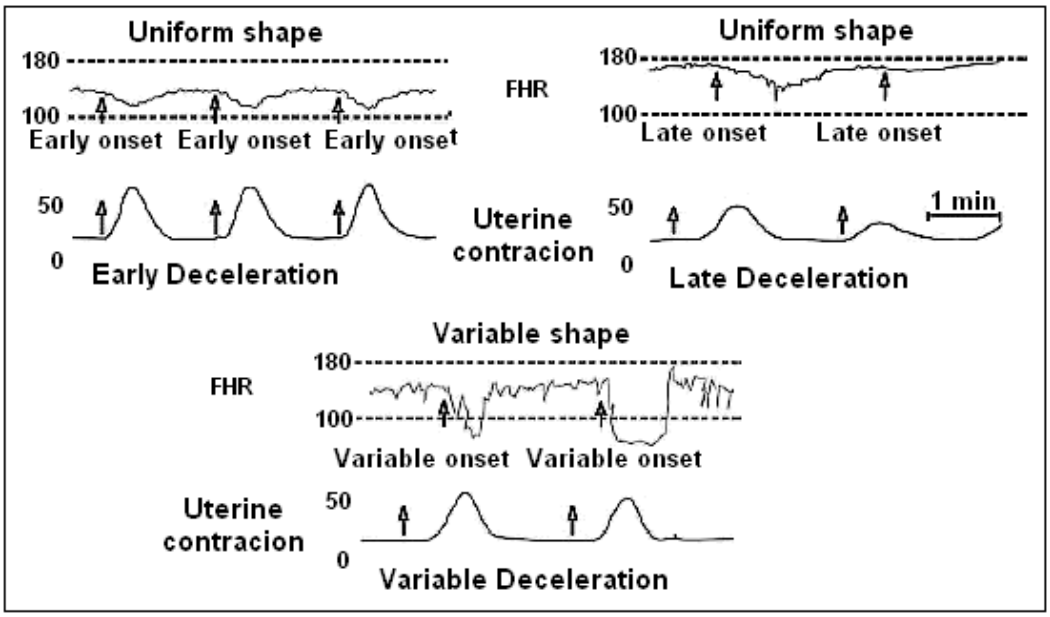
Continuous electronic fetal monitoring

The monitors simultaneously record FHR and uterine activity.

- Baseline fetal heart rate (Baseline FHR)
  - The baseline FHR is the average rate between uterine contractions.
  - Normally, it is between 110 and 160 beats/minute.
  - Baseline fetal tachycardia (FHR >160 beats/minute), may result from a fetal hypoxia, dysrhythmia, hyperthyroidism, maternal fever, or chorioamnionitis.
  - Baseline fetal bradycardia (FHR <110 beats/minute) may result from hypoxia, congenital heart block associated with congenital heart malformation or maternal lupus.
- Beat-to-beat variability
  - In the normal mature fetus, there are slight rapid fluctuations in the interval between beats (beat-to-beat variability) and the heart rate varies from beat to beat by approximately 5-25 beats/minute. This indicates a functioning sympathetic-parasympathetic nervous system interaction.
  - Reduced beat-to-beat variability may result from depression of the fetal central nervous system due to fetal immaturity, hypoxia, fetal sleep, or specific maternal medications such as narcotics, sedatives, β-blockers, and IV magnesium sulfate.
- Accelerations
  - These are often associated with fetal movement, and are reassuring.
- Decelerations
  - Early decelerations
    - They are symmetric in shape and closely mirror uterine contractions in time of onset, duration, and termination. They are benign and are not associated with fetal compromise.
    - These decelerations are commonly seen in active labor when the fetal head is compressed in the pelvis, resulting in a parasympathetic effect.
  - Late decelerations
    - They are visually apparent decreases in the FHR in association with uterine contractions. The onset, nadir, and recovery of the deceleration occur after the beginning, peak, and end of the contraction, respectively.
    - Late decelerations result from uteroplacental insufficiency and possible fetal hypoxia.

- As the uteroplacental insufficiency/hypoxia worsens: (i) Beat-to-beat variability will be lost, (ii) Decelerations will last longer, (iii) They will begin sooner following the onset of a contraction, (iv) They will take longer to return to baseline, and (v) The rate to which the fetal heart slows will be lower.
- Maneuvers such as maternal oxygen supplementation and maternal positioning in the left lateral decubitus position should be attempted.

- Variable decelerations
  - They vary in their shape and in their timing relative to contractions.
  - Usually they result from fetal umbilical cord compression.
  - Variable decelerations are a cause for concern if they are severe (down to a rate of 60 beats/minute or lasting for 60 seconds or longer, or both), associated with poor beat-to-beat variability, or mixed with late decelerations.



FHR: Fetal heart rate

Figure (2-1): Pattern of fetal heart rate decelerations

Fetal scalp blood sample

- Fetal scalp blood sampling is used during labor to determine the fetal acid-base status when the FHR tracing is non-reassuring or equivocal.
- It can be performed only after rupture of membranes.
- It is contraindicated in cases of possible blood dyscrasias in the fetus and with maternal infections caused by herpes virus or HIV.
- An intrapartum scalp pH >7.20 with a base deficit <6 mmol/L is normal.
- Many obstetric units have replaced fetal scalp blood sampling with noninvasive techniques to assess fetal status.

Chapter 3

Maternal Disorders Affecting Fetus or Newborn

Maternal Disorders Affecting Fetus or Newborn

High risk neonates, as an outcome of high risk pregnancies and/or problematic pregnancies, are in need of close observations immediately after birth.

High risk pregnancies are characterized by factors that increase the likelihood of abortion, fetal demise, preterm labor, IUGR, congenital malformations, and mental retardation. An active partnership between obstetric and neonatal teams should be developed for the management of high-risk pregnancies and newborns.

Factors Associated with High Risk Pregnancy

- Maternal age: less than 18 years or more than 35 years old
- Poverty
- Social and behavioral factors:
  - Low educational status
  - Cigarette smoking
  - Drug addiction
  - Poor nutrition
- Obstetric factors:
  - Previous cesarean section
  - Multiple pregnancies
  - Prior infertility
  - Previous preterm birth
  - Previous postterm birth
  - Pre-eclampsia
- Medical conditions:
  - Diabetes mellitus
  - Hypertension
  - Pregnancy induced hypertension (PIH)
  - Congenital heart disease
  - Auto-immune diseases
  - Infections **(Table 3-1)**.

Factors Associated with High Risk Delivery

- Prolonged or precipitate labor
- Instrumental (forceps/vacuum) delivery
- Cesarean section
- Analgesia

- Signs in placenta, umbilical cord, amniotic membranes and amniotic fluid (e.g., placental pallor, edema, retro-placental hematoma, whitish nodules, meconium staining, or single umbilical artery)

Table (3-1): Important maternal medical conditions and associated risk for fetus or neonate

Maternal disorder	Adverse effects on fetus or neonate
Diabetes mellitus	• Intrauterine fetal demise • RDS, hypoglycemia, polycythemia • Macrosomia, birth injury • Congenital anomalies
Thyroid disease	Goiter, hypothyroidism, hyperthyroidism
Heart, lung disease	IUGR, prematurity
Systemic lupus erythematosus	Congenital heart block, rash, anemia, thrombo-cytopenia, neutropenia
Renal disease	IUGR, prematurity
Urinary tract infection	Prematurity, sepsis
Hypertension (chronic or PIH)	IUGR, intrauterine fetal demise, asphyxia, prematurity
Anemia	IUGR, asphyxia, prematurity, hydrops
Rhesus or other blood group sensitization	Fetal anemia, hydrops, neonatal jaundice
Iso-immune thrombocytopenia	Thrombocytopenia and bleeding
Myasthenia gravis	Transient neonatal myasthenia
Hyperparathyroidism	Neonatal hypocalcemia
Infections:	
• *Group β Streptococci, E.Coli*	Ascending cervical sepsis, pneumonia
• *Rubella virus*	Congenital rubella
• *Cytomegalovirus* (CMV)	Congenital CMV
• *Hepatitis B virus*	Neonatal hepatitis, chronic carrier
• *Hepatitis C virus*	Uncommon but possible neonatal hepatitis chronic carrier

PIH: Pregnancy induced hypertension, IUGR: Intrauterine growth restriction

Fetal and Neonatal Thyroid Disorders

Goiter

Most neonatal goiters result from maternal iodine deficiency or occasionally from maternal antibodies or maternal thyroid medications (e.g., propylthiouracil (PTU) induced fetal hypothyroidism). Prominent goiter is only occasionally present at birth in infants with familial dyshormonogenesis. Congenital neoplasms of the thyroid gland rarely occur.

Congenital Hypothyroidism

Thyroid hormones are integral to the development and maturation of CNS as well as normal growth and development; CNS is thyroid hormone dependent for 2-3 years, as well as growth during the first two decades of life.

Congenital hypothyroidism (CH) represents one of the most common preventable causes of mental retardation. The prevalence of CH in Egypt is about 1:2,500.

Etiology

- Thyroid dysgenesis (aplasia, hypoplasia, or ectopic thyroid).
- Inborn errors of thyroid hormone metabolism (Dyshormonogenesis); most cases are inherited as autosomal recessive disorders. Pendred syndrome is a familial organification defect associated with sensorineural deafness.
- Thyroid hormone receptor abnormalities.
- TSH or thyrotropin-releasing hormone (TRH) deficiencies; either as an isolated problem or in conjunction with other pituitary deficiencies.
- Transient conditions:
  - Maternal autoimmune thyroiditis (thyroid blocking antibodies)
  - Maternal use of iodine in excess, radioactive iodine therapy
  - Transient hypothyroxinemia of prematurity

Clinical manifestations

- Even in athyreotic infants, the classic clinical features of CH are usually absent at birth and appear only gradually over about 6 weeks.
- Early manifestations:
  - Lethargy, poor activity and hypotonia
  - Periorbital edema
  - Large anterior and posterior fontanelles
  - Feeding difficulty (infant falls asleep after sucking for a short period and needs a prolonged period to complete his feed)
  - Respiratory distress
  - Prolonged jaundice
  - Pallor, perioral cyanosis, mottled skin
  - Poor or hoarse crying

  - Constipation
  - Hypothermia
  - Umbilical hernia
  - Distended abdomen
- Neonatal goiters may be extremely large and asymmetric or small.

Screening for congenital hypothyroidism

In order to decrease the incidence of mental retardation caused by CH, the Ministry of Health implements a program for early detection of cases of CH, so as to provide early and proper treatment for the discovered cases.

- A blood sample is taken from the newborn from the beginning of the third to the end of the seventh day of life.
- Method of screening: TSH is measured from a dry blood spot on filter paper taken from a heel prick capillary blood sample.
- Date for sampling: Saturday and Tuesday every week are scheduled for sample collection in all primary health care units, irrespective of official vacation days.
- Interpretation
  - Level (Cutoff point): TSH level >15 μu/ml is considered positive for full-term as well as preterm babies.
  - Borderline Cases: When neonatal TSH level = 15-40 μu/ml, another dry blood sample should be taken for confirmation.
  - Cases with neonatal TSH level >40 μu/ml do not need another sample and should be sent immediately for confirmation and treatment.
- Screening programs can miss cases due to:
  - Laboratory error
  - Improper or no specimen
  - Sick neonates
- Babies in the neonatal care units
  - The receiving units should ask whether newborn screening has been done. If not, the neonate should have newborn screening done from the beginning of the 3rd to the end of the 7th day of life and this should be documented in the record and reported to the transferring hospital.
  - The newborn screening test should be done before transfusion is given.
  - Unscreened infants transfused before admission to the NICU should be screened regardless but will need rescreening 6-8 weeks' post-transfusion.
  - Very sick babies receiving dopamine should be rescreened one week after stoppage of the drug or before discharge from the NICU.
- Confirmation:
  - In primary hypothyroidism, confirmation is done by demonstrating low serum levels of thyroid hormone (free T_4 <10 pmol/L) and elevated TSH levels (>9 μu/ml).

- Measurement of maternal or neonatal antithyroid antibodies may be required to confirm the diagnosis of maternal antibody–mediated hypothyroidism.
- Thyroid scanning (using technetium 99 m).

Management

Infants (term or preterm) with low T4 and elevated TSH

- These infants should be treated as primary hypothyroidism. All infants treated should have trial off medication at 3-4 years to determine if this condition is transient or permanent.
- L-thyroxine should be initiated immediately after obtaining the blood sample for confirmatory test, and without waiting for the results. L-thyroxine is administered at a dose of 10-15 µg/kg/day oral (usually 37.5-50 µg/day).
- L-thyroxine doses should be adjusted to keep T_4 10-16 pmol/L, and TSH <5 µu/ml.
- Tablets should be crushed, mixed with one tablespoon of breast milk, formulas (not Soya bean containing formulas) or water. It is given immediately after preparation (morning undivided dose) half an hour before feeding.
- Follow-up:
  - Clinical parameters: linear growth, weight gain, bone age, developmental progression, and overall well-being.
  - Measurements of T_4 and TSH should be made:
    - 4 weeks after starting L-thyroxine and 2 weeks after a dosage change.
    - Every 2 months during the first year of life.
    - Every 3 months during the second and third years.
    - Every 6 months until adulthood is reached.

Preterm infants with transient hypothyroxinemia

- The serum T_4 and free T_4 levels are low in comparison with those of full-term infants, but the TSH levels are normal.
- Treatment with thyroid hormone is not currently indicated in these infants.

Neonatal Hyperthyroidism

Neonatal hyperthyroidism usually results from thyroid stimulating antibodies crossing from the mother to fetus towards the end of pregnancy [thyroid receptor antibodies (TRAb) in women with Graves' disease]. Rarely, hyperthyroidism may occur in infants born to mothers with Hashimoto's thyroiditis or in infants with activating mutations of the TSH receptor (autosomal dominant disorder).

Clinical manifestations

When neonatal thyrotoxicosis occurs in the infant born to a mother with untreated Graves' disease, the clinical manifestations of hyperthyroidism may become apparent within the first 24 hrs of life.

- Infants born prematurely and with LBW
- Microcephaly, cranisynostosis

- Exophthalmos (usually mild when present)
- Goiter (varies in size; it may be large enough to cause tracheal compression)
- Irritability, jitteriness, and poor sleeping
- Tachycardia
- Hypertension
- Flushing
- Vomiting and diarrhea
- Failure to thrive; despite increased appetite
- Generalized enlargement of reticuloendothelial system, causing generalized lymph-adenopathy, hepatosplenomegaly, thrombocytopenia, and hypoprothrombinemia. This is unique to the neonate with severe Graves' disease.
- In severe cases, hyperthermia, arrhythmia, and high-output cardiac failure may occur. If the condition remains untreated, death may ensue.

Investigations

Newborn infants born to mothers with Graves' disease and suspected of hyperthyroidism should have free T4 and TSH levels measured soon after delivery.

Management

In most cases, the course is self-limiting. The signs and symptoms subside spontaneously after 3 weeks to 6 months, depending on the severity of the disease.

- Supportive care to maintain adequate oxygenation, and adequate fluid and caloric intake.
- Antithyroid drugs:
  - PTU (5-10 mg/kg/day) or methimazole (0.5-1 mg/kg/day). If no response in 36-48 hrs, increase drug by 50%.
  - Lugol’s iodine (1 drop 3 times per day). If no response in 48 hrs, increase drug by 25%, given only 10-14 days.
- Propranolol (2 mg/kg/day) to control tachycardia, infants are weaned off as indicated by heart rate.
- A large goiter compressing the trachea and resulting in asphyxia must be treated surgically by splitting the isthmus.
- Digoxin may be needed in cases with CHF.

Treatment may be needed for 4-12 weeks. Once improvement is evident, PTU should be gradually tapered and then discontinued as allowed by T_4 level and clinical situation.

Congenital Infections

Congenital infections are either transmitted via the placenta during pregnancy or acquired from birth canal at the time of labor.

Traditionally congenital infections were known as the TORCH infections, referring to *Toxoplasmosis*, Other [*Treponema pallidum*, *Varicella-zoster* virus (VZV), *Parvovirus* B19], *Rubella* virus, *Cytomegalovirus* (CMV), and *Herpes simplex* virus (HSV). This acronym was too limiting and several additional infectious agents should be considered in this category, such as human immunodeficiency virus (HIV).

Clinical findings are rarely disease specific **(Table 3-2)** but may include: LBW, IUGR, microcephaly, prematurity, seizures, cerebral calcification, chorioretinitis, cataract, micro-ophthalmia, chronic rash, jaundice, anemia, purpura, hepatosplenomegaly and pneumonitis.

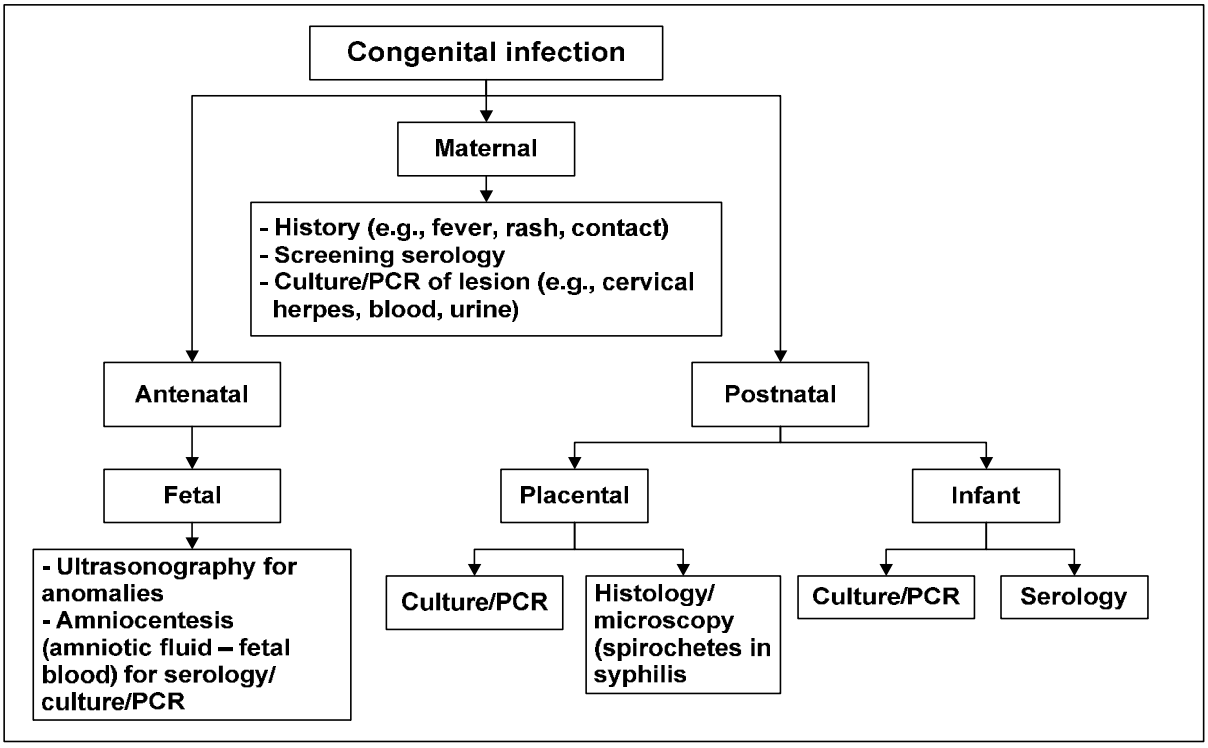
Table (3-2): Clinical findings caused by congenital infections

Micro-organism	Clinical Manifestations
Toxoplasma gondii	• One of many patterns: ▸ Symptomatic disease in the first 3 months, predominately with neurologic signs ▸ Unidentified infection with sequelae in infancy ▸ Subclinical infection • Hydrocephalus, chorioretinitis and intracranial calcification are the classic triad
Rubella virus	• Cataract, sensorineural hearing loss and CHD (most common PDA and pulmonary artery stenosis) • Other common features: meningoencephalitis, microphthalmia, retinopathy, purpura, hepatosplenomegaly, and IUGR
Cytomegalovirus	• Two presentations: ▸ Early presentation with acute fulminant infection involving multiple organs (e.g., petechiae, jaundice, hepatosplenomegaly) ▸ Early presentation without life threatening complications as microcephaly, and intracranial calcifications (especially peri-ventricular) • Sensorineural hearing loss is the most common sequela
Herpes Simplex Virus	• Three categories: ▸ Localized infection to skin, eye and/or mouth: vesicles typically appearing on the 6^{th} - 9^{th} day of life ▸ Encephalitis with or without localized mucocutaneous disease: fever, lethargy, and seizures by the 10^{th} - 14^{th} day of life ▸ Disseminated disease within the 1^{st} week of life in the form of shock, seizures, pneumonia and DIC with a high mortality
Treponema pallidum	• Bullous, macular, and eczematous skin lesions involving the palms and the soles; rhinorrhea, dactylitis and other signs of osteochrondritis and periostitis

Table (3-2): Clinical findings caused by congenital infections (continued)

Micro-organism	Clinical Manifestations
Varicella-zoster virus	• Fetal varicella-zoster syndrome: ► Hypoplasia or atrophy of an extremity, paralysis with muscular atrophy, and hypoplastic or missing fingers ► Microphthalmos, chorioretinitis, cataracts, optic atrophy, and Horner's syndrome ► Cicatricial skin lesions ► Microcephaly, seizures, encephalitis, cortical atrophy mental retardation and intracranial calcifications • Neonatal varicella-zoster infection: ► Centripetal rash begins as red macules and progresses to vesicles and encrustation ► Lung involvement: □ Usually appearing 2-4 days after the onset of rash, but may be seen up to 10 days after □ Fever, cyanosis, rales, and hemoptysis ► Other organs: □ Focal necrosis in the liver, adrenals, intestines, and kidneys □ Glomerulonephritis, myocarditis, encephalitis, and cerebellar ataxia
Parvovirus B19	Diffuse edema (in-utero hydrops fetalis)

An approach to diagnose congenital infections is illustrated in **(Figure 3-1).**



PCR: Polymerase chain reaction

Figure (3-1): A diagnostic approach for congenital infections

Toxoplasmosis

Maternal infection in the first trimester is less likely to infect the fetus (10%) but if it occurs the damage is more severe. Mid or late trimester infections are more likely to infect the fetus (30-50%) but the effects are milder.

Clinical manifestations (Table 3-2)

Investigation

- CBC, liver function tests
- Maternal serum for toxoplasma IgG and IgM
- Infant's serum for toxoplasma IgG, IgM and infant's blood for PCR
- Cranial ultrasound and CT scan

Management

- Spiramycin with or without pyrimethamine and sulfadiazine for pregnant women with positive toxoplasmosis screen will prevent most of the newborn manifestations.
- Treatment of newborns (whether symptomatic or asymptomatic) with:
  - Pyrimethamine (1 mg/kg every 12 hrs for 2 days, then daily until 2-6 months of age, then 3 times weekly until 1 year of age); and
  - Sulfadiazine (50 mg/kg every 12 hrs until 1 year of age).

Rubella Virus Infection

Infection of the fetus is chronic, so congenitally infected infant will shed virus at a high titer for many months.

Clinical manifestations (Table 3-2)

Investigations

- Serum (cord or infant's blood) for rubella IgM.
- Rubella virus detection from the nasopharynx, CSF, and urine by PCR.

Management

- The best therapy is prevention.
- Treatment is only supportive.
- Isolation:
  - Contact isolation: the infant is considered infectious for the first year of life.
  - Only those known to be immune should care for the baby in hospital and pregnant visitors at home should be warned.

Cytomegalovirus (CMV) Infection

Clinical manifestations (Table 3-2)

Investigations

- Viral cultures in body fluids (oral secretions or urine) in the first three weeks of life

(after 3 weeks, the infant may have acquired the organism at the time of delivery or postnatally via breast milk).

- Test cord or infant's blood for CMV detection by PCR.
- CMV IgG and IgM are of limited usefulness but negative titers in maternal and infant's sera are sufficient to exclude congenital CMV.
- Long term follow up tests include serial audiology and developmental assessment, head circumference, ophthalmology.

Management

- Asymptomatic congenital infection: treatment is not indicated.
- Symptomatic infants:
  - Ganciclovir is indicated for CMV retinitis, colitis, meningoencephalitis, esophagitis, hepatitis, and pneumonitis. Gancyclovir is given at a dose of 10-15 mg/kg/day IV infusion over >1 hr, divided every 12 hrs for 3-6 weeks.
  - The use of CMV hyperimmune globulin has not been evaluated extensively for the treatment of congenital CMV disease.

Herpes Simplex Virus (HSV) Infection

Most mothers whose infants have neonatal herpes do not have a history of symptomatic genital herpes.

Clinical manifestations (Table 3-2)

Investigations

- Swab for viral culture and HSV-PCR from skin vesicles, eyes, or mouth/ nasopharynx.
- CSF: cells, protein, glucose, culture, viral culture and PCR.
- CT brain, EEG.

Management

- Infant born vaginally to a mother with a first episode or primary genital infection has a risk of infection 33-50%.
- If the mother is recognized as having primary disease or develops genital herpetic lesions at the time of delivery, elective cesarean section or cesarean section within 4-6 hrs of rupture of membranes is indicated.
- Acyclovir is the drug of choice for neonatal HSV infections. It is administered at a dose of 20 mg/kg every 8 hrs for 14 days for skin, eye, and mouth disease, and for 21 days for either CNS or disseminated disease.
- Women with a history of recurrent genital infection can be delivered vaginally as the risk of neonatal infection is very low (3-5%). Prophylactic acyclovir therapy to the baby is unproven.
- Isolation:
  - Contact isolation required, especially if skin lesions present.
  - Isolate infants born vaginally to mothers with active genital infection for 4 weeks.

- Rooming-in with mother in isolation, if possible.

Varicella-Zoster Virus (VZV) Infection

- 15% of pregnant women are susceptible to varicella (chickenpox).
- Usually, the fetus is unaffected but will be at risk if the mother develops chickenpox:
  - In the first half of pregnancy (<20 weeks' gestation); risk of developing severe scarring of the skin and possibly ocular and neurological damage and digital dysplasia.
  - Within 5 days before or 2 days after delivery; the fetus is unprotected by maternal antibodies and the viral dose is high.

Fetal varicella syndrome

This form occurs in 2% of infants born to women who develop varicella during the first or second trimester of pregnancy.

Clinical manifestations (Table 3-2)

Diagnosis

- Fetal infection can be demonstrated by detection of VZV-DNA by PCR in fetal blood and amniotic fluid or by detection of the specific IgM antibody, in the same fluids.

Management

- Mother
  - If the mother is exposed to VZV infection in the first or second trimester, treat with varicella-zoster immune globulin (VZIG) if the history of varicella is negative or uncertain.
  - If chickenpox is diagnosed during pregnancy, antiviral therapy with acyclovir should be considered.
- Infant
  - Isolation is not necessary.
  - Provide supportive care.
  - Acyclovir therapy may be helpful.

Neonatal varicella infection

This form occurs after transplacental maternal varicella in late gestation. Neonatal varicella can be a serious illness, depending on the timing of maternal varicella and delivery (i.e., whether transplacental passage includes only the virus or includes both the virus and the antibodies):

- If the mother develops varicella within 5 days before or 2 days after delivery; varicella infection in these babies is likely to be severe and disseminated because there is insufficient time for maternal antibody formation; the resulting death rate is 30% in untreated affected infants.
- If the onset of maternal disease is >5 days before delivery transplacental antibody transmission occurs and generally results in a milder case of varicella and deaths are infrequent.

Clinical manifestations

Manifestations may be mild with vesicles on the skin, or severe **(Table 3-2).**

Diagnosis

- PCR for detection of VZV-DNA in skin swab, biopsies
- VZV can be isolated from cultures of vesicular lesions during the first 3 days of the rash
- Detection of IgM antibodies in the infant's serum

Management

- Varicella-zoster immunoglobulin (VZIG)
  - Infants of mothers who develop VZV infection within 5-7 days before or 48-72 hrs after delivery should receive 125 units of VZIG as soon as possible and not later than 96 hrs.
  - These infants should be placed in strict respiratory isolation for 28 days after receiving VZIG because treatment will prolong the incubation period.
- Acyclovir therapy at a dose of 10-15 mg/kg every 8 hrs in symptomatic infants.
- Antibiotics if secondary bacterial skin infections occur.

N.B.: VZIG is not recommended in such cases with the onset of maternal varicella >5 days antepartum. Acyclovir may be used, depending on individual circumstances.

Hepatitis B Infection

Transplacental passage of Hepatitis B virus is uncommon. Vertical transmission is more common in HBeAg-positive mother.

Clinical manifestations

Usually subtle and the baby may be completely asymptomatic.

Management

- All newborns of HBsAg-positive mothers should receive hepatitis B immune-globulin (0.5 ml/kg IM) as soon as possible after birth (within 12 hrs), followed by HBV vaccine (0.5 ml IM) injection. With appropriate hepatitis B immunoprophylaxis, breastfeeding should be started.

HIV Infection

Vertical transmission of HIV can occur at any time during gestation and delivery, and postpartum through breast milk. The rate of vertical transmission of HIV varies from approximately 15-40% in the absence of antiretroviral therapy.

Clinical manifestations

Usually asymptomatic during the neonatal period but may present with lymphadenopathy and/or hepatosplenomegaly. Occasionally poor weight gain or neuromotor abnormalities may occur.

Investigations

- Serology is of limited value in diagnosing vertically transmitted HIV infection in infants <15 months old (because maternal IgG crosses the placenta and can persist in infants throughout the first year or more of life). Viral detection tests should be used to identify infected infants born to HIV-infected mothers. These include:
  - PCR to detect viral DNA in peripheral blood cells
  - PCR for viral RNA in plasma
  - In-vitro cell culture
- In-vitro cell culture

Management

- Zidovudine: prophylactic therapy of infants born to HIV-infected mother at a dose of 1.5 mg/kg IV, infused over 1 hr (PO: 2 mg/kg/dose) every 8-12 hrs.
- Multiple drug therapy: for infected infant, into consultation with a pediatric infectious disease specialist.
- Breastfeeding in HIV-infected mother:
  - The most appropriate infant feeding option for an HIV-infected mother depends on her and her infant's individual circumstances, including her health status, but should take into consideration the health services available and the counseling and support she is likely to receive.
  - When replacement feeding is **A**cceptable, **F**easible, **A**ffordable, **S**ustainable and **S**afe (AFASS), avoidance of all breastfeeding by HIV-infected women is recommended.
  - Mixed feeding in the first 6 months of life (that is, breastfeeding while also giving other fluids, formula or foods) should always be avoided by HIV-infected mothers.

Chapter 4

Neonatal Resuscitation

Neonatal Resuscitation

Most newborn babies are vigorous. Only about 10% require some kind of assistance and only 1% needs major resuscitative measures (intubation, chest compressions, and/or medications) to survive.

Within seconds after birth, fluid in the alveoli is absorbed, air enters the lungs, blood vessels in the lung relax, pulmonary blood flow increases, and umbilical arteries and vein constrict**,** thus increasing blood pressure. Lack of ventilation of the newborn's lungs results in sustained constriction of the pulmonary arterioles preventing systemic arterial blood from becoming oxygenated. Prolonged lack of adequate perfusion and oxygenation to the infant's organs can lead to brain damage, damage to other organs, or death.

Primary and Secondary Apnea

When a fetus/newborn first becomes deprived of oxygen, an initial period of attempted rapid breathing is followed by primary apnea and dropping heart rate that will improve with tactile stimulation.

If oxygen deprivation continues, secondary apnea ensues; it is accompanied by a continued fall in heart rate and blood pressure. Secondary apnea cannot be reversed with stimulation; assisted ventilation must be provided, resulting in a rapid improvement in heart rate.

Risk Factors

The majority of, but not all, neonatal resuscitations can be anticipated by identifying the presence of antepartum and intrapartum risk factors associated with the need for neonatal resuscitation **(Table 4-1).**

Table (4-1): Antepartum and intrapartum risk factors

Antepartum risk factors	Intrapartum risk factors
• Rupture of membranes for a period of ≥18 hrs • Pre-eclampsia and eclampsia • Maternal infection – Malaria, HIV • Premature labor • Multiple births	• Excessive bleeding • Breech presentation • Meconium staining amniotic fluid • Non-reassuring fetal heart rate patterns (e.g., lost beat-to-beat variability, late deceleration, bradycardia) • Prolapsed or nuchal cord • Rapid, hard labor • Foul-smelling amniotic fluid • Prolonged labor • Shoulder dystocia

Personnel

Every delivery should be attended by at least one trained person whose only responsibility is the infant, and who is capable of initiating resuscitation. Either that person or someone else who is immediately available should have the skills required to perform a complete resuscitation. When resuscitation is anticipated, additional personnel should be present in the delivery room before the delivery occurs.

Equipment

- Turn on the radiant warmer
- Check resuscitation supplies and equipments **(Refer to Chapter 1)**
  - Suction equipment
  - Bag-and-mask equipment
  - Intubation equipment
  - Umbilical vessel catheterization tray with (3.5Fr, 5Fr) catheters, and three-way stopcocks
  - Medication
    - Epinephrine (1:10,000 solution)
    - Normal saline or Ringer's lactate
    - Glucose 10% solution
    - Sterile water
    - Naloxone hydrochloride
  - Miscellaneous
    - Stethoscope (neonatal head preferred)
    - Feeding tubes (6Fr, 8Fr)
    - Warmed linens
    - Clock
    - Oropharyngeal air ways

N.B.: Pulse oximetry can be applied for information on oxygen saturation and heart rate, and should be available for premature infant.

Initial Assessment

- All newborns require initial assessment to determine whether resuscitation is required. The following questions must be asked:
  - Term gestation?
  - Clear amniotic fluid?
  - Breathing or crying?
  - Good muscle tone?
- If the answer to any of these questions is “No”, resuscitation should be started.
- Resuscitation should proceed rapidly:
  - You have approximately 30 seconds to achieve a response from one step before deciding whether you need to go on to the next.
  - Evaluation and decision making are based primarily on respirations, heart rate, and color.

Steps of Neonatal Resuscitation

The Apgar score **(Refer to Appendix 1)** is assigned at 1, 5, and, occasionally, 10-20 minutes after delivery. It gives a fairly objective retrospective idea of how much resuscitation a term infant required at birth and the infant's response to resuscitative efforts.

The Apgar score is not used to determine when to initiate resuscitation or in making decisions about the course of resuscitation. Resuscitation is in seconds not minute.

N.B.: Simultaneous assessment of respiratory activity, heart rate and skin color provides the quickest and most accurate evaluation of the need for continuing resuscitation.

Initial steps

- **Provide warmth** by placing the infant under radiant warmer.
- **Dry** the infant thoroughly and gently, the wet towels should be promptly removed to avoid evaporative heat loss.
- **Position** head and **clear airway** as necessary, by placing the newborn on the back with head in midline position and with slight neck extension "sniffing position". Suction the mouth first, and then the nose gently and briefly by suction bulb or a large-bore suction catheter **(Figure 4-1)**. Suctioning should limited to 5 seconds at a time.

N.B.: Deep and aggressive pharyngeal stimulation with a suction catheter may cause arrhythmia and should be avoided.

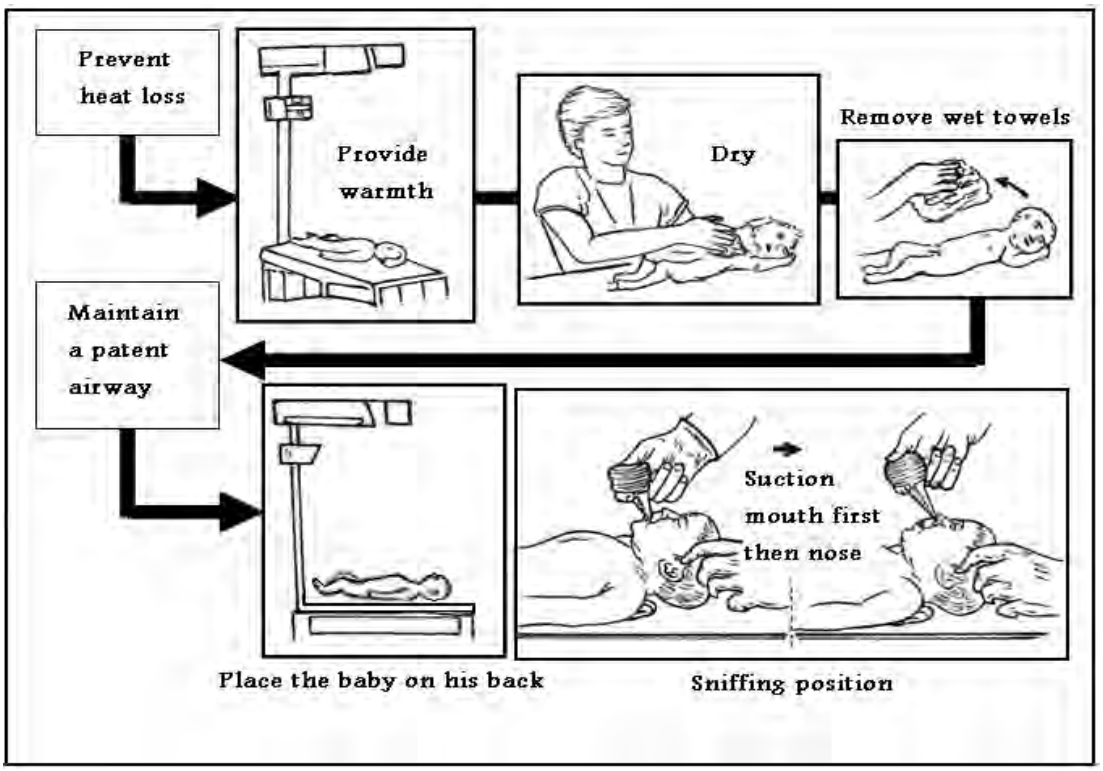
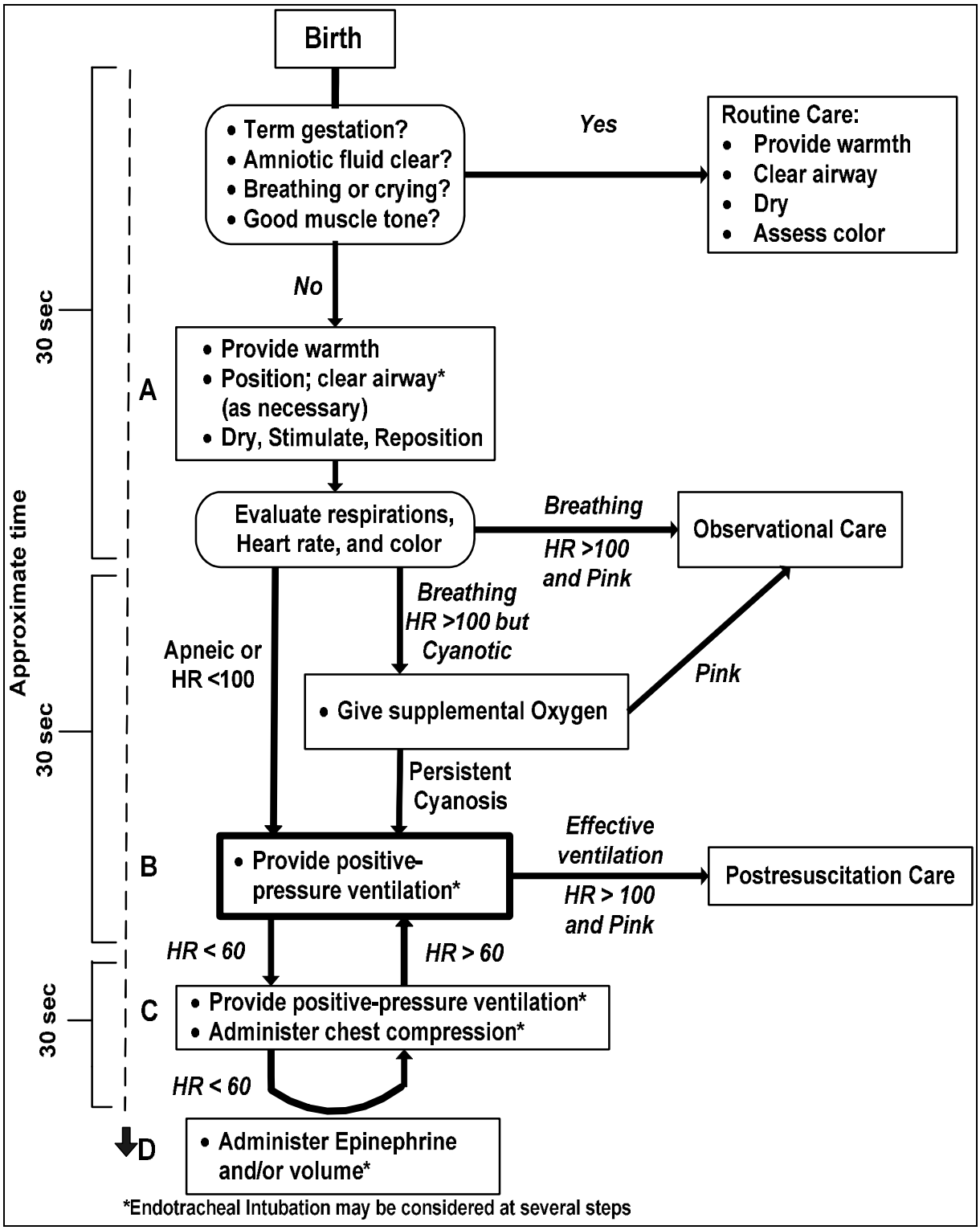


Figure (4-1): Initial steps of neonatal resuscitation



HR: Heart rate

Figure (4-2): Neonatal resuscitation flow chart

Adapted from American Heart Association and American Academy of Pediatrics. Neonatal Resuscitation Guidelines, Pediatrics 2006; 117(5): e1029-e1038. Reproduced with permission from Pediatrics.

If meconium is present

Evaluate the newborn's respiratory effort, heart rate and muscle tone **(Figure 4-3)**

- If the infant is vigorous (has strong respiratory effort, good muscle tone, and heart rate >100 beats/minute): suction the mouth and nose only, and proceed with resuscitation as required.
- If the infant is not vigorous:
  - Insert an endotracheal tube and attach it to a meconium aspirator which has been connected to a suction source; then suction the infant's trachea while the tube is slowly withdrawn before proceeding with any other steps.
  - Repeat as necessary until little additional meconium is recovered, or until the infant's heart rate indicates that resuscitation must proceed without delay.

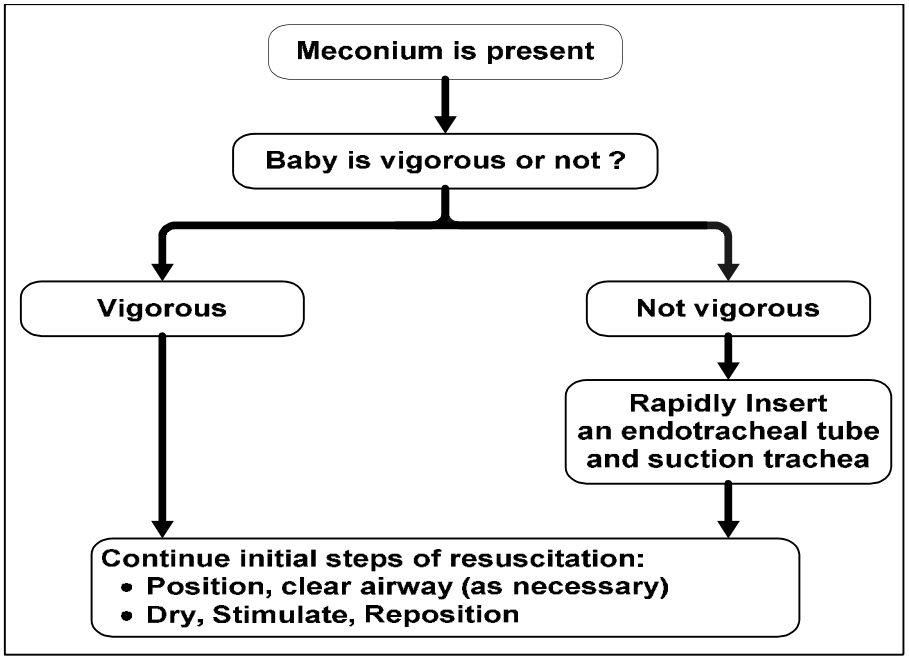


Figure (4-3): Initial steps of resuscitation in presence of meconium

Stimulate the infant to breathe

If the infant is still apneic, tactile stimulation is performed by slapping or flicking the soles of the feet or by gently rubbing the back once or twice.

Evaluate

Evaluate respiration, heart rate (counted in 6 seconds then multiplied by 10) and color.

- If the infant is breathing and heart rate is more than 100 beats/minute but with central cyanosis, free-flow oxygen (5-8 L/minute) is administered by an oxygen mask held firmly over the infant's face, or oxygen tubing cupped closely over the infant's mouth and nose.
- If the infant is apneic/gasping or heart rate is less than 100 beats/minute, even if breathing or central cyanosis persists despite 100% free flow oxygen, positive-pressure ventilation is indicated.

N.B.: Continued use of tactile stimulation in a newborn who is not breathing wastes valuable time. For persistent apnea give positive pressure ventilation.

Positive pressure ventilation (PPV)

- Ventilation of the lungs is the single most important and most effective step in cardiopulmonary resuscitation of the compromised newborn infant.
- Positive pressure ventilation (PPV) is performed using a resuscitation self-inflating bag with a reservoir.
- The Neonatal Resuscitation Program (NRP) recommends use of 90-100% oxygen when (PPV) is required during neonatal resuscitation. If oxygen is unavailable, use room air to deliver PPV (21% oxygen).
- Before beginning PPV; select appropriate-sized mask which should cover tip of chin, mouth and nose and leave eyes uncovered, be sure airway is clear, position infant's head in sniffing position by placing a small roll under the shoulders, and position yourself at infant's side or head.
- An airtight seal is essential to achieve effective positive pressure in order to inflate the lungs when the bag is squeezed.
- Ventilate with a rhythm of (breathe, two, three, breathe, two, three…), and at a rate of 40-60/minute.
- You should ventilate with the lowest pressure required to move the chest adequately. The first few breaths will often require higher pressures (30-40 cmH_2O) and longer inflation time than subsequent breaths (15-20 cmH_2O).

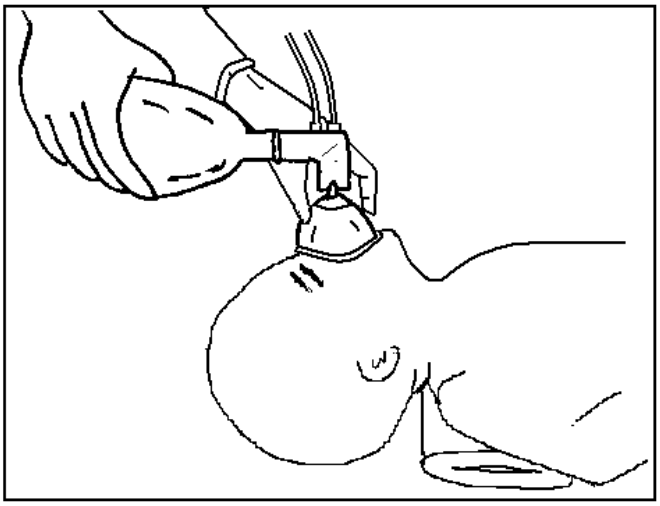


Figure (4-4): Positive pressure ventilation using a flow-inflating bag

- Don't allow your fingers to rest on the infant's eyes, and don't let the mask go down on the face.
- Improvement during PPV is indicated by a rapid increase in heart rate and subsequent improvement in color and oxygen saturation, muscle tone and spontaneous breathing.
- If there is no physiologic improvement and no perceptible chest expansion during PPV, the following actions should be attempted:
  - Reapply mask to face using light downward pressure and lifting the mandible up toward the mask.
  - Reposition the head.
  - Check for secretions; suction mouth and nose.

- Ventilate with the infant's mouth slightly open.
- Increase pressure of ventilations.
- Recheck or replace the resuscitation bag.
- After failure of reasonable attempts, consider intubation of the infant.

- Newborns requiring PPV with a mask for longer than several minutes should have an orogastric tube inserted and left in place.
- After 30 seconds of PPV, evaluate the heart rate:
  - Heart rate >100 beats/minute → evaluate the color and if cyanosed give free flow oxygen as before.
  - Heart rate >60 but <100 beats/minute → repeat PPV for 30 seconds.
  - Heart rate <60 beats/minute → provide PPV with chest compressions for 30 seconds.

Chest compression

- It is indicated when the heart rate remains less than 60 beats/minute, despite 30 seconds of effective PPV.
- It compresses the heart against the spine, increases intra-thoracic pressure and circulates blood to the vital organs, including the brain.
- Two persons are needed, one that performs chest compression while the other continues ventilation.
- The most efficient method of delivering chest compression is to stand at the foot of the infant and grip the chest in both hands in such a way that the two thumbs can press at the junction of the middle and lower thirds of the sternum, just below an imaginary line joining the nipples, with the fingers wrapped around and supporting the back. Alternatively, one can stand at the side of the infant and compress the lower third of the infant's sternum with the index and third fingers of one hand and with the second hand supporting the back.
- The two-finger technique may be preferable when access to the umbilicus is required during insertion of an umbilical catheter.
- To ensure proper rate of chest compressions and ventilation, the compressor repeats "One-and-Two-and-Three-and-Breathe-and..."
- During chest compressions, the breathing rate is 30 breaths/minute, and the compression rate is 90 compressions/minute. This equals 120 "events" per minute. One cycle of three compressions and one breath takes 2 seconds.
- During chest compression, ensure that chest movement is adequate during ventilation, supplemental oxygen is being used, compression depth is one third the diameter of the chest, pressure is released fully to permit chest recoil during relaxation phase of chest compression, thumbs or fingers remain in contact with the chest at all times. The duration of the downward stroke of the compression is shorter than duration of the release and chest compressions and ventilation are well coordinated.

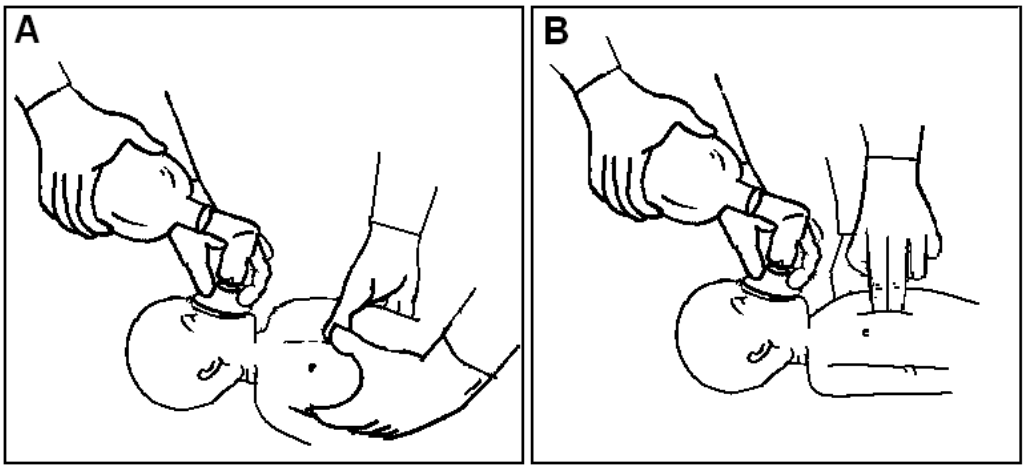


Figure (4-5): The two-thumb encircling hands method for chest compressions (A) is preferred over the two-finger method (B)

- After 30 seconds of well coordinated chest compressions and ventilation, suspend both ventilation and compression, and check the heart rate:
  - If heart rate is >100 beats/minute, discontinue compressions and gradually discontinue ventilation, if the newborn is breathing spontaneously.
  - If heart rate is >60 beats/minute, discontinue compressions and continue ventilation at a rate of 40-60 breaths/minute.
  - If heart rate is <60 beats/minute, give epinephrine**,** preferably intravenously**,** and intubate the newborn if not already done. Intubation provides a more reliable method of continuing ventilation.

Endotracheal intubation

- A person experienced in endotracheal intubation should be available to assist at every delivery.
- Indications for endotracheal intubation:
  - To suction trachea in presence of meconium when the newborn is not vigorous.
  - To improve efficacy of ventilation after several minutes of bag and mask ventilation or ineffective bag-and-mask ventilation.
  - To facilitate coordination of chest compressions and ventilation and to maximize the efficiency of each ventilation.
  - To administer epinephrine, if required, to stimulate the heart while intravenous access is being established.
  - When a diaphragmatic hernia is suspected or known to exist.
- Intubation procedure ideally should be completed within 20 seconds.
- The laryngoscope is always held in the operator's left hand, use blade No.1 for a term newborn and No.0 for a preterm newborn, the proper endotracheal tube size is based on weight **(Table 4-2)**.

Table (4-2): Endotracheal tube (ETT) sizes

Gestational age (weeks)	Weight (gm)	Tube size (mm) (inside diameter)	Distance of tip of ETT (6 + Body weight)
<28	<1,000	2.5	7 cm
28-34	1,000-2,000	3.0	8 cm
34-38	2,000-3,000	3.5	9 cm
>38	>3,000	3.5-4	10 cm

- Steps for intubation:
  - Stabilize the newborn's head in the "sniffing" position and deliver free flow oxygen during the procedure.
  - Consider cutting the tube to a shorter length (13-15 cm) before the intubation process.
  - Slide the laryngoscope over the right side of the tongue, pushing the tongue to the left side of the mouth, and advancing the blade until the tip lies just beyond the base of the tongue.
  - Lift the blade slightly and raise the entire blade, not just the tip.
  - Look for landmarks. Vocal cords should appear as vertical stripes on each side of the glottis or as an inverted letter "V" **(Figure 4-6).**
  - Suction, if necessary, for visualization.
  - The tube is held with the right hand, inserted into the right side of the mouth with the curve of the tube lying in the horizontal plane, and then passed between the vocal cords approximately 2 cm below the glottis (the tip of the tube is inserted until the vocal cord guide is at the level of the cords). If the vocal cords are closed, wait for them to open.
  - Hold the tube firmly against the infant's palate while removing the laryngoscope. Hold the tube in place while removing the stylet (if it was used).
  - Be certain that you visualize the glottis before inserting the tube, watch the tube enter the glottis between the vocal cords.
  - Proper depth of insertion can be estimated by calculating the depth at the lips according to the following formula:

Weight (kg) + 6 cm = insertion depth at lip in cm

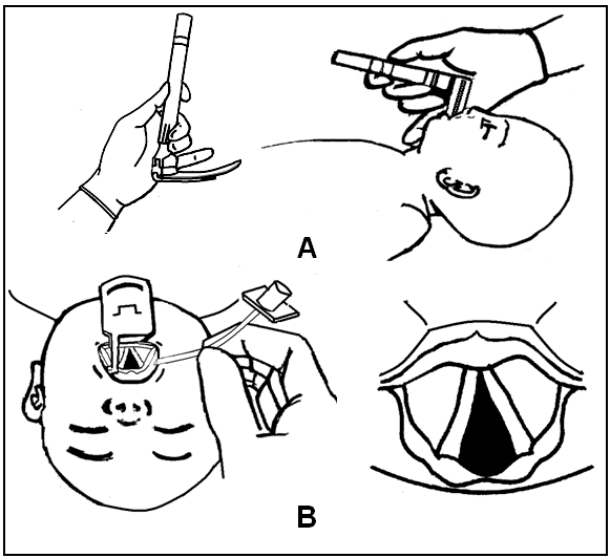


Figure (4-6): Endotracheal intubation

A) Holding and lifting the laryngoscope blade, B) Identification of landmarks, and endotracheal tube insertion

- After endotracheal intubation, confirm the position of the tube by:
  - Observing symmetrical chest-wall motion.
  - Listening for equal breath sounds, especially in the axillae, and for absence of breath sounds over the stomach.
  - Confirming absence of gastric inflation.
  - Watching for a fog of moisture in the tube during exhalation.
  - Noting improvement in heart rate, color, and activity of the infant
  - Chest x-ray confirmation, if the tube is to remain in place past initial resuscitation.
- If the tube is inserted too far, it will pass into the right main bronchus, resulting in overventilation of one lung and pneumothorax.

Medications

Epinephrine

- A cardiac stimulant, that is indicated when the heart rate remains below 60 beats/minute, despite 30 seconds of assisted ventilation followed by another 30 seconds of coordinated chest compressions and ventilation.
- Route: IV (through the umbilical vein). Endotracheal administration may be considered while IV access is being established.
- Dose: 0.1-0.3 ml/kg (consider higher dose, 0.3-1 ml/kg, for endotracheal route only); dose can be repeated after 3-5 minutes.
- Preparation: 1:10,000 solution.
- Rate: rapidly, as quickly as possible.

Volume expansion

- Indicated if an infant is not responding to resuscitation and appears in shock (pale color, weak pulses, persistently low heart rate, no improvement in circulatory status despite resuscitation efforts) and there is a history of condition associated with fetal blood loss (e.g., extensive vaginal bleeding, abruptio placentae, placenta previa, twin-to-twin transfusion,…etc).
- Recommended volume expander is normal saline, Ringer's lactate, or O Rh-negative blood packed RBCs.
- Route: umbilical vein.
- Dose: 10 ml/kg (another dose may be needed).
- Preparation: correct volume drawn into large syringe.
- Rate: slowly (over 5-10 minutes).

Sodium bicarbonate

- Not useful during the initial resuscitation. However, after prolonged resuscitation, it may be indicated for correction of documented severe metabolic acidosis.
- **Do not** give sodium bicarbonate unless the lungs are being adequately ventilated.
- Route: umbilical vein.
- Sodium bicarbonate is very caustic and **should not** be given through the ET tube.
- Dose: 2 mEq/kg (8.4% concentration).
- Preparation: diluted 1:1 with appropriate diluent (glucose 5% or sterile water "concentration 0.5 mEq/ml").
- Rate: slowly, no faster than a rate of 1 mEq/kg/minute (to minimize the risk of intra-ventricular hemorrhage).

Special Considerations

The appropriate action for an infant who fails to respond to resuscitation will depend on the presentation:

- Failure to ventilate
- Persistent cyanosis or bradycardia
- Failure to initiate spontaneous breathing

PPV fails to produce adequate ventilation in

- Mechanical blockage of airway:
  - Meconium or mucus plug
  - Choanal atresia
  - Airway malformation (e.g., Robin syndrome)
  - Other rare conditions (e.g., Laryngeal web)
- Impaired function:
  - Pneumothorax

  - Congenital pleural effusion
  - Congenital diaphragmatic hernia
  - Pulmonary hypoplasia
  - Extreme prematurity
  - Congenital pneumonia
- Symptoms from choanal atresia can be helped by placing an oral airway. An endotracheal tube, inserted through the mouth, may be needed.
- Airway obstruction from Pierre Robin syndrome can be helped by inserting a nasopharyngeal tube and placing the infant prone.
- In an emergency, a pneumothorax can be detected by transillumination and treated by inserting a needle in the chest.
- If diaphragmatic hernia is suspected (persistent respiratory distress, scaphoid abdomen, and diminished breath sounds on the side of the hernia), avoid positive-pressure ventilation by mask. Immediately intubate the trachea and insert an orogastric tube.

Persistent cyanosis and bradycardia

- These are rarely caused by congenital heart disease. More commonly, the persistent cyanosis and bradycardia are caused by inadequate ventilation.
  - Ensure chest is moving with ventilation.
  - Listen for equal bilateral breath sounds.
  - Confirm 100% oxygen is being given.
  - Consider congenital heart block or cyanotic heart disease (rare).

Failure to initiate spontaneous respirations

- Consider:
  - Brain injury (hypoxic ischemic encephalopathy)
  - Severe acidosis, congenital neuromuscular disorder
  - Sedation, secondary to maternal drugs
  - If a mother has recently received narcotics within 4 hrs of delivery and her infant fails to breathe, first assist ventilation with positive pressure, and then consider giving naloxone to the infant (0.1 mg/kg, 1mg/ml solution, I.V. or I.M).

Resuscitation of Preterm Newborns

- Preterm babies are at additional risk for requiring resuscitation because of their:
  - Excessive heat loss
  - Vulnerability to hyperoxic injury
  - Immature lungs and diminished respiratory drive
  - Vulnerability to infection
  - Low blood volume, increasing the implications of blood loss

- Additional resources needed to prepare for an anticipated preterm birth include:
  - Additional trained personnel, including intubation expertise
  - Careful attention for maintaining temperature
  - Compressed air
  - Oxygen blender
  - Pulse oximetry
- Premature babies are more vulnerable to hyperoxia; use an oximeter and blender to gradually achieve oxygen saturations in the 85-95% range during and immediately following resuscitation.
- Decrease the risk of brain injury by:
  - Handling the infant gently
  - Avoiding the Trendelenburg position
  - Avoiding high airway pressures, when possible
  - Adjusting ventilation gradually, based on physical examination, oximetry, and blood gases.
  - Avoiding rapid intravenous fluid boluses and hypertonic solutions because of the risk of intraventricular hemorrhage
- After resuscitation:
  - Monitor and control blood glucose level
  - Monitor for apnea, bradycardia, or desaturations, and intervene promptly
  - Monitor and control oxygenation and ventilation
  - Consider delaying feeding if perinatal compromise was significant
  - Increase your suspicion for infection

Post-resuscitation Care

- An infant who has required resuscitation must have close monitoring and management of oxygenation, infection, blood pressure, fluids, apnea, blood sugar, feeding, and temperature. Be careful not to overheat the infant during or following resuscitation.
- The Apgar scores should be recorded in the neonate's birth record. Complete documentation of the events taking place during resuscitation must also include a description of interventions performed and their time.

Withdrawal of Resuscitation

- Discontinuation of resuscitation effort may be appropriate if there are no signs of life (no heart rate and spontaneous breaths) in an infant after 15 minutes of complete and adequate resuscitation effort with no evidence for other causes of newborn compromise.

Chapter 5

Care of the Well Newborn

Care of the Well Newborn

Delivery Room Care

Infection control measures

Strictly follow the infection control guidelines.

Thermoregulation

- Stabilization of temperature is the first step. Newborns should be dried thoroughly, except for the hands, with warm towels immediately after birth. Once it is clear that the infant has a good color and is active (usually within 1-3 minutes), he/she can be given to the mother and placed between the mother's breasts or on her abdomen and wrapped with her.
- Early skin to skin contact (SSC) between mother and infant is important for several reasons:
  - A fall in newborn's temperature can be reduced.
  - Psychologically, SSC stimulates mother and infant to get acquainted with each other (mother-newborn bonding).
  - After birth, babies are colonized by bacteria, for this reason it is advantageous that babies come in contact with their mother’s skin bacteria, and that they are not colonized by bacteria from care givers or from the hospital.
  - SSC is considered a critical component for successful breastfeeding initiation.

Assessment

Assessments of the newborn begin immediately. One of the first checks is the Apgar score, at 1 and 5 minutes after birth, to evaluate the condition of the newborn.

Physical examination

- A brief physical examination is performed to check that the infant is healthy (i.e., has no major anomalies or birth injuries, his/her tongue and body appear pink, and has normal breathing). For high-risk deliveries, this examination should focus on congenital anomalies and pathophysiologic problems that may interfere with normal cardiopulmonary and metabolic adaptation to extrauterine life.
- The hips of all newborns should be examined with specific maneuvers to rule out developmental dysplasia of the hip (DDH) **(Refer to Chapter 37).**

Umbilical cord care

- Fix the cord clamp two inches away from the umbilicus.
- Cut the umbilical cord 3-5 cm from the abdomen using clean and sterile scissors or scalpel.
- Examine the umbilical cord for any abnormality (e.g., single umbilical artery).
- Wipe the umbilical stump with antiseptic solution.

Identification

- Footprints are often taken and recorded in the medical record.

- Before the newborn leaves the delivery room, identification bracelets with identical hospital numbers are placed on the infant and mother. Babies often have two- one on the wrist and the other on the ankle. These should be checked each time the infant comes or goes from the mother's room.

Transitional Care

- The transition period (the transition from life in uterus to existence outside) is usually defined as the first 4-6 hrs after birth. During this period, the infant's pulmonary vascular resistance decreases, blood flow to the lungs is greatly increased, overall oxygenation and perfusion improve, and the ductus arteriosus begins to constrict or close.
- Common signs of disordered transitioning are:
  - Respiratory distress
  - Poor perfusion with cyanosis or pallor
  - Need for supplemental oxygen
  - Hypothermia.
- Transitional care of the newborn can take place in the mother's room:
  - Infants are evaluated for problems that may interfere with the normal transition, such as congenital malformations.
  - The infant should be evaluated every 30-60 minutes during this period, including assessment of heart rate, respiratory rate, axillary temperature, color and tone, and observation for signs of withdrawal from maternal medications.
  - With suspicion of disordered transitioning:
    - Hemodynamically stable infant can be observed closely for a brief period of time.
    - Infants with persistent signs of disordered transitioning require transfer to a higher level of care.

Routine Care

Healthy newborns should be with their mothers, all or nearly all the time (rooming-in). When possible, physical assessments, administration of medications, and bathing should occur in the mother's room.

Infection control measures

Proper hand washing is essential before handling the newborn.

Thermoregulation

The newborn's temperature is stabilized with one of three possible modalities:

- Open radiant warmer on servo-mode
- Skin to skin contact with the mother
- Hats and proper clothes

Gestational age assessment

Assessment of gestational age is performed on all newborns using the expanded Ballard Score.

Anthropometric measurements

The newborn's weight, head circumference, and length are recorded and then plotted against the estimated gestational age (GA).

Bathing

- Do not bathe immediately after birth; for thermoregulation keep the newborn warm and wrapped in dry cloth.
- Blood, meconium and some of the vernix caseosa will have been wiped off during drying at birth. The remaining vernix does not need to be removed as it may reduce heat loss.
- The first bath is given with non-medicated soap and warm tap water once an infant's temperature has stabilized (4-6 hrs after delivery). Later, the infant can be cleaned with water and soap as necessary.
- Initially, only sponge baths are allowed. Do not bathe the infant in a basin until after the umbilical cord has fallen off.

Skin care

- Examine for trauma or signs of infection.
- If *Staphylococcus aureus* epidemic is present, use hexachlorophene soap (potentially toxic to neonates, thus leave 5 minutes on skin then rinse well).
- Clean skin abrasions carefully with soap and water. Topical antibiotics are used for special indications for short periods, as prolonged use will lead to emergence of multiple antibiotic resistant strains.

Umbilical cord care

- Rooming-in and skin-to-skin contact with the mother to promote colonization with non-pathogenic bacteria from the mother's skin flora.
- Keep the stump dry and loosely covered with clean sterile gauze.
- The diaper should be folded below the umbilicus.
- If the stump becomes soiled, wash it with soap and clean water and dry it well.
- Apply alcohol after each diaper change.

Infant sleep position

The AAP recommends that healthy infants be placed supine (on the back) to sleep, not prone (on the stomach).

Routine Medications

- Apply eye drops (e.g., tobramycin eye drops) or erythromycin eye ointment 0.5% within one hour of delivery to protect against ophthalmia neonatorum.
- Vitamin K_1 (0.5-1 mg) should be administered within 2 hrs of life to prevent hemorrhagic disease of the newborn as a single IM injection.

Routine Assessments

- After a stable delivery, a second and more detailed examination should be performed within 24 hrs of birth.
- Vital signs: respiratory rate, heart rate, and axillary temperature are recorded every 8-12 hrs, and every 4 hrs if at risk for cardiac or pulmonary disease.
- Each urine and stool output is recorded in the infant's chart. The first urination should occur by 30 hrs of life. The first passage of meconium is expected by 48 hrs of life. Delayed urination or stooling is cause for concern and must be investigated.
- Daily weights are recorded in the infant's chart.
- All the neonatal care staff must be alert for the signs and symptoms of illness, including temperature instability, change in activity, refusal to feed, pallor, cyanosis, early or excessive jaundice, tachypnea and respiratory distress, delayed passage of first stool or voiding of urine, and bilious vomiting.

Feedings

- Supporting and facilitating the bonding process and immediate and exclusive breastfeeding should be the priority during the first hour postpartum preferably in the delivery room. The infant’s lips are placed near or on the mother’s nipple immediately after birth. Babies should never be forced on the breast.
- Washing infant’s hands and mother’s breasts should be delayed so that the taste and smell of the mother’s amniotic fluid is not removed.
- Early initiation of breastfeeding has many advantages:
  - For the mother
    - Nipple sucking stimulates uterine contractions that minimize postpartum hemorrhage.
    - Early and frequent feeding may bring in the mother's milk more quickly.
    - Early breastfeeding helps to enhance emotional bonding between mother and infant.
    - Avoids breast engorgement.
  - For the infant
    - Importance of colostrum to the infant.
    - Early passage of meconium.
    - Prevents infection from prelacteal feeding, such as diarrhea.
    - Prevents development of protein intolerance from artificial feeding and allergies such as eczema.
- Standard term formula is offered to infants for whom breastfeeding is contraindicated. Infants are fed at least every 3-4 hrs. The frequency and volume of each feed is recorded in the infant's chart.

Newborn Male Circumcision

- Appropriate testing to exclude a bleeding disorder must be done if there is a family history of bleeding disorders, such as hemophilia.
- Complications: Infection and bleeding.
- Contraindications:
  - Sick or unstable infant.
  - Congenital bleeding disorder. It can be performed if the infant receives appropriate therapy before the procedure.
  - Anomalies in the penis (e.g., hypospadias, ambiguity, or micropenis).
  - It should be delayed in infant with bilateral cryptorchidism.
- After circumcision:
  - There may be a gauze dressing with petroleum jelly or an antibiotic cream. This may be removed at the first diaper change and a new dressing applied.
  - The head of the penis may be very raw and red looking.
  - There may be a small amount of blood at first or yellow-colored drainage later (these are part of normal healing).
  - The infant may have some discomfort with diaper changes in the first few days.
  - Keep the penis clean with soap and water.
- Circumcision usually heals within one to two weeks.

Screening

- Congenital hypothyroidism (CH) screening: from 3rd to 7th day of life.
- Bilirubin screening: before discharge, it is recommended to screen all newborns for the risk of subsequent, significant hyperbilirubinemia.

Documentation

All the newborn's data should be properly documented in the infant's chart.

Parental Education

- Instruction by the nurse on feeding and infant care.
- Distribution of books and pamphlets on care of healthy newborn.
- Availability of continuous maternal and child health teaching programs.

Vaccination

- Educate parents about vaccination schedule.
- Hepatitis B immunoglobulin (HBIG) (0.5 ml/kg IM) should be administered to all newborns of HBs Ag-positive mothers as soon as possible after birth (within 12 hrs), followed by HBV vaccine (0.5 ml IM).

Discharge Examination

Answer any questions, review certain issues, and observe for:

- Jaundice
- Skin infection
- Subtle signs of illness (fever, lethargy and change in feeding behavior)
- Adequacy of breast milk intake

Pediatric Follow-up Appointment

- Healthy newborn infants are usually seen 2-3 days after discharge.
- Copies of initial and discharge summaries are given to parents.

Chapter 6

Levels of Neonatal Care Units

Levels of Neonatal Care Units

The Egyptian National Neonatal Care Program (ENNCP) provides services nationwide. The number of neonatal units is steadily increasing and differences between the units are characterized by available spaces, quantity and types of equipment and supplies, the number and qualifications of available staff, case loads and quality of services.

Improving community access to quality of care in the Neonatal Care Units is a major focus of the perinatal/neonatal health care strategy. All communities should have adequate access to care for the majority of newborn illnesses, whether mild or severe.

To meet this goal neonatal intensive care units (NICU) will be reassessed and upgraded into a new multilevel system of neonatal care.

Neonatal Functional Units

A neonatal service should have the facilities available to perform these functions:

- Resuscitation and stabilization
- Admission and observation
- Normal neonatal nursery care
- Continuing care
- Intermediate care
- Intensive care
- Isolation
- Visitation
- Support services

Local circumstances should be considered in the design and management of these neonatal care services.

Levels of Neonatal Care

Level I-basic neonatal care

Function of the unit

- Care of neonates with uncomplicated conditions, availability of emergency measures, and plan for transfers to Levels II and III
- Risk assessment
- Plan for well child post-discharge care
- Parent education and discharge planning
- Continuing education

Criteria for admission

- Normal, stable, full term neonate with a body weight ≥2,500 gm
- No risk factors

Physical facility

- Space allocation: rooming-in with the mother at the post-delivery room.
- The number of bassinets (cribs) should be at least equal to the number of obstetric beds.
- The room temperature should be maintained at 24º-26ºC.

Equipment, supplies, and medications

- Resuscitation box with equipment, supplies and medications necessary for neonatal resuscitation
- Neonatal stethoscope
- Newborn scale
- Neonatal thermometer
- Alcohol 70%
- Antibiotic eye drops

Personnel

- Nurses and physicians must be trained in basic neonatal care and resuscitation
- Staffing requirements should reflect a nurse-infant ratio of 1:6-8

Level II-special neonatal care units

Function of the unit

- Management of moderately ill newborns expected to improve rapidly
- Management of extremely ill newborns requiring stabilization and transfer to Level III
- Management of recovering neonates transferred back from Level III or Level IV centers
- Risk assessment
- Continuing education

Criteria for admission of neonates at level II units

- Preterm infant 32 weeks' gestation (<37 weeks)
- Low Birth Weight (LBW) infant ≥1,500 gm
- Infant of a diabetic mother (IDM)
- Affected infant born to high risk pregnancy and delivery
- Respiratory distress not needing assisted ventilation
- Hyperbilirubinemia, needing phototherapy
- Neonatal sepsis
- Hypothermia

Personnel

- Nurse-infant ratio of 1:4 during each shift

- Resident trained in neonatology available 24 hrs/day
- Pediatrician with special neonatal training available 24 hrs/day

N.B.: Level II units are subdivided into 2 categories (Level IIA and IIB) on the basis of their ability to provide continuous positive airway pressure (CPAP). Level IIB is capable to provide CPAP.

Level III-neonatal intensive care units

Function of the unit

- Care of moderately ill and extremely ill newborns
- Transport system
- Regional and in-house continuing education
- Assist region in assessing unmet needs in perinatal health
- Evaluation and research

Criteria for admission of neonates at level III units

Any infant whose clinical condition is such that they cannot be appropriately cared for in Level II:

- Infant with hemodynamic compromise (shock)
- Moderate or severe respiratory distress, needing short-term mechanical ventilation for less than 7 days
- Very low birth weight (VLBW) infant <1,500 gm
- Infant with an abnormal neurologic examination
- Infant with seizures or sever hypoxic-ischemic injury
- Infant requiring an exchange transfusion for hyperbilirubinemia or polycythemia
- Total parenteral nutrition for less than 7 days

Personnel

- Nurse-infant ratio of 1:1-2
- Nurse specialized in NICU
- Resident available 24 hrs/day
- Consultant available 24 hrs/day

Level IV-neonatal intensive care units (University Hospitals)

Criteria for admission of neonates at level IV units

- ELBW infant (<1,000 gm)
- Prolonged mechanical ventilation for more than 7 days
- Surgery; pre and postoperative care
- Suspected metabolic or endocrine disorders

- Hydrops fetalis
- Life threatening anomalies
- Total parenteral nutrition for more than 7 days

Personnel

- Nurse-infant ratio of 1:1
- High Institute Graduate Nurses
- Neonatologist available 24 hrs/day
- Neonatology Consultant available 24 hrs/day

For more details on this topic, please refer to Input Standards of the Neonatal Care Units

Chapter 7

Stabilization Guidelines

Stabilization Guidelines

The normal neonate's requirements for stabilization are provided through routine care, but a full term neonate who is at-risk and a preterm infant will require special care. This means that a thorough immediate assessment and proper management in the delivery room and upon admission to the special care neonatal unit must take place. The obstetrical team of doctors and nurses must work effectively with the neonatal team to ensure that the neonate is stabilized and transferred to the special care neonatal unit as soon as possible. When the neonate is admitted to the unit, the neonatal team of doctors and nurses must assess and manage the neonate and work together to ensure that optimal care is provided during neonatal stabilization.

Definition

- Stabilization is a series of activities which begin with resuscitation and continue through those interventions necessary to help the infant achieve normal transition.
- Careful stabilization of the infant prior to transport will enhance long-term outcomes for the infant and minimizes the risks of adverse events occurring during transport.

Assessment and Management

Stabilization focuses on five basic physiologic areas: airway and breathing, temperature, blood pressure and cardiovascular system, metabolic and fluid status, and laboratory and sepsis work-up.

Neonatologists should anticipate, promptly recognize, and effectively correct problems as they arise.

Airway and breathing

Just as in neonatal resuscitation, a patent, stable airway continues to be of primary importance during stabilization.

- Ensure a patent and stable airway:
  - Position with the neck slightly extended; use shoulders roll, if needed (improper positioning may lead to obstructive apnea, especially in the preterm neonates)
  - Suction
  - Insert an oral airway, if needed
  - An endotracheal tube may be needed
- Once a patent airway is achieved, evaluate:
  - Respiratory effort, rate, and pattern
  - Color
  - Air entry by auscultation
  - Oxygen saturation
  - Oxygen requirement to keep an adequate O_2 saturation
  - Presence of apnea

- Assist ventilation, if needed by:
  - Bag and mask ventilation
  - Endotracheal intubation and mechanical ventilation
  - Decompression of pneumothorax, if present
  - Continuously monitor degree of respiratory distress and response to therapy
- Blood gas evaluation:
  - Sample may be obtained from radial, posterior tibial, or umbilical artery; or capillary sample obtained by heel puncture.

Thermoregulation

- Normal neonatal core temperature is 36.5-37.5°C.
- Hypothermia or hyperthermia may increase oxygen consumption and metabolic demands.
- Sick infants, small for gestation (SGA) and preterm infants are particularly vulnerable to cold stress.
- Prevention of heat loss is easier than overcoming the detrimental effects of cold stress once it has occurred.
  - Before the delivery of the infant, neonatal hypothermia could be prevented by:
    - Closing all the doors and windows.
    - Turning off all fans in the room.
    - Pre-warming towels and other linens which will be used in wrapping of the infant.
    - Keeping delivery room warm using a heater (radiator), if available. The Delivery room temperature should be kept within 24-26°C.
  - Immediately after delivery, dry the infant, and remove wet linens from around the infant.
  - The neonate should be undressed except for a diaper and centered under pre-heated radiant warmer.
  - Encourage direct skin-to-skin contact with the mother. Wrap both mother and neonate in blankets or clothing.
  - Prevent contact with cold or wet surfaces or exposure to turbulent air currents.
  - Cover infant with clear plastic sheet or acrylic heat shield; use double-walled isolette.
  - Cover infant's head with a cap.
- Warming the infant:
  - Place under radiant warmer; skin probe should be on abdomen with desired skin temperature set at 36.5°C.

- If the infant is cold, place in isolette with temperature set at 1-1.5°C above body temperature. As infant warms, increase by 1-1.5°C until temperature is normal. It is important note that re-warming should take place slowly (with a rate not to exceed 1°C/hr).
- Use warmed blankets, or heat lamps, and avoid using hot water bottles.

Circulatory status

- Assessment of the circulatory status and perinatal volume loss:
  - Perfusion: capillary refill time (>3 seconds), pallor, mottling, cool skin, decreased peripheral pulses with poor peripheral perfusion.
  - Heart rate: tachycardia (>170 beats/minute at rest), or bradycardia (<100 beats/minute).
  - Blood pressure: may be normal or low; a fall in blood pressure is a late sign of shock (as the blood vessels may constrict and redirect blood away from non-vital organs to maintain blood flow to the heart and brain).
  - Urine output.
  - Blood gas analysis: evaluate for acidosis/hypoxemia.
- Obtain an intravenous access:
  - Peripheral intravenous line: the first choice, insert cannula under aseptic conditions.
  - Umbilical vein catheter: the second choice, if trained personnel and equipment are available.
- Treatment for circulatory failure:
  - Support oxygenation/ventilation and reverse effects of asphyxia.
  - Improve circulating blood volume by giving normal saline, Ringer's solution, packed RBC's, or whole blood 10 ml/kg over 15-30 minutes. Volume expansion may need to be repeated up to two times in severe shock.
  - Improve myocardial contractility:
    - Dopamine: 5-20 μg/kg/minute via a continuous infusion.
    - Other inotropic agents can be used as dobutamine, and epinephrine.

Metabolic and fluid status

- Blood glucose levels should be monitored regularly and maintained at 50-125 mg/dl.
- In case of symptomatic hypoglycemia (serum glucose <45 mg/dl), give 2 ml/kg glucose 10% IV over 1 minute, followed by IV infusion of 4-8 mg/kg/minute.
- Calculate fluid requirement according to gestational age, day of life, hydration state and disease state.
- When available, evaluation of blood gases for acid-base balance can be helpful to identify respiratory or metabolic acidosis. Establishing and maintaining adequate ventilation and perfusion are much more important to a successful resuscitation than the vigorous use of alkali solution.

- Administration of alkali is limited to situations where:
  - Provision of adequate pulmonary ventilation has been assured.
  - Tissue oxygenation and perfusion are maximized and the blood pH remains <7.20 and base deficit >10.
  - Documented or suspected metabolic acidosis diagnosed during cardiopulmonary resuscitation.
- Calculate the dose of bicarbonate using the following formula:

Body weight in kg × HCO_3 deficit (desired - actual) × (0.3) = mEq $NaHCO_3$

Administer half of the calculated dose, infused over >20-30 minutes, and then assess need for the remainder.

Evaluate for sepsis

- Evaluation for infection requires a thorough review for potential risk factors, including:
  - Preterm labor and delivery
  - Rupture of membranes (≥18 hrs)
  - Prolonged length of labor
  - Presence of maternal fever during labor
  - Elevated maternal WBCs count
  - Low neonatal WBCs count
- Obtaining CBC with differential, WBCs count, absolute neutrophil count, immature to total (I/T) ratio, platelet count, and blood culture.
- Treating suspected infection:
  - Initiate IV antibiotic therapy (ampicillin and gentamicin) after obtaining the appropriate cultures, and continue close observation until results of blood culture and sensitivity are available.

Chapter 8

Neonatal Referral and Transport

Neonatal Referral and Transport

Neonatal referral is an integral part of perinatal care programs. The goal is to reduce neonatal mortality and morbidity when the management of a sick infant exceeds the ability of the level of care provided in a district hospital.

All hospitals with established maternity services and level I or II neonatal care units should have agreements with higher perinatal care centers for perinatal consultations and neonatal transfer.

Types of Neonatal Transport

- Intrauterine transport: transfer of the mother prior to delivery of a high-risk infant to a hospital capable of providing suitable care for the neonate.
- One-way transport: transfer of the neonate from a Level II to a Level III unit at another facility.
- Two-way transport: transfer of the neonate to a higher level care center and back again by a specialized team from the Level III unit facility.
- Return (reverse) transport: transfer of the infant from a Level III care unit to a Level II care unit, after resolution of the acute condition for which the neonate had been transferred.

Indications for Maternal/Neonatal Referral

Referral of the pregnant mother to

A hospital with level III NICU

When the mother is suspected to deliver a baby with:

- Very low birth weight (<1,500 gm) or gestational age <32 weeks
- Anomalies affecting transition (e.g., diaphragmatic hernia)
- Severe hemolytic jaundice
- Any level I risk baby with complications **(Refer to Chapter 1)**

A hospital with level IV NICU (University Hospitals)

When the mother is suspected to deliver a baby with:

- Extreme low birth weight (<1,000 gm)
- Anomalies needing immediate surgical intervention
- Life threatening anomalies
- Hydrops fetalis

Referral of the newborn infant to

Level III-neonatal intensive care unit

Criteria for admission of a newborn at level III care units **(Refer to Chapter 6).**

Level IV-neonatal intensive care unit

Criteria for admission of a newborn at level IV care units **(Refer to Chapter 6).**

Referral of the neonate to another hospital

If procedures needed are unavailable at referring hospital

Arranging for Transport

Communication

Communication with the referral center is done prior to transport to ensure the availability of a bed and availability of the services required for the baby (e.g., surfactant, surgery...).

Information that should be available at the time of the consultation call:

- Parent's consent for referral and documented in the patient's medical record
- Patient's name and date of birth
- Names of the patient's mother and father
- Prenatal history
- Labor and Delivery Record
- Neonatal Resuscitation Record
- Apgar scores
- Gestational age and birth weight
- Vital signs (temperature, heart rate, respiratory rate, blood pressure)
- Oxygen/ventilatory support requirements
- Laboratory data obtained (glucose, calcium, hematocrit, blood gas value)
- Vascular access

Role of the referring hospital

Stabilization of the newborn

(Refer to Chapter 7)

- Airway and breathing support
- Thermoregulation; temperature should be taken every 30 minutes until transfer.
- Circulatory support; in cases of shock, volume expansion (10 ml/kg IV over 15-30 minute) is required using normal saline, Ringer's solution, whole blood, packed RBC's. It can be repeated, if necessary.
- Obtain an intravenous access: insert a peripheral IV line (cannula) under aseptic conditions.
- Adjust metabolic and fluid status; maintain plasma glucose levels between 50-125 mg/dl. When available, evaluation of blood gases can be helpful to identify respiratory or metabolic acidosis.
- Evaluate the risk of infection; in case of suspected infection, obtain appropriate cultures and give first dose of IV antibiotics (ampicillin and gentamicin).

Special considerations

- Esophageal atresia and tracheo-esophageal fistula: place a multiple end-hole suction catheter in the proximal pouch and put on to intermittent suction immediately to protect the lungs.
- Diaphragmatic hernia: initiate immediate endotracheal intubation (avoid bag and mask ventilation), and then insert a large nasogastric tube into the stomach and aspirate its contents immediately.
- Abdominal wall defect (gastroschisis or omphalocele): cover the sac with warm, sterile, saline soaked gauze, and wrap with a sterile transparent plastic bag (care must be taken to prevent twisting and infarction of the bowel), then a nasogastric tube is inserted to decompress the intestine, thus minimizing intestinal distention.
- Neural tube defects (e.g., myelomeningocele): keep the newborn in the prone position, with a sterile saline-moistured gauze sponge placed over the defect. Use latex free products including gloves (risk of anaphylaxis).
- Bilateral choanal atresia: insert an oral airway.
- Pierre Robin syndrome: place the infant in the prone position, in more severe cases; nasopharyngeal tubes are required.

Discussion

The referring hospital should discuss the newborn's condition and potential therapies with team members before departure.

Documentation

All newborn’s data and his/her clinical condition should be properly documented in the referral report.

Role of the Transport Team

Preparation

Personnel

Transport teams consist of a combination of at least two or three trained and fully skilled personnel in the care of the high-risk neonate for adequate stabilization before, and effective management during, transport. The team may include a physician, neonatal nurses, respiratory therapists and specially trained transport nurses.

Vehicle and equipment

An ambulance should be prepared with the following:

- Transport incubator
- Monitors for:
  - Heart rate
  - Respiratory rate
  - Temperature
  - Arterial blood pressure with different sizes of neonatal blood pressure cuff
  - Inspired oxygen concentration

  - Oxygen saturation
- Oxygen delivery system (cylinder, regulator and tubing)
- Intravascular infusion equipment
  - IV cannulae (sizes 22 and 24)
  - Syringes (sizes 2.5, 3, 5, 10, 20 and 50 ml)
  - IV infusion sets
  - Adhesive tape
  - Alcohol swabs
  - Gauze
- Suction equipment
- Ambubag with face masks; term and preterm sizes
- Intubation equipment
- Umbilical vessel catheterization tray
- Medications for resuscitation
- Other equipments:
  - Stethoscope
  - Oral airways (neonatal size)
  - Light source
  - Source of electrical power
  - Feeding tubes: 6Fr and 8Fr
  - Thermometer
  - Assisted ventilation equipment, if available

For more details **(Refer to Chapter 1)**

Records

Records of each transport should include complete prenatal history, delivery record and Apgar scores from the hospital of origin and the referral form.

Upon arrival to the referring hospital

- The transport team will assess the infant's condition by performing a physical examination, reviewing x-ray and/or laboratory results and obtaining vital signs, a blood glucose level, and blood gas levels as appropriate.
- The transport team will rely upon the staff of the referring hospital to supply the prenatal history, labor and delivery record, neonatal resuscitation record, Apgar scores and the gestational age and birth weight of the neonate.
- If the infant has unstable vital signs, the transport team will remain at the referring hospital until he/she is sufficiently stabilized to ensure a safe transport. It is unsafe to transport an unstable infant, so, depending on his/her condition, the team may stay at the referring hospital for a prolonged time.

During transport

- Checking vital signs and temperature frequently. However, the benefit of handling the patient and taking vital signs must be weighed against the possibility of an accidental extubation or thermal loss incurred by opening the transport incubator.
- Monitoring oxygen saturation with pulse oximetry.
- Documentation of any important event that may occur during the trip and contact the referring or the receiving hospital to find out the solution.
- The transport team should use cell phones to maintain contact with the NICU and seek advice for unexpected events.
- Registration of the time of leaving and arrival.

Upon arrival to the receiving hospital

- The team should give the NICU staff compete clinical information (handoff) and copies of charts, consents and radiographs.
- A team member should telephone the parents and the referring physicians to inform them about the patient's status.

Role of the receiving hospital

Prior to infant arrival (preparation of the place)

- Ensure presence of vacant incubator for the referred baby.
- Get an updated report (e.g., phone call) for case progress from the referring place prior to admission, anticipate respiratory needs and ask the nurse to prepare needed equipment.

Upon arrival to the hospital

- Assess and stabilize the newborn **(Refer to Chapter 7)**
- Check the referral documents:
  - Referral letter for case progress
  - Investigations and radiology
  - Medications given, doses and last given dose
  - Steps and procedures done in the referring hospital
  - Fill in the relevant part of referral sheet
- Fill in the Admission Sheet
- Ensure contacting the parents for:
  - Re-evaluating the history
  - Discussing the plan of care
  - Getting contact information such as phone and address
  - Getting consent for procedures
  - Highlighting the importance of family visits, breastfeeding and regular expression of breast milk every 3 hrs

- Orientation of parents to system of NICU visits and infection control measures

Feedback

This can be obtained through a communication between the physician of the receiving hospital and that of the referring one, to know the status and the progression of the infant's illness.

Records

An accurate record of each transport is made for quality assurance and documentation.

N.B.: The most important factor is to always ensure the safety of the transport team while en-route. In most circumstances, stabilize the infant at the referring hospital before entering the ambulance.

Chapter 9

Newborn Admission in Neonatal Care Units

Newborn Admission in Neonatal Care Units

The Egyptian National Neonatal Care Program (ENNCP) provides optimal care for Egyptian neonates through:

- Proper identification of risk factors
- Evaluation of neonatal signs and symptoms of illness and/or disease
- Development and implementation of an appropriate care plan

Neonates considered by the physician to need the services of the Special Care Unit (for any reason) should be admitted. All neonates in the hospital must have a physician responsible for their daily care.

Indications for Admission

- Prematurity ≤34 weeks' gestation
- Low Birth Weight (LBW) <1,800 gm
- Cardiopulmonary problems:
  - Central cyanosis
  - Respiratory distress
  - Apnea/Bradycardia
  - Meconium suctioned below the vocal cords
- Neurologic problems:
  - Seizures
  - Impaired consciousness
  - Abnormal neonatal reflexes
  - Severe hypotonia
  - Low 5-minute Apgar score
- Gastrointestinal and genitourinary problems:
  - Delayed passage of meconium beyond 48 hrs
  - Bile stained vomiting, or other signs suggesting bowel obstruction
  - Feeding problems severe enough to cause clinical concern
  - Abdominal masses
  - Delayed passage of urine beyond 24 hrs
- Hematologic problems:
  - Pallor
  - Polycythemia with venous hematocrit ≥65%, or 60-64% with clinical symptoms
  - Petechiae and purpura
- Hyperbilirubinemia requiring treatment
- Neonatal infection (acquired or congenital)

- Metabolic problems:
  - Hypoglycemia and IDM: inability to maintain a serum glucose concentration ≥45 mg/dl despite adequate feeding
  - Dehydration
  - Electrolyte disturbances
- Congenital malformation:
  - Major malformations or minor malformations that need special care as:
    - Chromosomal disorders (trisomies 13, 18, and 21)
    - Pierre Robin syndrome
    - Osteogenesis imperfecta
    - Asphyxiating thoracic dystrophy
- Birth injuries

Important Note
Any infant that is causing concern to such a degree that the attending doctor feels that the infant requires observation or treatment should be admitted. It is better for an infant to be admitted unnecessarily than for an infant requiring admission to be left on the ward.

Admitting Orders

- At the time of admission, the physician must provide standard orders for the management of each neonate after full history taking and complete thorough clinical examination. All admitting orders are reviewed and modified by the physician, as needed.
- List of standard admitting orders should include:
  - Place of admission: incubator or crib depending on weight and clinical condition.
  - Checking vital signs every 30 minutes for the first two hours, then every hour until stable, then every 4 hrs.
  - Assessing neonate's weight, length, and head circumference; estimating gestational age by using the New Ballard Score, and then plotting these measures against the estimated GA **(Refer to Chapter 11).**
  - Bedside glucose monitoring until stable or per physician's order.
  - Prophylactic antibiotic eye drops administration within one hour after birth.
  - Vitamin K_1 administration within 1-2 hrs after birth.
  - Recording weight daily.
  - Nutritional plan: breastfeeding on demand is the usual order; or any other special fluid or nutrition order needs to be specified and documented.
  - Bathing the neonate when generally and vitally stable and after his/her temperature is stable for at least 2 hrs.
  - Provision of umbilical cord care

- Admitting procedures
  - Completion of the Data Collection Forms
  - Completion of the Admission Log Book
  - Completion of the Daily Neonatal Clinical Record
  - Notification of hospital administration of admission to ensure appropriate staffing support and equipment availability
  - Orientation of parents to the unit environment and routines
- Determination of specific interventions based on the neonate's risk factors and assessment. Examples:
  - Daily measurement of head circumference for suspected hydrocephalus
  - Assessment of abdominal circumference every 6-8 hrs for suspected necrotizing enterocolitis (NEC)

Chapter 10

Physical Assessment of the Newborn

Physical Assessment of the Newborn

The whole key to the management of the newborn infant lies in a proper assessment of the infant at birth.

Importance

- The conduct of a physical examination as soon as possible after delivery is essential for early detection of deviations from the normal. This is particularly important in certain cases (e.g., esophageal atresia, imperforate anus, or diaphragmatic hernia) where the early diagnosis enables treatment which may make the difference between life and death and in some cases (e.g., congenital dislocation of the hips and club feet) where early diagnosis and initiation of treatment may reduce the incidence of permanent or severe disability.
- It establishes a baseline for subsequent examinations, and enables the doctor to give parents a true account of the infant's physical state.

When?

- The initial examination should be performed as soon as possible after delivery. Infants should have temperature, heart rate, respiratory rate, color, type of respiration, tone, activity, and level of consciousness monitored every 30 minutes after birth for 2 hrs or until stabilized. For high-risk deliveries, this examination should take place in the delivery room and focus on congenital anomalies and pathophysiologic problems that may interfere with normal cardiopulmonary and metabolic adaptation to extrauterine life.
- After a stable delivery, a second and more detailed examination should be performed within 24 hrs of birth.
- Before discharge from the maternity unit or neonatal care unit; no infant should be discharged from the hospital without a final examination, because certain abnormalities, particularly heart murmurs, often appear or disappear in the immediate neonatal period.
- An examination is indicated whenever there is any concern about the infant's progress.

Points to be Remembered

- Examining a newborn requires patience, gentleness, and procedural flexibility.
- It is better to perform a physical examination in a fixed order so that nothing is forgotten. However, if the infant is quiet and relaxed at the beginning of the examination, palpation of the abdomen or auscultation of the heart should be performed first, before other more disturbing manipulations are attempted.
- Whenever possible, the infant's mother should be present.
- The environment should be warm and a good light source must be present.
- Wash your hands before examining the infant.
- The infant should be completely undressed.
- Make sure to document the assessment appropriately.

Physical Examination

Gestational age assessment

(Refer to Chapter 11)

Vital signs

Stable growing neonates should have vital signs taken and systems assessment before feeding time. Unstable neonates and neonates on ventilators should have vital signs taken and systems assessment at least every 1-2 hrs.

Temperature

It should be obtained as axillary temperatures.

- The normal temperature for a neonate is 36.5-37.5^{o}C.
- A neonate in a warmer bed should have a skin probe thermometer attached at all times and an axillary temperature taken every hour until stable.
- Some neonatal units routinely obtain a rectal temperature as soon as the neonate is admitted, in order to check patency of the anus. However, a soft flexible catheter can be a safer method for determining anal patency while reducing the risk of rectal perforation.

Heart rate

Heart rate should be assessed by auscultation and counted for a full minute.

- A normal heart rate in neonates is 120-160 beats/minute at rest.
- If the neonate is tachycardic (heart rate >170 beats/minute), make sure the neonate is not crying or moving vigorously.
- If the neonate is bradycardic (heart rate <100 beats/minute), assess the neonate's color and pattern of breathing and start bag and mask ventilation, if necessary.
- Peripheral pulses of upper and lower limbs should be palpated for possibility of coarctation of aorta.

N.B.: Bradycardia is sometimes normal in term sleeping neonates.

Respiratory rate

Respiratory rate should be obtained by observation for one full minute.

- The normal respiratory rate of a neonate is 40-60 breaths/minute.
- Newborns have periodic rather than regular breathing. Apnea is abnormal.

Blood pressure

Measuring blood pressure is not a routine part of vital signs in most newborn nurseries. But once the newborn is admitted to NICU, blood pressure readings should be obtained on all four limbs using an automated blood pressure machine (DINAMAP machine) with the following considerations:

- Blood pressure varies with change in activity level (may increase with crying and decrease with sleeping).

- Appropriate cuff size (should cover only 2/3 of upper arm) is important for accurate reading.
- Normal blood pressure varies with gestational and postnatal ages **(Refer to Appendix 3).**
- It is measured in upper limbs and lower limbs (to rule out coarctation of aorta). Calf systolic pressure 6-9 mmHg less than systolic pressure in upper extremities may be indicative of coarctation of the aorta.

Growth measurements

There are three components for growth measurements in neonates:

- Weight should be obtained daily.
- Length should be obtained on admission and weekly.
- Head circumference should be obtained on admission and weekly.

N.B.: Measurements should be plotted on the corresponding growth curves related to gestational age.

Weight

- Weight should be obtained every day (twice daily, if infant <1,000 gm), at a fixed time of the day, in conjunction with routine care and isolette cleaning.
- Weight should be plotted on the weight chart upon admission and daily **(Refer to Appendix 2).**
- Normal birth weight in term newborn is 2,500-4,000 gm.
- If the weight is significantly different than the previous day, it should be checked twice.
- If a neonate is too unstable to be moved and weighed, a physician's order not to weigh the neonate must be obtained.

Length

- Crown-to-heel length should be obtained on admission and weekly.
- Length should be plotted on the length chart weekly.
- Neonate should be in transverse position while measuring the length. Avoid disturbing the neonate during measurement.
- Crown-heel length of the average newborn at term is 50 cm and 95% measures between 46 and 56 cm.

Head circumference

Head circumference should be measured on admission and weekly.

- Occipitofrontal head circumference is measured by placing a paper tape measure around the head to encircle the occiput, the parietal bones, and the forehead (one cm above the nasal bridge), i.e. the largest circumference.
- Measure at least daily in neonates with neurological problems, such as intraventricular hemorrhage, hydrocephalus or asphyxia.

- Head circumference of the average infant at term is 35 cm, though any measurement from 33-38 cm can be normal.

General appearance

Observe the infant and record the general appearance (e.g., activity, skin color, and obvious congenital abnormalities).

Skin

- Color: pink (normally), jaundice, pallor, plethora or acrocyanosis
- Texture: dry, wrinkled, covered with vernix caseosa. Superficial peeling is common in the first week of life
- Look for non pathologic conditions: milia, erythema toxicum, mongolian spots, benign pustular melanosis, salmon patch nevus, lanugo hair, and neonatal acne.
- Look for abnormal conditions: petechiae, bruising, strawberry hemangioma, port wine stains, pigmented nevi, and forceps marks.

Head and Neck

Assessment of head and neck should include the parameters listed in **(Table 10-1)**.

Table (10-1): Head and neck assessment parameters

Parameter	Normal	Abnormal
Skull	• Molding • Caput succedaneum • Craniotabes • Anterior fontanelle (2.5-3 cm)	• Cephalhematoma • Fracture • Sutures fused • Fontanelle (full or depressed)*
Face	• Normal configuration	• Face asymmetry • Abnormal (odd) facies • Mandibular hypoplasia • Forceps injury • Facial palsy
Eyes	• Symmetrical • Open • Red reflex (by ophthalmoscope)	• Asymmetry • Subconjunctival hemorrhage • Corneal opacities • Congenital glaucoma (large and cloudy) • Cataracts • Coloboma • Conjunctivitis
Nose	• Symmetrical • Patent	• Deformity • Nasal flaring • Choanal atresia
Ears	• Normal configuration (shape and perpendicularity to skull) • Response to sound	• Abnormal configuration • Low set • No response to sound • Forceps injury • Accessory auricle(s)/tags

Table (10-1): Head and neck assessment parameters (Continued)

Parameter	Normal	Abnormal
Mouth	• Normal configuration • Epstein's pearl	• Cleft lip/palate • High arched palate • Precocious teeth • Macroglossia • Tongue tie
Neck	• Normal mobility	• Webbing • Masses (sternomastoid tumor, goiter, or cystic hygroma) • Fracture clavicle

***** Fontanelle may be bulging during crying; examine when the baby is quiet.

Extremities

Observe and examine for:

- Polydactyly, syndactyly, abnormal palmar creases, and talipes.
- Developmental dysplasia of the hip (DDH), palsies (e.g., Erb's palsy) and fractures (swelling and crepitus).

Back and spine

Palpate the entire spine and examine for:

- Scoliosis
- Pilonidal sinus
- Spinal defects: meningomyelocele, lipoma, or tuft of hairs or dimple overlying spina bifida occulta

Lymph nodes

Palpable lymph nodes are found in approximately 1/3 of normal neonates. They are usually less than 12 mm in diameter and are often found in the inguinal and cervical areas, and occasionally in the axillary area.

Genitalia

Assessment of the genitalia should include the parameters listed in **(Table 10-2).**

Table (10-2): Genital assessment

Parameter	Normal	Abnormal
Female	• Normal configuration • Mucous vaginal discharge • Grayish white mucoid vaginal discharge • Pseudo-menstruation • Mucosal tag from the vaginal wall	• Ambiguous genitalia • Labia fused • Imperforate hymen
Male	• Normal configuration • Testes in scrotum • Hydrocele • Penile length 2.5 cm • Retractile testes	• Ambiguous genitalia • Phimosis • Hypospadias • Epispadias • Undescended testes

Anus and rectum

- Check patency (using a soft catheter), position and size (normal diameter is 10 mm).
- Abnormalities: imperforate anus, fistula, or patulous.

Systems assessment

Neurological assessment

- A full neurological assessment should be done every day. For unstable neonates and neonates with neurological problems, it should be done more frequently, as indicated by the physician's order.
- Neurological assessment should include the parameters in **(Table 10-3).**

Table (10-3): Neonatal neurological assessment parameters

Parameter	Comments
Activity	Quiet, awake, irritable or sleeping
Level of consciousness	Lethargic, alert or sedated
Posture	While observing neck position, look for symmetry between the sides and compare the upper and lower extremities
Movements	Spontaneous, to pain or absent
Tone	Hypertonic, hypotonic, normal or weak
Pupil	• Size: right, left • Reaction: sluggish, brisk or absent
Eye opening	To pain, to sound, none or spontaneous
Cry	Weak, full or high-pitched
Fontanelle (s)	Sunken, bulging or flat
Sutures	Over-riding or separated
Seizures	If present, write a complete description

- Normal neonatal reflexes
  - There are several reflexes that can be normally elicited in the newborn. These reflexes can be classified as tendon reflexes and primitive reflexes.
  - Primitive reflexes are peculiar to newborn; they are present since birth and occur at the subcortical level (as the cerebral cortex is functionally deficient). They usually disappear by 4-6 months of age (with maturation of the cerebral cortex). Persistence of these reflexes indicates a neurological problem.
  - Commonly evaluated neonatal reflexes are listed in **(Table 10-4)**.

Table (10-4): Neonatal reflexes

Reflex	Testing method	Normal responses
Babinski (plantar)	• Stroke one side of the neonate's foot upward from the heal and across the ball of the foot	• Neonate hyperextends the toes. Dorsi-flexes the great toe and fans the toes outward
Grasp	• Palmer reflex; place a finger in the neonate's palm • Plantar reflex; place a finger against the base of the neonate's toe	• Neonate grasps the finger • Neonate toes curl downward and grasp the finger
Moro	• Suddenly but gently drop the neonate's head backward (relative to the trunk)	• Neonate extends and abducts all extremities bilaterally and symmetrically, then adducts and flexes the extremities
Rooting	• Touch a finger to the neonate's cheek or the corner of mouth (the mothers nipple also should trigger this reflex)	• Neonate turns the head toward the stimulus, opens the mouth and searches for the stimulus
Stepping (automatic walking)	• Hold the neonate in an upright position and touch one foot lightly to a flat surface (such as the bed)	• Neonate makes walking motions with both feet
Sucking	• Place a finger in the neonates mouth (the mother's nipple also should trigger this reflex)	• Neonate sucks on the finger (or nipple) forcefully and rhythmically; sucking is coordinated with swallowing

Respiratory and chest wall assessment

- Breasts of male and female newborns may be swollen, and even occasionally engorged and secreting a white substance (witch's milk) due to maternal hormone stimulation. The enlargement persists for several weeks and may still be present at the end of the first year in girls. It should not be squeezed.
- Prominent xiphoid: this visible, firm lump in the midline of the chest is a frequently observed finding in newborns.
- An assessment should done every shift or with any change in the clinical condition.
- Respiratory assessment should include the parameters in **(Table 10-5).**

Table (10-5): Neonatal respiratory assessment parameters

Parameter	Comments
Skin color	Pink, cyanotic, pale, dusky, mottled or jaundiced
Breathing	Unlabored or labored, grunting, nasal flaring or retractions
Chest wall	Deformity, symmetrical or asymmetrical movement
Breath sounds	Distant, shallow, stridor, wheezing, or diminished, equal or unequal
Apnea/ bradycardia/ desaturation	Lowest observed heart rate, color, oximeter reading and duration of episode
Secretion	• Amount: scant, moderate or large • Color: white, yellow, clear, green or blood-tinged • Consistency: thick, thin or mucoid
Endotracheal tube	Length at the level of skin

Cardiovascular assessment

- An assessment should be done every shift or with any change in clinical condition.
- The heart lies in a relatively transverse position and the apex beat can be detected by palpation in the third or fourth intercostal space just outside the mid-clavicular line.
- Cardiovascular assessment should include the parameters listed in **(Table 10- 6).**

Table (10-6): Neonatal cardiovascular assessment parameters

Parameter	Comment
Precordium	Quiet or active
Skin color	Pink, cyanotic, acrocyanotic, pale, dusky, mottled
Heart sounds	Diminished or easily audible
Rhythm	Normal or describe any arrhythmia
Murmur	Describe, if any
Capillary refill	How many seconds? Where to be elicited?
Peripheral pulses; femoral and brachial	Normal, weak or absent

Gastrointestinal and abdominal assessment

Gastrointestinal assessment should be done daily or with any change in clinical condition and should include the parameters listed in **(Table 10-7)**.

Table (10-7): Neonatal gastrointestinal assessment parameters

Parameter	Comment
Abdominal shape	Slightly prominent (normal), distended, scaphoid
Abdominal girth	Record the measurement in cm daily
Umbilical stump	• Number of umbilical arteries • Meconium staining • Drying, inflamed, or discharges • Omphalocele
Emesis (or residuals)	Volume and description
Abdominal wall	• Red or discolored, defects • Distended or any visible loops of bowel
Palpation	Soft, tender or rigid liver (normally, liver is palpated 2 cm below costal margin in the newborn)
Bowel sounds	Present, absent, hyperactive or hypoactive

Other assessments

Other assessments should be obtained as applicable, examples:

- Wound and dressing description
- Colostomy output description

Chapter 11

Gestational Age Assessment

Gestational Age Assessment

All infants admitted to neonatal care units should have a complete gestational age (GA) assessment. If possible, this should be done within one hour after birth. The purpose of the Gestational Age Assessment is to:

- Compare a given infant against the standardized norms of neonatal growth based on gestational age. Findings are considered accurate within a range of 2 weeks.
- Verify the obstetrical estimate for gestational age and identify infants that are preterm, post-term, large or small for gestational age.
- Observe and treat for possible complications.

How to Assess the Gestational Age?

Antenatal

- Obstetric estimation of GA is based on dating from the first day of the last menstrual period.
- Ultrasonic scanning for the size of the fetal biparietal diameter can provide information about GA and fetal growth and development before birth.

Postnatal

- New Ballard Score
- Direct ophthalmoscopy of the anterior vascular capsule of the lens:
  - This technique allows for accurate determination of GA at 27-34 weeks' gestation.
  - Pupils must be dilated under the supervision of an ophthalmologist, and the assessment must be performed within 48 hrs of birth before the vessels atrophy.
  - Grading system
    - Grade 4 (27-28 weeks): vessels cover the entire anterior surface of the lens or the vessels meet in the center of the lens.
    - Grade 3 (29-30 weeks): central portion of the lens is not covered by vessels.
    - Grade 2 (31-32 weeks): vessels reach only to the middle-outer part of the lens. The central clear portion of the lens is larger.
    - Grade 1 (33-34 weeks): vessels are seen only at the periphery of the lens.

New Ballard Score

The Ballard Maturational Score has been expanded and updated to include extremely premature infants. It has been renamed the New Ballard Score. It is best performed at <12 hrs of age if the infant is <26 weeks' gestation. If the infant is >26 weeks' gestation, there is no optimal age of examination up to 96 hrs.

Accuracy

Examination is accurate to $\pm$2 weeks. It overestimates GA by 2-4 days in infants between 32 and 37 weeks' gestation.

Criteria

Examination consists of six neuromuscular criteria and six physical criteria.

Procedure

- GA assessment should be unhurried, systematic**,** and performed when the infant is stable and in a quiet, alert state.
- Examination is performed twice by two different examiners to ensure objectivity, and the data are entered on the chart **(Figure 11-1)**.
- Examination consists of two parts: neuromuscular maturity and physical maturity. The 12 scores are totaled, and maturity rating is expressed in weeks of gestation, estimated by using the chart provided on the form.
- Review the birth history and record the following information in **(Figure 11-1)** Maturational Assessment of Gestational Age.
  - Name - Date/time of birth - Sex - Race
  - Date/time of examination - Postnatal age (in hours) when examined
  - Birth weight - Length - Head circumference
  - Apgar score: at 1, 5, and 10 minutes
- Physical maturity is most accurately assessed immediately after birth. If the infant was compromised during labor and delivery or was affected by labor medications, neurological maturity may not be accurately assessed at this time and should therefore be repeated after 24 hrs of age. If the neurological assessment is not performed, the GA estimate can be based upon a doubling of the physical assessment score.
  - Assess the infant's physical maturity and place an (X) in the box on the form which best describes the infant. When a second examination is performed, place a (0) in the appropriate box.
  - Assess the infant's neuromuscular maturity and place an (X) in the box on the form which best describes the infant. When a second examination is performed, place a (0) in the appropriate box.

Neuromuscular maturity

Posture

- The infant is placed supine and the examiner waits until the infant settles into a relaxed or preferred posture.
- Observe the flexion of the arms and legs.
- Compare with the figures on the diagram and place an (X) through the figure most similar **(Figure 11-1).**

Square window

- Flex the infant's hand at the wrist and observe the angle between the thumb and forearm. Apply gentle pressure to get as much flexion as possible.
- Compare the angle at the thumb with the figures on the diagram and choose the figure most similar.

Arm recoil

- Place the infant in the supine position.
- Flex the forearms for 5 seconds; then grasp the hand and fully extend the arm and release. Observe the infant's arm reaction to the release.
  - Score (0): Infant' arm remains extended
  - Score (1): Partial flexion to 140-180º
  - Score (2): Flexion to 110-140º
  - Score (3): Flexion to 90-100º
  - Score (4): Brisk return to full flexion

Popliteal angle

- With infant lying supine, and with diaper removed and pelvis flat on the examining surface.
- Hold the thigh in the knee-chest position with the left index finger and the thumb supporting the knee. Then extend the leg by gentle pressure from the right index finger behind the ankle.
- Compare the angle behind the knee or the popliteal angle, with the figures on the diagram **(Figure 11-1)**.

Scarf sign

- Place the infant in the supine position.
- Hold the infant's hand and draw the arm as far across the neck (like a scarf) to the opposite shoulder as possible.
- To perform this maneuver the elbow may need to be lifted across the body, but both shoulders should remain on the examining surface and the head should remain midline.
- The point on the chest to which the elbow moves easily prior to significant resistance is noted.
- Observe the position of the elbow on the infant's chest and compare it to the figures on the diagram.
- Landmarks noted in order of increasing maturity are:
  - Score (-1): Full scarf at the level of the neck
  - Score (0): Contralateral axillary line
  - Score (1): Contralateral nipple line
  - Score (2): Xyphoid process
  - Score (3): Ipsilateral nipple line
  - Score (4): Ipsilateral axillary line

Heel-to-ear-maneuver

- The infant is placed supine and the flexed lower extremity is brought to rest on the mattress alongside the infant's trunk.

- Support the infant's thigh laterally alongside the body with the palm of one hand. Hold the infant's foot between the thumb and index finger of the other hand and draw it to as near the head as possible towards the ipsilateral ear without forcing it. Keep the pelvis flat on the examining surface.
- Note the location of the heel where significant resistance is appreciated.
- Observe the distance between the foot and the head and the degree of extension at the knee and compare this to the figures on the diagram **(Figure 11-1)**.
- Landmarks noted in order of increasing maturity include resistance felt when the heel is at or near the: ear (-1); nose (0); chin level (1); nipple line (2); umbilical area (3); and femoral crease (4).

Physical maturity

These characteristics are scored as shown in **(Figure 11-1)**.

Skin

- Carefully look at the skin and grade according to the diagram.
- Extremely premature infants have sticky, transparent skin and receive a score of (-1).

Lanugo hair

- Examine on the infant's back; between and over the scapulae.

Plantar surface

- Measure foot length from the tip of the great toe to the back of the heel; give a score of (-2) if the result is <40 mm, assign a score of (-1) if it is between 40 and 50 mm, and a score of (0) if the measurement is >50 mm and no creases are seen on the plantar surface.
- If there are creases, score accordingly.

Breast

- Palpate any breast tissue and score according to the diagram.

Eye and ear

- Loosely fused eyelids are defined as closed, but gentle traction opens them; score this as (-1). Tightly fused eyelids are defined as inseparable by gentle traction; scored as (-2).
- Base the rest of the score on open lids and the examination of the ear.

Genitalia

- Score according to the diagram **(Figure 11-1)**.

Scoring and maturity rating

- After completing the physical and neuromuscular assessment, add up the scores received for each of the checked boxes and record the total scores on the worksheet. If the examination only consisted of a physical assessment; multiply the total score by 2.
- Maturity rating: compare the total score obtained from the assessment in the score column to the estimated GA in the weeks' column.

- Be certain to record the date and time of examination and the GA by dates and ultrasound.

Classification

Intrauterine Growth Chart **(Figure 11-2)** is then used to classify the newborns, based on maturity and intrauterine growth, by plotting the infant's weight, length, and head circumference against the estimated GA to determine whether the infant is SGA, AGA, or LGA. These are called Lubchenco Charts.

Classification of newborns

Based on gestational age (GA)

- Preterm: less than 37 weeks completed weeks (259 days)
- Term: 37-41 weeks and 6/7 days (260-294 days)
- Post-term: 42 weeks (295 days) or more

Based on birth weight

- Normal birth weight: from 2,500-3,999 gm
- Low birth weight (LBW): less than 2,500 gm. Can be further classified to
  - Very low birth weight (VLBW): less than 1,500 gm
  - Extremely low birth weight (ELBW): less than 1,000 gm

Based on maturity and intrauterine growth

- Small for gestational age (SGA): defined as 2 standard deviations below the mean weight for GA or below the 10^{th} percentile **(Refer to Chapter 13).**
- Appropriate for gestational age (AGA): 10^{th} to 90^{th} percentile.
- Large for gestational age (LGA): defined as 2 standard deviations above the mean weight for GA or above the 90^{th} percentile. LGA can be seen in infants of diabetic mothers, infants with Beckwith's syndrome, constitutionally large infants with large parents, or infants with hydrops fetalis.

MATURATIONAL ASSESSMENT OF GESTATIONAL AGE (New Ballard Score):

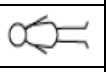
Name: _____ Date/Time of birth: _____ Sex: _____ SCORE: _____

Hospital No.:_____ Date/Time of Exam._____ Birth weight: _____ Neuromuscular: ____

Race: _____ Age when examined: _____ Length: _____ Physical: _____

Apgar score: 1 minute:__ 5 minutes:___10 minutes___Head circ.: _____ Total: _____

Examiner: _____

Neuromuscular maturity sign	Score							Record score here
	-1	0	1	2	3	4	5	
Posture								
Square window (wrist)								
Arm recoil								
Popliteal angle								
Scarf sign								
Heel to ear								
Total neuromuscular maturity score								

Score	weeks
-10	20
-5	22
0	24
5	26
10	28
15	30
20	32
25	34
30	36
35	38
40	40
45	42
50	44

Physical maturity signs	-1	0	1	2	3	4	5
Skin	Sticky, friable, transparent	Gelatinous, red, translucent	Smooth, pink, visible veins	Superficial peeling and/or rash, few veins	Cracking, pale areas, rare veins	Parchment, deep cracking, no vessels	Leathery, cracked, wrinkled
Lanugo	None	Sparse	Abundant	Thinning	Bald areas	Mostly bald	
Plantar surface	Heel-toe 40-50 mm: -1 < 40 mm: -2	> 50 mm No crease	Faint red marks	Anterior transverse crease only	Creases anterior 2/3	Crease over entire sole	
Breast	Imperceptible	Barely Perceptible	Flat areola, no bud	Stippled areola, 1-2 mm bud	Raised areola, 3-4mm bud	Full areola, 5-10 mm bud	
Eye/Ear	Lids fused loosely:-1 Tightly: -2	Lids open Pinna flat, stays folded	Slightly curved pinna; soft slow recoil	Well-curved pinna, soft but ready recoil	Formed and firm, instant recoil	Thick cartilage, ear stiff	
Genitals (male)	Scrotum flat, smooth	Scrotum empty, faint rugae	Testes in upper canal, Rare rugae	Testes descending, few rugae	Testes down, good rugae	Testes pendulous, deep rugae	
Genitals (female)	Clitoris prominent, labia flat	Prominent clitoris, labia minora	Prominent clitoris, enlarging minora	Majora and minora equally prominent	Majora large, minora small	Majora cover clitoris and minora	

Figure (11-1): Maturational assessment of gestational age (New Ballard Score)

(From Ballard JL et al: New Ballard Score expanded to include extremely premature infants. J Pediatr 1991; 119:417). With permission from Elsevier

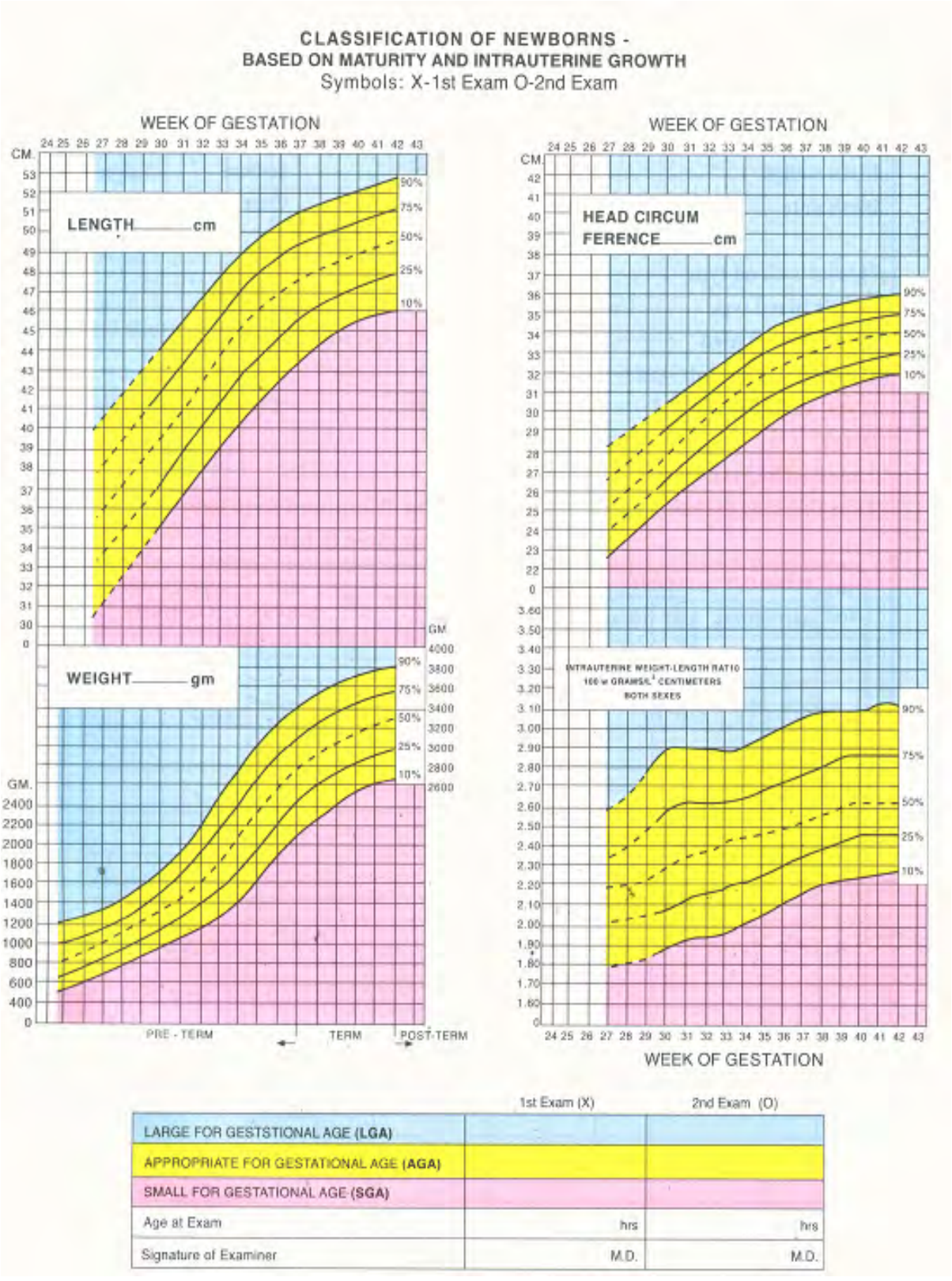


Figure (11-2): Classification of newborns (both sexes) by intrauterine growth and gestational age

(From Lubchenco LO, Hansman C, Boyd E. Intrauterine growth in length and head circumference as estimated from live births at gestational ages from 26 to 42 weeks. Pediatrics 1966; 37:4; Battaglia FC, Lubchenco LO: A practical classification for newborn infants by weight and gestational age. J Pediatr 1967; 71:159. With permission from Pediatrics and Elsevier)

Chapter 12

Thermoregulation

Thermoregulation

- Thermoregulation is a balance between heat loss and heat gain.
- The main goal is to control the neonate's environment, to maintain a neutral thermal environment**,** and to minimize energy expenditure.
- Normal temperature ranges in neonates:
  - Core (rectal) temperature is 36.5-37.5°C
  - Axillary temperature may be 0.5-1°C lower
  - Skin temperature is 36-36.5°C
- Neutral Thermal Environment (NTE): the environmental conditions under which the core body temperature is normal with minimal caloric expenditure and oxygen consumption.

Mechanism of Thermoregulation

Heat production

Term newborns have a source of thermogenesis in the brown fat, which is highly vascularized and innervated by sympathetic neurons. When these infants face cold stress, norepinephrine levels increase and act in the brown fat tissue to stimulate lipolysis. Most of the free fatty acids (FFAs) are re-esterified or oxidized; both reactions produce heat. Hypoxia decreases this response.

N.B.: Because neonates do not shiver, they must rely on non-shivering or chemical thermogenesis, to produce heat.

Heat loss

- Methods of heat loss are:
  - **Evaporation:** heat loss from fluid on the neonate's skin or mucous membranes to the room air.
  - **Conduction: d**irect heat loss from the infant to the surface with which he or she is in direct contact.
  - **Radiation:** when heat is transferred from the neonate to another solid object not in direct contact.
  - **Convection:** heat loss from the neonate's skin to the moving air.

  All of these methods can be a problem in Egyptian hospital nurseries.
- Preterm infants are predisposed to heat loss because they have:
  - A higher skin surface area to body weight ratio
  - Little subcutaneous fat, with less insulative capacity
  - Highly permeable skin leading to increased transepidermal water loss
  - Reduced heat production because of inadequate brown fat and glycogen stores, and inability to shiver

- Inability to take in enough calories**;** to provide nutrients for thermogenesis and growth
- The hypotonic (frog) posture limiting the ability of the infant to curl up to reduce the skin area exposed to the colder environment

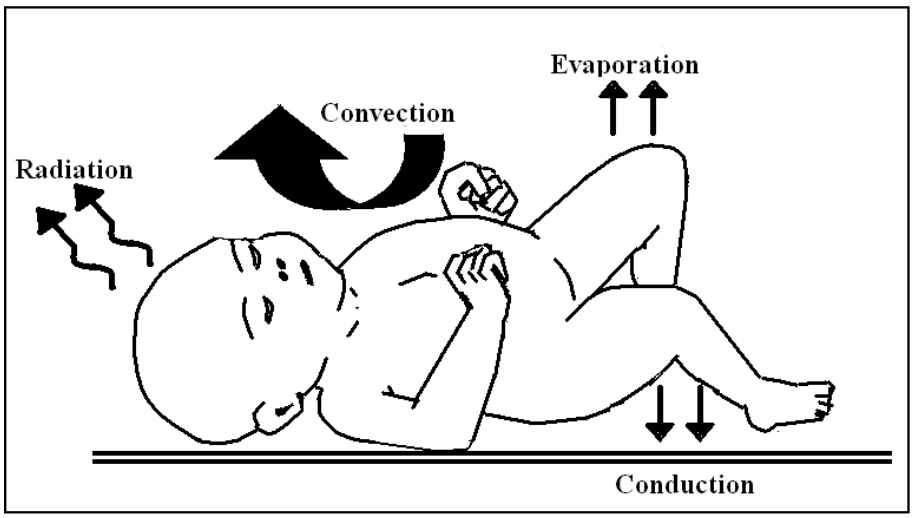


Figure (12-1): Methods of heat loss

Disorders of Thermoregulation

Hypothermia

It is defined as a core body temperature below 36.5°C.

Etiology

- Cold environment
- Incorrect care of the neonate immediately after birth:
  - Inadequate drying
  - Insufficient clothing
  - Separation from the mother
  - Inadequate warming procedures (before and during transport)
- Diseased and stressed infants

Clinical manifestations

- Measuring the neonate's temperature may not detect early changes of cold stress, as the neonate will initially use energy stores to maintain his/her core temperature.
- Initial signs are:
  - Feel cold to touch
  - Weak sucking ability or inability to nurse
  - Lethargy and weak cry
  - Skin color changes from paleness and cyanosis to peripheral mottling or plethora
  - Tachypnea and tachycardia

- Later signs include:
  - Apnea and bradycardia
  - Hypoglycemia, metabolic acidosis, respiratory distress, and bleeding disorders as disseminated intravascular coagulation (DIC), intraventricular hemorrhage, and pulmonary hemorrhage may occur.

Hyperthermia

It is defined as a core body temperature above 37.5°C.

Etiology

- High environmental temperature:
  - Overbundling of the infant
  - Placement of the incubator in sunlight
  - A loose temperature skin probe with an incubator or radiant heater on a servo-control mode, or a servo-control temperature set too high
- Dehydration
- Infection
- Intracranial hemorrhage

Clinical manifestations

- Warm skin, that may appear flushed or pink initially and pale later.
- A pattern similar to hypothermia may develop as the problem continues, including increased metabolic rate, irritability, tachycardia and tachypnea.
- Dehydration, intracranial hemorrhage, heat stroke and death may occur.
- Lack of sweating in neonates may be a major part of this problem.

N.B.: If environmental temperature is the cause of hyperthermia, the temperatures of the trunk and extremities will be the same and the infant appears flushed. In contrast, infants with sepsis are often vasoconstricted and the extremities are colder than the trunk.

Management of Disorders of Thermoregulation

Temperature assessment

Rectal temperature

- The rectal glass thermometer is inserted less than 3 cm (to avoid rectal perforation) and held in place at least 3 minutes (to obtain an accurate reading).
- Disadvantages:
  - This is an invasive procedure.
  - Not always reliable; if there is peripheral vasoconstriction and the neonate is centralizing its circulation, the cold blood running from the legs will significantly lower the measured rectal temperature.

- Rectal temperature should not be taken on a routine basis in neonates due to risks of vagal stimulation and rectal perforation.

Axillary temperature

- Put the thermometer high in the middle of the axilla with the arm held gently but firmly at the neonate's side for approximately 5 minutes.
- Advantages:
  - Decreased risk to neonates and maintenance of hygiene.
  - Easy and accurate assessment; although the temperature is slightly lower than the true core temperature, it will change in the same way as the core temperature.
  - The skin at this site does not react to a lower temperature with vasoconstriction.

Skin temperature

- A skin probe is secured to the right upper quadrant of the abdomen.
- Advantages:
  - Continuous monitoring of abdominal skin temperature with newborn lying supine is a noninvasive method.
  - Because the infant responds to cold stress by vasoconstriction, a drop in skin temperature may be the first sign of hypothermia. The core temperature may not fall until the infant is no longer able to compensate. Also, the axillary temperature may remain normal because of close proximity to brown fat stores.

Environmental temperature

- Each room should have a wall thermometer.
- Keep the environmental room temperature between 24-26°C.

Temperature control

In the delivery room

- Provide a warm environment that is free from air currents.
- Dry the neonate immediately and remove any wet towels.
- Direct skin-to-skin contact with the mother will serve as a heat source. Wrap both mother and neonate in blankets or clothing.
- Use radiant warmers at birth for all neonates who had low Apgar scores, exhibited signs of stress during delivery**,** and/or whose mothers have had prenatal and intrapartum risk factors.
- Cover the neonate's head with a cap.

On admission to the neonatal care unit

- The neonate should be undressed except for a diaper and centered under the radiant heater of the warmer.
- The skin temperature probe must be placed flat on the neonate's skin, usually on the abdomen (right hypochondrium).
- The servo temperature should be set at 36.5^{o}C.

- Temperature should be taken every 30 minutes or per the physician's order to assess that the neonate's temperature is maintained within the proper range.

During the neonatal care unit stay

- Ensure that all personnel involved with newborn care are capable of using the incubator properly, monitoring the neonate's temperature and adjusting the incubator temperature to maintain a neutral thermal environment.
- Incubators require an uninterrupted electrical supply. Ensure the availability of trained personnel for maintenance/repair, and available spare parts for repair.
- Keep the incubator away from uninsulated windows or sunlight.
- The room temperature should be adequate and room drafts minimized.

N.B.: Incubators should be monitored closely for incorrectly high, as well as incorrectly low, temperatures. If the incubator is located in direct sunlight or if phototherapy lights are being used, frequent monitoring of the neonate's temperature and incubator temperature adjustments are required to prevent the overheating of the neonate.

- When a neonate requires incubator care, it is important to encourage parents to visit and hold the neonate as much as possible, utilizing skin-to-skin contact for temperature stabilization.
- The neonate's temperature should be monitored every 3-4 hrs or per the physician's order to maintain the core temperature at 36.5-37.5^{o}C.
- The portholes should be used as much as possible during care of the neonate, instead of opening the larger door.
- Double walled incubators limit radiant heat loss and decrease convective and evaporative losses as well.
- Radiant warmer should be used during the performance of medical procedures. Temperature can be maintained in:
  - Servo-mode (using skin probe): if the temperature falls, additional heat is delivered. As the target skin temperature is reached, the heating unit turns off automatically. A potential disadvantage is that overheating may occur if the skin sensor is detached.
  - Nonservo-mode (Manual mode): maintains a constant radiant energy output regardless of the infant's temperature. If the radiant warmer is used in the manual mode, the infant should be observed very carefully to avoid overheating; this mode should be used only for a limited period, such as in the delivery room.
  - Servo-controlled open warmer beds may be used for very sick infants when access is important. The use of a tent made of plastic wrap is effective in preventing both convection heat loss and insensible water loss.

Management of hypothermia

- Rewarm at a rate of 1°C/hr. However, infants weighing <1,200 gm, those with gestational age <28 weeks and those with temperature <32°C, can be rewarmed more slowly (with a rate not to exceed 0.6°C/hr).

- During rewarming, the skin temperature should not be >1°C warmer than the coexisting rectal temperature.
- Rewarming may induce apnea and hypotension; therefore, the hypothermic infant should be continuously and closely monitored.

Management of hyperthermia

- Defining the cause of the elevated body temperature is the most important initial issue.
- Other measures: turning down any heat source and removing excessive clothing.

Table (12-1): Neutral thermal environmental temperature

Age and Weight	Temperature	
	At start (°C)	Range (°C)
0-6 hours		
• Under 1,200 gm	35	34-35.4
• 1,200-1,500 gm	34.1	33.9-34.4
• 1,501-2,500 gm	33.4	32.8-33.8
• Over 2,500 gm	32.9	32-33.8
6-12 hours		
• Under 1,200 gm	35	34-35.4
• 1,200-1,500 gm	34	33.5-34.4
• 1,501-2,500 gm	33.1	32.2-33.8
• Over 2,500 gm	32.8	31.4-33.8
12-24 hours		
• Under 1,200 gm	34	34-35.4
• 1,200-1,500 gm	33.8	33.3-34.3
• 1,501-2,500 gm	32.8	31.8-33.8
• Over 2,500 gm	32.4	31-33.7
24-36 hours		
• Under 1,200 gm	34	34-35
• 1,200-1,500 gm	33.6	33.1-34.2

Table (12-1): Neutral thermal environmental temperature (Continued)

Age and Weight	Temperature	
	At start (°C)	Range (°C)
• 1,501-2,500 gm	32.6	31.6-33.6
• Over 2,500 gm	32.1	30.7-33.5
36-48 hours		
• Under 1,200 gm	34	34-35
• 1,200-1,500 gm	33.5	33-34.1
• 1,501-2,500 gm	32.5	31.4-33.5
• Over 2,500 gm	31.9	30.5-33.3
48 -72 hours		
• Under 1,200 gm	34	34-35
• 1,200-1,500 gm	33.5	33-34
• 1,501-2,500 gm	32.3	31.2-33.4
• Over 2,500 gm	31.7	30.1-33.2
72-96 hours		
• Under 1,200 gm	34	34-35
• 1,200-1,500 gm	33.5	33-34
• 1,501-2,500 gm	32.2	31.1-33.2
• Over 2,500 gm	31.3	29.8-32.8
4-12 days		
• Under 1,500 gm	33.5	33-34
• 1,501-2,500 gm	32.1	31-33.2
• Over 2,500 gm		
▸ 4-5 days	31	29.5-32.6
▸ 5-6 days	30.9	29.4-32.3

Table (12-1): Neutral thermal environmental temperature (Continued)

Age and Weight	Temperature	
	At start (°C)	**Range (°C)**
▸ 6-8 days	30.6	29-32.2
▸ 8-10 days	30.3	29-31.8
▸ 10-12 days	30.1	29-31.4
12-14 days		
Under 1,500 gm	33.5	32.6-34.0
1,501-2,500 gm	32.1	31-33.2
Over 2,500 gm (and >36 weeks' gestation)	29.8	29-30.8
2-3 weeks		
Under 1,500gm	33.1	32.2-34
1,501-2,500 gm	31.7	30.5-33
3-4 weeks		
Under 1,500 gm	32.6	31.6-33.6
1,501-2,500 gm	31.4	30-32.7
4-5 weeks		
Under 1,500 gm	32	31.2-33
1,501-2,500 gm	30.9	29.5-35.2
5-6 weeks		
Under 1,500 gm	31.4	30.6-32.3
1,501-2,500 gm	30.4	29-31.8

(From: Klaus M, Fanaroff A. The physical environment. In: Care of the high risk neonate. 5th Ed. Philadelphia.WB Saunders 2001)

Chapter 13

Preterm and Low Birth Weight Infants

Preterm and Low Birth Weight Infants

A live-born infant born before 37 completed weeks of gestation (<259 days after the date of the mother's last menstrual period) is defined as preterm.

A low birth weight (LBW) infant is one whose birth weight is less than 2,500 gm. The terms very low birth weight (VLBW) and extremely low birth weight (ELBW) have been applied to infants whose birth weight is less than 1,500 gm and 1,000 gm respectively.

Growth charts against gestation are used to determine whether an infant's weight is appropriate for gestational age or not.

Low-birth weight may be due to:

- Prematurity
- Intrauterine growth restriction (IUGR)
- Both

The two main groups of LBW infants have different problems so early and accurate assessment is necessary.

Preterm Infants

Etiology

Unknown in most cases, preterm delivery is associated with the following conditions:

Maternal factors

- Low socioeconomic status
- Mothers younger than 16 years or older than 35 years
- Chronic medical illness (e.g., cyanotic heart disease, renal disease)
- Infection (e.g., *Listeria monocytogenes*, urinary tract infection)
- Drug abuse (e.g., cocaine)

Fetal factors

- Fetal distress (e.g., late deceleration, non-reassuring biophysical profile)
- Multiple gestations
- Erythroblastosis fetalis
- Nonimmune hydrops

Obstetric factors

Uterine

- Bicornate uterus
- Incompetent cervix

Placental

- Placenta previa
- Abruptio placentae

Others

- Premature rupture of membranes
- Amnionitis
- Hypertensive disorders (e.g., pre-eclampsia)
- Polyhydramnios
- Trauma

Prior poor birth outcome

A preterm first birth is the best predictor of a preterm second birth.

Iatrogenic

Incorrect estimation of GA may result in unintentionally early delivery.

Problems of Prematurity

Respiratory difficulties

- Perinatal depression
- Respiratory distress syndrome (RDS)
- Increased risk of aspiration
- Pliable thorax and weak respiratory muscles
- Apnea
- Bronchopulmonary dysplasia (BPD)

Temperature instability

Preterm infants have special problems in temperature regulation. These infants are especially susceptible to hypothermia and hyperthermia **(Refer to Chapter 12).**

Gastrointestinal and nutritional problems

- Poor sucking and swallowing reflexes especially before 34 weeks' gestation
- Decreased intestinal motility
- Delayed gastric emptying
- Reduced digestion and absorption of fat-soluble vitamins
- Deficient lactase enzymes in intestinal brush border
- Diminished body stores of calcium, phosphorus, proteins and iron
- Increased risk of necrotizing enterocolitis (NEC): prematurity is the single greatest risk factor for NEC

Hepatic immaturity

- Impaired conjugation and excretion of bilirubin
- Deficiency of vitamin K dependent clotting factors

Renal immaturity

- Inability to excrete large solute load
- Accumulation of inorganic acids with metabolic acidosis
- Renal elimination of drugs may be diminished
- Electrolyte imbalance (e.g., hyponatremia or hypernatremia, hyperkalemia or renal glycosuria)

Immunologic immaturity

Preterm infants are at a high risk of infection because:

- Deficiencies in both humoral and cellular immunity:
  - Preterm infants lack the transplacental transfer of maternal IgG, as it is mostly transferred across the placenta during the last trimester of pregnancy.
  - Impaired phagocytosis

  - Decreased complement factors
- Deficient or breaking of physical barriers to infections:
  - Skin and mucous membranes are broken down easily
  - Invasive procedures are indicated (e.g., IV lines, endotracheal intubation)

Neurological problems

- Perinatal depression and hypoxic ischemic encephalopathy (HIE)
- Intraventricular hemorrhage (IVH)
- Periventricular leukomalacia and other neural injury
- Poor regulation of cerebral perfusion

Cardiovascular problems

- Hypotension; may be due to:
  - Hypovolemia
  - Cardiac dysfunction
  - Vasodilatation due to sepsis
- Patent ductus arteriosus (PDA) is common and may lead to congestive heart failure.

Hematological problems

- Anemia (early or late onset)
- Hyperbilirubinemia, mainly indirect
- Disseminated intravascular coagulation (DIC)
- Hemorrhagic disease of the newborn (HDN)

Metabolic problems

- Hypocalcemia
- Hypoglycemia or hyperglycemia

Ophthalmologic problems

- Retinopathy of prematurity (ROP)

Investigations

Laboratory

- CBC with differential
- Serial blood glucose measurement
- Serial Na, K, and calcium
- Serial serum bilirubin measurement, if indicated
- Arterial blood gases, if indicated
- CRP and cultures; to rule out infection

Radiological

- Chest x-ray; with evidence of respiratory distress.
- Cranial ultrasonography; must be done in all preterm infants <32 weeks' GA [on or around days 3, 7, 30, 60 (or just before discharge)] and in those >32 weeks' GA with risk factors (e.g., perinatal asphyxia or pneumothorax) or who present with abnormal neurologic signs to rule out intraventricular hemorrhage.
- Echocardiography; if PDA is suspected.

Management

Delivery room care

(Refer to Chapter 4)

- Delivery should be in an appropriately equipped and staffed hospital.
- Resuscitation and stabilization of preterm infant require the immediate availability of qualified personnel and equipment.
- Provide special attention for maintaining infant's temperature.
- Use an oximeter and blender to gradually achieve hemoglobin saturations between 85-95%.

Neonatal intensive care unit (NICU) care

Thermoregulation

Should be directed towards achieving a neutral thermal environment (NTE) according to the protocol **(Refer to Chapter 12)**

Respiratory support

Surfactant therapy, oxygen therapy and assisted ventilation

Apnea management

- Apply tactile stimulation.
- Start theophylline: a loading dose of 6 mg/kg/IV followed 8 hrs later by a maintenance dose of 2 mg/kg every 8 hrs. Caffeine citrate is safer than aminophylline (loading dose 20 mg/kg orally or IV over 30 minutes, followed 24 hrs later by 5-8 mg/kg orally or IV every 24 hrs).
- Start CPAP or assisted ventilation in recurrent and/or prolonged apnea.

Fluid and electrolyte therapy

- High insensible water losses (IWL) and large renal losses of fluids and electrolytes should be replaced to maintain proper hydration and plasma electrolyte concentration **(Refer to Chapter 15).** Some ELBW preterm infants may require up to 200 ml/kg/day, especially if using overbed warmer.
- Be aware that excessive fluid intake may contribute to the development of a hemodynamically significant PDA, and should be monitored closely.

Glucose homeostasis

- Blood glucose levels should be monitored and maintained between 50-125 mg/dl. Generally, glucose 7.5% or 5% solutions are used (Glucose infusion rate [GIR] 4-10 mg/kg/minute is usually sufficient).
- If hyperglycemia occurs, use lower glucose concentration but avoid hypo-osmolar formula (glucose <5%). Insulin therapy (at a dose 0.05-0.1 unit/kg/hr may be required in some infants with persistent hyperglycemia (>200-250 mg/dl).

Calcium homeostasis

- Generally, serum total Ca of >7 mg/dl does not need correction.
- Symptomatic hypocalcemia will not usually occur until ionized Ca^{++} is <4 mg/dl or <1 mmol/L).
- Preterm infants are started on calcium 40-50 mg elemental in their IV fluids. This can be advanced to reach calcium needs of 70-80 mg elemental/kg/day.

Nutrition

(Refer to Chapter 20)

Preterm infants may require gavage feeding or parenteral nutrition.

Cardiovascular support

Blood pressure

- Check normal systolic and diastolic blood pressure for gestational age **(Refer to Appendix 3)**
- The mean arterial pressure can be normal even when an infant is in shock and conversely**,** the mean arterial pressure may read low when the baby appears well perfused and clinically stable.
- Peripheral perfusion and capillary refill time (should be <2-3 seconds) must be assessed (capillary refill may be slower if the infant is cold).
  - Early hypotension is more commonly due to altered vasoreactivity than hypovolemia. Therefore, therapy with fluid boluses is limited to 10-20 ml/kg, after which pressor support, initially with dopamine, is started.
  - If an infant is truly hypotensive or in shock, treat with whole blood 10 ml/kg or more if blood loss has been obvious. Crystalloid may be used while waiting for blood.
  - Rapid infusions in preterm infants should be avoided due to risk of intraventricular hemorrhage (IVH).
  - A low mean arterial pressure secondary to a low diastolic blood pressure may indicate a PDA.

Patent ductus arteriosus

- Initial management is usually conservative and includes adequate oxygenation, fluid restriction**,** and diuretics (furosemide). This may help to minimize the effects of PDA, but should not be given to the point of dehydration as this can predispose to renal failure.

- A prostaglandin antagonist**,** such as indomethacin or ibuprofen**,** may be needed **(Refer to Chapter 35).**
- Surgical ligation may be necessary.

Blood transfusions

(Refer to Chapter 34)

In some cases, erythropoietin therapy in conjugation with adequate iron therapy may be considered.

Hyperbilirubinemia

(Refer to Chapter 21)

It is can be usually managed effectively by careful monitoring of bilirubin levels and use of phototherapy. Exchange transfusion may be needed in severe cases.

Infection

Broad-spectrum antibiotics should be started when suspicion of infection is strong. Consider anti-staphylococcal antibiotics for VLBW who have undergone multiple procedures or who have remained for a long time in the hospital.

Intrauterine Growth Restriction (IUGR)

Intrauterine growth restriction (IUGR) or small for gestational age (SGA) is defined as two standard deviations below the mean for gestational age or below the tenth percentile. Approximately one-third of LBW infant are SGA.

Etiology

Fetal growth is influenced by fetal, maternal and placental factors.

Fetal factors

- Constitutional: most of SGA infants are normal (genetically small)
- Chromosomal disorders (e.g., trisomies 13, 18, and 21)
- Congenital malformations (e.g., anencephaly, gastrointestinal atresia and Potter syndrome)
- Congenital infection (e.g., rubella or cytomegalovirus)
- Inborn errors of metabolism (e.g., galactosemia and phenylketonuria)

Maternal factors

- Pre-eclampsia and eclampsia
- Chronic renovascular disease
- Chronic hypertensive vascular disease
- Maternal malnutrition
- Maternal smoking
- Maternal hypoxemia associated with cyanotic congenital heart disease and sickle cell anemia
- Other maternal factors such as low socio economic status, young maternal age, short stature, primiparity and grand multiparity

Placental factors

- Placental insufficiency due to maternal disorders, such as pre-eclampsia and eclampsia, or due to post-term gestation
- Anatomic problems, such as multiple infarcts, umbilical vascular thrombosis and hemangiomas
- Multiple gestations may be associated with significant placental problems such as abnormal vascular anastomoses

Patterns of IUGR

Symmetric IUGR

- The head circumference, length and weight are all proportionately reduced for gestational age.
- Due to either a congenital infection or a genetic disorder occurring early in pregnancy, during the period of early fetal cellular hyperplasia.

Asymmetric IUGR

- Fetal weight is reduced out of proportion to length and head circumference. Brain growth is usually spared; hence the term**,** head sparing IUGR.
- It occurs late in pregnancy, during the phase of cellular hypertrophy, and is due to uteroplacental insufficiency or poor maternal nutrition.

Problems of IUGR

Fetal death

- 5-20 times higher in IUGR than AGA infants.
- Usually occurs between 38-42 weeks of gestation.
- Causes:
  - Placental insufficiency
  - Chronic hypoxia
  - Lethal congenital anomaly

Hypoxia

- Perinatal asphyxia
- Persistent pulmonary hypertension (PPHN)
- Meconium aspiration

Uterine contractions may add an additional stress on the chronically hypoxic fetus; this acute fetal hypoxia and acidosis may result in fetal death or neonatal asphyxia.

Hypothermia

- Hypothermia occurs due to diminished subcutaneous fat insulation and increased body surface area. Furthermore, hypoglycemia and hypoxia interfere with heat production in those infants.

Hypoglycemia

- Due to diminished glycogen stores and the decreased capacity for gluconeogenesis.
- Hypothermia may potentiate the problem of hypoglycemia.
- It occurs during the first 3 days.

Polycythemia

- Results from increased erythropoietin levels secondary to fetal hypoxia.
- Polycythemia may also contribute to hypoglycemia and lead to cerebral injury.

Developmental delay

- Occurs especially in premature, SGA infants and in infants with significant head growth restriction.
- It results from congenital infections, severe malformation, chronic hypoxia, postnatal asphyxia or hypoglycemia.

- It presents with delayed milestones at 2 and 5 years of age, and with poor school performance.

Immune depression

It occurs due to:

- Malnutrition, whether prenatal or postnatal, and
- Congenital infection (TORCH infections)
- Neutropenia

Investigations

- CBC with differential
- Serial blood glucose measurements
- TORCH screening
- Cranial sonar, if indicated
- Chest x-ray, if indicated

Management of IUGR

Delivery room care

- Be prepared for resuscitation to prevent HIE.
- Provide appropriate thermal environment.
- Initial assessment for gestational age.
- Assess for dysmorphic features and congenital anomalies.
- Check serum glucose level.

Neonatal intensive care unit (NICU) care

- Provide NTE, and check temperature every 4 hrs (more frequently if preterm).
- Initiate early feeding, if possible.
- Check for feeding intolerance.
- Start intravenous fluids, if feeding is not possible or not tolerated.
- Check hemoglobin level and treat polycythemia, if present.
- Check blood glucose level every 4 hrs during the first day of life, then every 8-12 hrs, if stable.

Long Term Follow-Up

- Adequate nutrition.
- Timely immunization.
- Developmental assessment with each routine visit.
- Early referral for developmental intervention and special educational programs.

- Maternal counseling for future conception is important; this is because IUGR commonly recurs. Specific recommendations include:
  - The mother should be cared for by personnel experienced in handling high-risk pregnancies.
  - The health of mother and fetus should be assessed throughout pregnancy by ultrasonography and non-stress tests.
  - Early delivery should be considered if fetal growth is poor.

Chapter 14

Post-term infants

Post-term Infants

Post-term infants are those born after 42 completed weeks of gestation (or >294 days) as calculated from the mother's first day of the last menstrual period, regardless of weight at birth. These infants are at an increased risk of perinatal mortality and morbidity.

Etiology

The cause of post-term birth is generally unknown. Very rarely, it may be caused by abnormalities that affect the fetal pituitary-adrenal axis (e.g., anencephaly or adrenal agenesis).

Clinical Manifestations

- Post-term infants often have increased birthweights and are characterized by the absence of lanugo, decreased or absent vernix caseosa, long nails, abundant scalp hair, white parchment-like or desquamating skin, and increased alertness.
- If placental insufficiency occurs, the amniotic fluid and fetus may be meconium stained, and abnormal fetal heart rates may be noted, and the fetus may have IUGR. After birth, these infants may have various physical signs:
  - Skin desquamation, long nails, abundant hair, decreased subcutaneous fat, and loose skin, especially around the thighs and buttocks (malnourished appearance)
  - Open-eyed and alert infant
  - Meconium-stained nails, skin, vernix, umbilical cord, and placental membranes

Management

- Careful obstetric monitoring: Non-stress test and biophysical profile, to provide a rational basis for choosing a course of nonintervention, induction of labor, or cesarean section.
- Intrapartum management: fetal monitoring and preparation for possible perinatal depression and meconium aspiration.
- Evaluation for problems related to postmaturity:
  - Congenital anomalies
  - Perinatal depression
  - Meconium aspiration
  - Persistent pulmonary hypertension
  - Hypoglycemia, hypocalcemia, and polycythemia
- Proper nutritional support

Chapter 15

Fluids and Electrolytes Management

Fluids and Electrolytes Management

Developmental changes in body composition in conjunction with functional changes in skin, renal, and neuroendocrine systems account for the fluid balance challenges faced by the neonatologists on daily basis.

Transition from fetal to neonatal life is associated with major changes in water and electrolyte homeostasis. During the first days of life, both term and preterm infants experience a reduction in body weight that is associated with a concurrent diuretic phase. This normal physiological weight loss is caused by interstitial fluid mobilization rather than by tissue loss. Term infants usually lose 5-8% of birth weight and preterm infants may lose up to 15% of birth weight. Failure to allow this normal postnatal contraction of extracellular fluid (ECF) in premature infants may increase the risk of significant PDA, NEC, and BPD.

General Principles

Total body water (TBW) = Intracellular fluid (ICF) + Extracellular fluid (ECF)

ECF = Intravascular fluid (plasma and lymph) + Interstitial fluid (between cells)

- At birth, the percentage of body weight represented by water is approximately 75% in term infants and greater in preterm infants. As gestational age increases, total body water and extracellular water decrease and intracellular fluid content increases.
- To maintain a stable water balance:
  - Water intake = Water for growth + insensible losses + sensible losses (urine + fecal losses)
    - Maintenance fluid should provide a net water balance of 10-15 ml/kg per day to allow the infant to grow at the rate of 10-20 gm/kg per day (as new tissue contains 70% water).
    - Water loss from stool output is minimal during the first few days of life. Once enteral feeds begin, the water loss in the stool is 5-10 ml/kg/day.

Sources of Water Loss

Insensible water loss

- Insensible water loss (IWL) is water loss that is not readily measured, and consists mostly of water lost via evaporation through the skin (two thirds) or respiratory tract (one third).
- The surface area of the newborn is relatively large and IWL increases with decreasing size. Therefore, insensible water losses will be greatest with small size and decreased gestational age **(Table 15-1)**.

Table (15-1): Insensible water loss (IWL)*

Birth weight (gm)	IWL (ml/kg/d)
750 - 1,000	82
1,001 - 1,250	56
1,251 - 1,500	46
> 1,501	26

* Values represent mean IWL for infants in incubators during the first week of life.

- A number of physiologic, environmental, and therapeutic factors can influence IWL, making it the most variable component of the maintenance fluid requirements in newborns **(Table 15-2)**.

Table (15-2): Factors that influence IWL*

Decrease IWL	Increase IWL
• Advanced GA and weight • Heat shield or double walled incubators, 10-30% • Plastic blankets, 30-50% • Clothes • High relative humidity (ambient ventilation gas), 20-30% • Emollient use	• Severe prematurity, 100-300% • Respiratory distress (Tachypnea, 20-30%) • Ambient temperature NTE • Radiant warmer, 50% • Phototherapy, 30-50% • Elevated body temperature, 10% for every 1˚C rise in temperature • Motor activity and crying, up to 70% • Congenital skin defects (e.g., large omphalocele)

*IWL is inversely related to GA and weight.

Sensible water loss

It includes other measurable sources of fluid loss:

Renal losses

- Neonates have a decreased capacity to concentrate or dilute urine in response to changes in intravascular fluid status and are at risk for dehydration or fluid overload.
- Immature sodium and water homeostasis is common in preterm infants.
- The normal maturation of renal function that occurs with increasing GA and postnatal age also plays a role in determining fluid requirements.

Others

Should be replaced if amount is significant; these include:

- Stools (diarrhea and osteotomy drainage)
- CSF (ventriculostomy and repeated lumbar punctures)
- Nasogastric and thoracostomy tube drainage

Fluid and Electrolytes Management

Calculation of fluid and electrolyte requirements in the newborn is based on maintenance needs, deficits, and ongoing losses.

Goal

To allow initial ECF loss over the first days of life as reflected by weight loss, while maintaining normal tonicity and intravascular volume as reflected by blood pressure, heart rate, urine output, serum electrolyte levels, and blood pH.

Fluid and electrolyte requirements

Fluid requirements **(Table 15-3)**

Table (15-3): Fluid therapy by infant's weight and postnatal age*

Birth weight	Glucose concentration	Fluid rate (ml/kg/day)$^{\Phi}$		
		Postnatal age		
		<24 hrs	24-48 hrs	>48 hrs
<1,000 gm	D5W - D7.5W	100-120	120-140	140-190
1,000- <1,500 gm	D7.5W - D10W	80-100	100-120	120-160
1,500- <2,500 gm	D10W	60-80	80-100	100-150
≥2,500 gm	D10W	60-80	80-100	90-150

*Infant under humidified incubator.

$^{\Phi}$The volume of fluids given should be estimated based on the clinical status of the infant.

- Term infants: depending on the tolerance of the previous day's fluid therapy, estimations of IWL, and clinical status of the infant, increases of 10-20 ml/kg/day may be considered.
- VLBW infants (during the first week of life): depending on weight and serum sodium levels, fluid therapy should be managed by increments or decrements of 20-40 ml/kg/day to keep sodium at a normal range (135-145 mEq/L).
- ELBW (especially those <750 gm) infants may have greatly increased IWL. Their fluid requirements may reach up to 200 ml/kg/day.
- Infants on mechanical ventilation, which provides a humidified oxygen delivery system, have reduced water evaporation from the respiratory tract (subtract 20 ml/kg from daily fluid intake).
- Infants under radiant warmers and phototherapy require higher initial fluid rates (increase the total fluid intake by 20 ml/kg/day).
- Give the initial glucose infusion rates of 4-6 mg/kg/minute in full term infants and 4-8 mg/kg/minute in preterm infants and adjusted to keep the serum glucose level between 50-125 mg/dl.
- Glucose infusion rate (GIR) can be calculated using this equation:

$$\textbf{GIR(mg/kg/min)} = \frac{\textbf{Fluid rate (ml/hr)} \times \textbf{Glucose concentration}}{\textbf{6} \times \textbf{Weight (kg)}}$$

N.B.: Do not infuse a higher concentration than D12.5W in a peripheral vein.

- ELBW infants are frequently glucose intolerant and frequently develop hyperglycemia, glycosuria and osmotic diuresis. Glucose delivery can be slowly advanced based on how well the infant tolerates this. Insulin may be needed in treating hyperglycemia in which glucose intolerance may necessitate decreasing glucose delivery to unacceptably low rates (<4 mg/kg/minute).
- TPN should be considered as soon as possible after birth (in the first 24 hrs) in neonates who are anticipated to be receiving <50% of total energy requirement by day

7 of life. Start an aminoacid infusion at 1.5-2 gm/kg/day. Intravenous lipids (20% emulsion) can be also started as early as the 1st day of life at 0.5-1 g/kg/day over 20-24 hrs through a separate IV line with a syringe pump **(Refer to Chapter 20)**.

- By the end of the first week of life, fluid requirements decrease toward 150 ml/kg/day in VLBW infants as the skin becomes more mature.
- If the infant is started on enteral feeding, the amount of feeds should be calculated per day and subtracted from total fluid intake. A combined fluid intake of ~150 ml/kg/day should be maintained.

N.B.: Any medication that needs dilution before administration (e.g., antibiotic, dopamine); its volume should be subtracted from the total volume of the IV fluids.

Electrolyte requirements

- For the first 24 hrs, supplemental sodium, potassium, and chloride are not usually required unless ECF expansion is required for shock or acidosis (normal saline is preferred over albumin).
- At the age of 24 hrs, assuming that urine production is adequate, the infant needs 1-2 mEq/kg/day of potassium and 2-3 mEq/kg/day of sodium.
- Extremely premature infants, who develop metabolic acidosis, may benefit from sodium acetate administration instead of sodium chloride
- During the active growth period after the first week, the need for potassium may increase to 2-3 mEq/kg/day, and the need for sodium and chloride may increase to 3-5 mEq/kg/day.
- Some of the smallest preterm infants have sodium requirements of as much as 6-8 mEq/kg/day because of the decreased capacity of the kidneys to retain sodium "syndrome of late hyponatremia".

Table (15-4): Initial electrolytes and mineral supplementation

Postnatal age	Sodium* (mEq/kg/day)	Potassium** (mEq/kg/day)	Calcium elemental*** (mg/kg/day)
<24 hrs	0	0	45
24-48 hrs	2-3	1-2	45
48-72 hrs	2-3	1-2	45

* Avoid adding sodium for VLBW infants unless serum Na^+ <135 mEq/L.
** **Do not** add potassium until urine output is established and normal renal function is ensured.
***Extravasation of calcium-containing solutions can cause tissue necrosis and skin sloughing.
The fluid administered must be recorded frequently (every hour) and the site should be observed for any signs of infiltration. Therefore, it is better not to add maintenance calcium to IV solutions infusing in peripheral veins; rather it should be given as an intermittent bolus over 5-15 minutes with total divided every 6 hrs. Maintenance requirements for the premature infant may reach 70-80 mg elemental/kg/day. Consider discontinuation of the maintenance IV calcium, if the infant is tolerating at least 15 ml of milk per feed every 3 hrs.

Estimating pathologic losses and deficit replacement

- The amount of extra water required can be determined by carefully measuring the volume lost.
- Electrolyte losses can then be calculated by multiplying the volume of fluid losses by the electrolyte content of the respective body fluids **(Table 15-5)**.

Table (15-5): Electrolyte content of body fluids

Fluid source	Na^+ (mmol/L)	K^+ (mmol/L)	CL^- (mmol/L)
Stomach	20-80	5-20	100-150
Small intestine	100-140	5-15	90-120
Bile	120-140	5-15	90-120
Ileostomy	45-135	3-15	20-120
Diarrheal stool	10-90	10-80	10-110

- Estimating replacement can be difficult in infants who accumulate fluid and electrolytes in static body fluid compartments (referred to as third spacing), occurring in several conditions (e.g., sepsis, NEC and hydrops fetalis). The most appropriate approach to manage these infants is to replenish the ECF compartments with colloid and crystalloid.

Monitoring of the fluid and electrolyte balance

- Appropriate fluid and electrolyte balance, as reflected by:
  - A urine output of approximately 1-3 ml/kg/hr and urine specific gravity of approximately 1,005-1,010
  - Approximate weight loss of 5% in term infants and 15% in premature infants over the first 5-6 days
- Bedside monitoring of weight gain is essential for monitoring the adequacy of fluid and calorie intake. Beyond the first week of life, infants should gain approximately 20-30 gm /day.
- Laboratory evaluation:
  - Serum electrolytes can be done at 8-24 hrs intervals, depending on illness severity and GA
  - BUN and creatinine
  - Hematocrit
  - Blood gas analysis
  - Measure magnesium in first few hours after birth, if the mother had received magnesium

N.B.: Assessment of the fluid and electrolyte status may be required initially and as frequently as every 6-8 hrs in ELBW infants

- Extracellular volume depletion is manifest by excessive weight loss, dry oral mucosa, sunken anterior fontanelle, capillary refill time >3 seconds, diminished skin turgor, increased heart rate, low blood pressure (with severe hypovolemia), elevated BUN, or metabolic acidosis.

Table (15-6): Assessment of hydration status of the neonate

Parameter	Frequency	Dehydration	Fluid overload
Weight (Daily weight loss should not exceed 1-3% in the first 4-5 days)	Daily, twice a day if <1,000 gm	Weight loss exceeding 3% per day	Weight loss <2% per day or weight gain
Skin and fontanelle*	Daily, every 8 hrs if <1,000 gm	Poor skin turgor and depressed fontanelle	Bulging fontanelle
Cardiovascular system	Every 4 hrs	Tachycardia, delayed capillary refill and hypotension	Hepatomegaly, tachycardia and hypertension
Serum sodium**	Daily, every 8-12 hrs if <1,000 gm	>145 mEq/L.	<130 mEq/L
BUN and creatinine		May rise due to decreased ECF and GFR	
Hematocrit		Increased	Decreased
• **Urine volume** (1-3 ml/kg/hr) • **Specific gravity†** (1,005-1,010) • **Glycosuria‡**	With every diaper[a] change	Urine volume deceases (<1 ml/kg/hr) and specific gravity rises	Increased urine volume and decreased specific gravity

* Altered skin turgor, a sunken anterior fontanelle, and dry mucous membranes are not sensitive indicators of dehydration in babies.

** Serum sodium is the most useful parameter to follow in VLBW infants during the first few days of life, although its value reflects mother's value during the first few hours of life.

° BUN and creatinine values may also reflect mother's values in the first 12-24 hrs of life.

† Urine volume and specific gravity are useful in assessment of fluid status, although reduced function of the immature kidney in the preterm infant may make these parameters less useful.

‡Glycosuria can cause osmotic diuresis and dehydration. If the urine glucose level is 2+, measure the serum glucose and consider adjusting the glucose infusion or the insulin administration.

[a] All diapers should be pre-weighed on a gram scale and marked with dry weight. After each stool or void urine the diaper is reweighed; the difference equals the amount of loss.

Fluid and electrolyte therapy in common neonatal conditions

- Congestive heart failure: infants usually require fluid restriction (-30 ml/kg).
- PDA: restrict fluid administration. This is especially important when indomethacin is prescribed to treat PDA (as indomethacin can decrease urine output).

- RDS: infants with RDS need appropriate fluid therapy because:
  - Excessive fluid administration can lead to hyponatremia, volume overload, worsening the pulmonary condition and increasing the risk of developing BPD.
  - Inadequate fluid administration leads to hypernatremia and dehydration.
- BPD: diuretics (e.g., furosemide) are often prescribed in these infants to treat pulmonary edema, which can lead to electrolyte disturbances.
- Perinatal asphyxia: These infants are prone to acute tubular necrosis and significant oliguria, and the CNS injury may produce syndrome of inappropriate release of antidiuretic hormone (SIADH). Restricting fluid intake to minimize the risk of volume overload is often required.

Insulin Infusion

Almost all infants weighing <800 gm become hyperglycemic as full calories are approached between days 5-7, as do 40% of infants weighing between 800-1,000 gm. This happens even when glucose intake is carefully calculated and slowly increased.

First, evaluate and reverse all correctable causes of hyperglycemia and relieve the underlying stress factor. If hyperglycemia is mild, a decrease in GIR is frequently successful. Use of hypotonic solution (<5% dextrose) should be avoided.

Low dose insulin therapy may be useful in case of persistent hyperglycemia when blood glucose level is consistently >200-250 mg/dl despite of all the above measures. Frequent monitoring of the plasma glucose concentration is mandatory **(Refer to Chapter 17).**

Example

A full term, 8 days old neonate, weighing 3.5 kg on enteral feeding 10 ml term formula every 3 hrs. He was admitted to NICU because of RD and pneumonia. Now he is more stable but still on mechanical ventilator (MV).

- Volume of fluid intake
  - Total fluid requirement = 150 ml/kg/day subtract 20 ml/kg (MV) = 455 ml
  - Enteral intake = total amount of formula/day = 10(ml) × 8(feeds/day) = 80ml/day
  - The net amount of IV fluid needed = 455 ml - 80 ml = 375 ml/day
- Type of IV fluid
  - Sodium requirement = 3.5 × 4 (mEq) = 14 mEq

    (20 ml saline 0.9% contains 3 mEq then 14 mEq are present in 93 ml saline)
  - Potassium requirement = 3.5 × 2 = 7 mEq

    (one ml KCl contains 2 mEq then 7 mEq are present in 3.5 ml KCl)
  - Calcium requirement = 3.5 × 45 (mg) = 157.5 mg

    (one ml calcium gluconate contains 9 mg elemental calcium then 157.5 mg are present in 17.5 ml calcium gluconate)
  - The rest of the IV fluids is glucose = 375 - (93 + 3.5 + 17.5) = 261 ml glucose 10%
- Calculate GIR as follows:

$$\frac{\text{Glucose concentration (10)} \times \text{Rate of glucose infusion (261/24 hrs)}}{6 \times \text{Body weight}}$$

$$= 5.2 \text{ mg/kg/minute}$$

- Rate of the total working IV fluid = 375/24 hrs = 15 ml/hr
- Calculate total caloric intake
  - Enteral caloric intake (from the formula): Every 100 ml gives 67 kcal, then 80 ml gives 53.6 kcal
  - Parenteral caloric intake (total caloric intake from IV fluids) = 100 ml glucose 10% contains 10 gm of glucose, then 261 ml contains 26.1 gm glucose. Since each gm glucose gives 3.4 kcal, then 26.1 gm gives 89 kcal.
  - Total daily caloric intake = enteral caloric intake (53.6 kcl) + parenteral caloric intake (89 kcl) = 148.6/3.5 (kg) = 42.5 kcal/kg/day
  - Total caloric intake needed for this baby is 120 kcal/kg/day; thus this baby receives insufficient caloric intake, it should be increased; either by increasing the amount or the enteral intake; as tolerated, or starting total parenteral nutrition.
- Since IV fluids contain solutes other than glucose, then glucose concentration in IV fluids is adjusted as follows: glucose 10% means (100 ml containing 10 gm), then 261 ml of glucose 10% contains 26.1 gm, then; to have 26.1 gm in 375 ml, approximately glucose7% [(26.1/375) × 100] is used.

Chapter 16

Water and Electrolyte Imbalance

Water and Electrolyte Imbalance

Disorders of Sodium Balance

Normal serum Na^+ value is 135-148 mEq/L.

Hyponatremia

It is defined as serum sodium level of <130 mEq/L.

Causes

Water overload

- Maternal water overload before birth
- Iatrogenic water overload following birth
- Syndrome of inappropriate release of antidiuretic hormone (SIADH)
  - Cerebral disease (e.g., birth asphyxia and meningitis)
  - Respiratory disease (e.g., pneumonia and pneumothorax)

Sodium depletion

This is usually accompanied by a lesser degree of water depletion.

- Excessive GIT losses (vomiting, diarrhea, nasogastric aspirate, or enterostomy loss).
- Excessive fluid removal (repeated drainage of ascites, pleural fluid or CSF).
- Excessive renal losses:
  - Primary renal tubular problems, late hyponatremia of prematurity, or following relief of obstructive uropathy.
  - Congenital adrenal hyperplasia.
- Third space loss (e.g., NEC).

Clinical manifestations

- Hypotonia, lethargy and convulsions. These symptoms are not usually seen until plasma sodium falls to <125 mEq/L, and are partly related to the acuteness of the fall.
- Inappropriate weight gain with iatrogenic water overload in early postnatal life or weight loss with sodium depletion in later postnatal life.
- Features associated with the underlying disease.
- Syndrome of inappropriate antidiuretic hormone secretion (SIADH):
  - Suspected clinically when decreased serum sodium and decreased urine output occur.
  - Criteria include: (a) low serum sodium, (b) urine sodium loss, (c) urine osmolality > plasma osmolality, and (d) normal adrenal and renal function.

Management

Appropriate treatment may be either fluid restriction or sodium supplementation:

- Over hydration
  - Restrict fluid intake.
  - Add maintenance sodium (2-4 mEq/kg/day) to IV fluids.
  - Correct serum sodium using replacement formula, if serum level is <120 mEq/L.
- Renal losses
  - Increase maintenance sodium (some VLBW infants may have sodium requirements of as much as 6-8 mEq/kg/day).
  - Replace sodium loss using replacement formula.
- Gastrointestinal losses:
  - Replace nasogastric drainage ml/ml with glucose 5% and normal saline 0.9% (1:1 ratio). Add potassium, if needed.
  - Replace sodium loss using replacement formula, if the infant is still hyponatremic.
- SIADH
  - Restrict fluid intake to (IWL + 1/3 to 1/2 urine output).
  - Furosemide, at a dose of 1 mg/kg IV every 6 hrs, can be initiated with sodium replacement using hypertonic NaCl 3% (1-3 ml/kg) as an initial dose, if:
    - Serum Na^+ is <120 mEq/L.
    - Neurologic signs such as seizures develop.
  - Once serum Na^+ >120 mEq/L and neurologic signs abort, fluid restriction alone can be utilized.

N.B.: Rapid correction of hyponatremia may lead to central pontine myelinolysis.

Sodium replacement formula

Total Na^+ replacement = Desired Na^+ (mEq) - Actual Na^+ (mEq) × Weight (kg) × 0.6

- Give 1/2 replacement (over at least 6-8 hrs) in the maintenance IV fluid.
- Check serum Na^+ level after the first replacement. If additional sodium is needed, give the second half over the next 16 hrs.
- Correct by hypertonic saline 3% (1 mEq in 2 ml).

Table (16-1): Sodium concentration of various fluids

Solution	Na^+ Concentration (mEq/L)
3% NaCl in water	513
0.9% NaCl in water	154
Ringer's lactate	130
0.45% NaCl in water	77
0.2% NaCl in water	34

Hypernatremia

It is defined as a serum sodium level of >150 mEq/L.

Causes

Water depletion

- Inadequate free water intake
- Excessive transepidermal water loss (e.g., skin sloughing)
- Excessive renal losses:
  - Glycosuria
  - Diabetes insipidus (congenital or acquired e.g., IVH)

Sodium overload

- Excessive administration of sodium-containing solution (sodium bicarbonate bolus infusion and sodium-containing medications) especially in the face of reduced cardiac output.

Clinical manifestations

- Hypertonicity occurs and convulsions may ensue.
- A full fontanelle may suggest hypernatremic dehydration.
- The diagnosis may be delayed as signs of hypovolemia and decreased skin turgor occur late.
- Severe hypernatremia may cause permanent CNS damage.

Management

Treatment is difficult as persistence of hypernatremia is associated with cerebral hemorrhage and renal vein thrombosis in the newborn but aggressive correction may cause cerebral edema as water enters cells down the osmotic gradient.

Hypernatermia with deficient ECF volume

- Increase free water administration.
- Use D5W/0.3-0.45% saline solution IV in volumes equal to the calculated fluid deficit, given over 48-72 hrs to avoid a rapid fall in serum osmolality, which can lead to cerebral edema. Reduce serum Na^+ level no faster than 0.5-1 mEq/L/hr.
- Body weight, serum electrolytes, and urine volume and specific gravity must be monitored regularly so that fluid administration can be adjusted appropriately.
- Once adequate urine output is demonstrated, potassium is added to provide maintenance requirements or replace urinary losses. Maintenance fluids should be provided concurrently.

Hypernatremia with ECF volume excess

- Restrict sodium administration.

N.B.: Plasma osmolality can be estimated using the formula [2 × Plasma Na^+ (mEq/L)] + [Blood glucose (mg/dl)/18] + [BUN (mg/dl)/2.8] (N: 285 - 295 mOsm/L).

Disorders of Potassium Balance

Normal serum K^+ value is 3.5-5.5 mEq/L. However, serum potassium levels often do not accurately indicate total-body potassium stores (as most of the potassium in the body is contained in the intracellular compartment). A low pH level shifts K^+ out of the cell, whereas alkalosis drives K^+ into the cell 0.1 units of pH change, results in a 0.3-0.6 mEq/L change in the serum potassium level).

Hypokalemia

It is defined as a serum potassium level of <3.5 mEq/L. Hypokalemia is rarely a cause for concern until the serum potassium level is <3.0 mEq/L, unless the patient is receiving digoxin therapy.

Causes

Potassium loss by:

- Chronic diuretic use
- Renal tubular defects
- Nasogastric drainage, or ileostomy drainage

Clinical manifestations

- It may be asymptomatic, or may has the following manifestations:
  - Weakness and paralysis
  - Lethargy
  - Ileus
  - Arrhythmia

ECG changes (Figure 16-1)

Flat T wave, prolonged QT interval, or the appearance of U wave

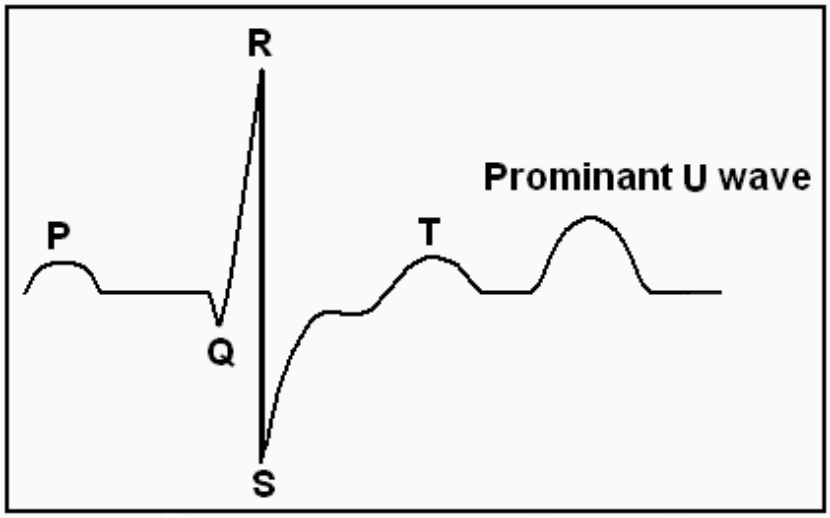


Figure (16-1): ECG changes in hypokalemia

Management

- Management is directed toward the causes e.g., diuretic-induced hypokalemia can be minimized by choosing a potassium sparing diuretic such as spironolactone.
- When significant, this condition is treated by slow potassium replacement either orally or intravenously (1 mEq/kg KCl should raise serum potassium 1 mEq/L).
  - Initial oral replacement therapy: 0.5-1 mEq/kg/day divided and administered with feedings (small, more frequent aliquots preferred). Adjust dosage based on monitoring of serum potassium concentration.
  - Constant IV potassium infusion: calculate the normal maintenance infusion of potassium that should be given and increase the amount accordingly 2-3 mEq/kg/day.
  - Intravenous therapy: KCl (1 mEq/kg) may be given, over a minimum of 4 hrs. For emergency treatment of symptomatic hypokalemia; as in case of cardiac arrhythmias, KCl (0.5-1 mEq/kg) IV may be given over 1 hr, then reassess (maximum infusion rate is 1 mEq/kg/hr).
  - The maximum concentration of potassium is 40 mEq/L for peripheral venous infusions, and 80 mEq/L for central venous infusions.
  - Rapid administration or a bolus dosing of potassium is **not** recommended as life-threatening cardiac arrhythmias may occur.
  - Do not give potassium to an infant who is not voiding.

Hyperkalemia

It is defined as a serum potassium level of >6 mEq/L, measured in a non-hemolyzed specimen. Hyperkalemia is of more concern than hypokalemia, especially when serum potassium levels exceed 6.5 mEq/L or if ECG changes have developed.

Causes

- Inadvertent excessive administration of potassium (e.g., supplementation for hypo-kalemia associated with diuretic therapy).
- Decreased potassium clearance due to renal failure, certain forms of congenital adrenal hyperplasia).
- Increased potassium release secondary to bleeding, tissue destruction, intraventricular hemorrhage, cephalhematoma, intravascular hemolysis, bowel infarction, trauma and hypothermia.
- Extracellular shift of potassium as severe acidosis.

Clinical manifestations

Hyperkalemia may be asymptomatic or may result in arrhythmias and cardiovascular instability.

ECG changes (Figure 16-2)

Peaked T waves, flattened P waves, increased PR interval, and widening of the QRS, bradycardia, tachycardia, supraventricular tachycardia (SVT), ventricular tachycardia, and ventricular fibrillation

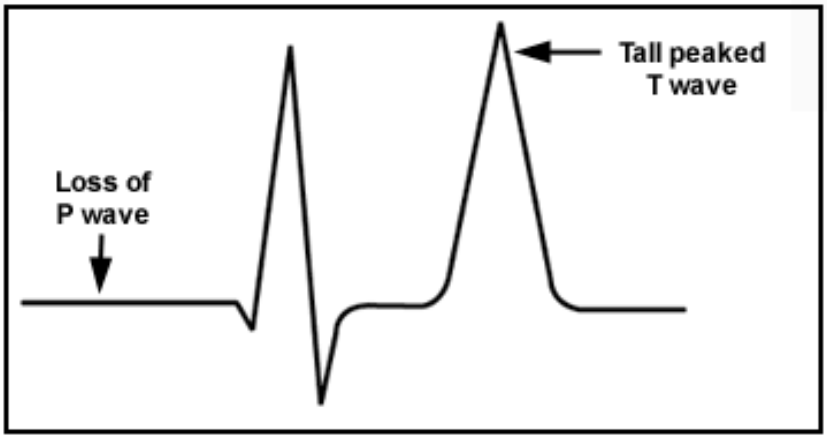


Figure (16-2): ECG changes in hyperkalemia

Management

- Discontinue all exogenous sources of potassium.
- Stabilization of the conducting system:
  - Calcium gluconate 10% (1-2 ml/kg) IV over 1 hr
  - Antiarrhythmic agents e.g. lidocaine and bretylium
- Dilution and intracellular shifting of K^+:
  - Sodium bicarbonate 1-2 mEq/kg (slowly, at least over 30 minutes). Avoid rapid infusion, may lead to IVH especially in preterm infants <34 weeks' gestation and younger than 3 days.
  - Human regular insulin (a bolus of 0.05 unit/kg), with glucose 10% (2 ml/kg), followed by a continuous infusion of insulin 10 units/100 ml, at a rate of 1 ml/kg/hr, with 2-4 ml/kg/hr glucose 10%. Monitor the infant for hypoglycemia.
  - β_2 agonists, such as albuterol, via nebulizer.
- Enhanced K excretion
  - Furosemide 1 mg/kg/dose in infants with adequate renal function.
  - Peritoneal dialysis or double volume exchange can be considered in infants with oliguria and reversible renal disease. Use fresh whole blood (<24 hrs). Peritoneal dialysis takes time to set up and it may be technically impossible in VLBW infants and when there is injured bowel, as in NEC.

Disorders of Calcium Homeostasis

Total serum calcium levels in term infants decline from values of 10-11 mg/dl at birth to 7.5-8.5 mg/dl over the first 2-3 days of life. Approximately 50% of the total calcium is in the ionized form and is the only biologically available form of calcium. Ionized calcium values, rather than total values, correlate better with calcium functions, such as cardiac contractility.

Calcium concentrations can be reported either in mg/dl or mmol/L (4 mg/dl of ionized calcium equals 1 mmol/L).

Hypocalcemia

It is defined as a total serum calcium concentration <7 mg/dl or an ionized calcium concentration <4 mg/dl (<1 mmol/L).

Early-onset hypocalcemia

- Occurs within the first 3 days of life, and is strongly associated with infants of diabetic mothers, asphyxia, and prematurity.
- Often asymptomatic in preterm infants but may show jitteriness, twitches, apnea, seizures, and abnormalities in cardiac function.
- Early onset hypocalcemia can be prevented by the infusion of 20-45 mg/kg/day elemental calcium in the admission IV fluids. Maintenance requirements for the premature infant may reach 70-80 mg/kg/day elemental calcium.
- If the infant is asymptomatic and has a total serum calcium level of >6.5 mg/dl or an ionized calcium level of >0.8-0.9 mmol/L, close observation alone is appropriate.
- Additional elemental calcium should be given intravenously if biochemical abnormality persists (total serum calcium level is <6.5 mg/dl or the ionized level is <0.8-0.9 mmol/L) at 10-20 mg/Kg elemental calcium for 4-6 hrs.
- Emergency calcium therapy (active seizures): 10-20 mg/Kg elemental calcium, given by IV infusion over 10-15 minutes.
- Care should be taken in administering the IV calcium:
  - Monitor for bradycardia or arrhythmia. Discontinue infusion if heart rate <100/minute.
  - Infants who are on digoxin receive calcium only by constant infusion.
  - The peripheral IV site should be checked for patency before and during administration, because of the potential for sloughing, and necrosis caused by infiltrated calcium.

Late-onset hypocalcemia

- It develops after the first week of life and usually has a specific cause such as high phosphate intake, malabsorption, hypoparathyroidism or vitamin D deficiency.
- It should be evaluated in details.

Hypercalcemia

Hypercalcemia is rarely observed in neonates and is defined as a total serum calcium concentration >11 mg/dl or an ionized calcium concentration >5 mg/dl (>1.25 mmol/L).

Oliguria

Oliguria is defined as a urine output of <1 ml/kg/hr. Urine output is often <1 ml/kg/hr during the first 12-18 hrs after birth. Most healthy term infants urinate within the first 12 hrs; however, a small number of healthy infants may not urinate until 24-36 hrs after birth. Persistent oliguria beyond 36 hrs should be evaluated in an otherwise healthy infant.

Etiology and Classification

Prerenal failure

It is a functional response of structurally normal kidneys to hypotension (e.g., shock, dehydration, or congestive heart failure).

Intrinsic renal failure

It is associated with structural renal damage, this includes:

- Acute tubular necrosis (ATN) from prolonged ischemia, drugs, or toxins
- DIC
- Renal artery or vein thrombosis
- Congenital malformation (polycystic, agenesis, dysplastic)

Postrenal failure

It is a consequence of mechanical or functional obstruction to the flow of urine, this includes:

- Posterior urethral valve (PUV)
- Neuropathic bladder
- Prune-belly syndrome

N.B.: Renal failure resulting from neonatal asphyxia and nephrotoxic injury is frequently non-oliguric type, is related to a less severe renal injury and has a better prognosis.

Diagnosis

History

- Maternal diabetes (renal vein thrombosis)
- Birth asphyxia (ATN)
- Oligohydramnios (Potter syndrome)
- Force of urinary stream (PUV)
- Nephrotoxic drugs (aminoglycosides, indomethacin, or furosemide)

Physical examination

Observe and examine for:

- Signs of ECF (intravascular) volume depletion (e.g., poor skin turgor, depressed fontanelles, tachycardia, and hypotension)
- Evidence of cardiac disease

- Signs of acute renal failure (volume overload as edema, congestive heart failure, hepatomegaly, and pulmonary edema)
- Presence of abdominal masses and ascites
- Presence of congenital anomalies

Laboratory investigations

- Urine analysis
  - A specimen is collected by:
    - Suprapubic bladder aspiration: it is the collection method of choice in infants without intra-abdominal pathology or bleeding disorders.
    - Cleaning the perineum and applying a sterile adhesive plastic bag (may give a false positive urine culture because of fecal contamination).
    - Bladder catheterization (may be technically difficult in preterm infants).
  - Analysis should include inspection, measurement of specific gravity, urinary dipstick assessment, and microscopic analysis.
- BUN and plasma creatinine:

  Normal plasma creatinine values are listed in **(Appendix 4).**
- Fractional excretion of sodium (FE-Na) is the ratio of sodium clearance to creatinine clearance, expressed as a percent. It is obtained from the following formula:

$$\textbf{FE-Na} = \frac{\textbf{Urine Na} \times \textbf{Plasma creatinine}}{\textbf{Plasma Na} \times \textbf{Urine creatinine}} \times \textbf{100}$$

  - Level of <1% suggests prerenal failure.
  - Level of 2.5% suggests acute renal failure.
  - Premature infants <32 weeks' gestation frequently show elevated values of FE-Na (>2.5%).
- Glomerular filtration rate (GFR) can be calculated using the following formula:

GFR (ml/min/1.73m^2) = k x Length (cm)/Plasma creatinine (mg/dl)

[k = 0.33 (in preterm infants) and 0.45 (in full-term infants)]

Fluid challenge test

- Administer normal saline (20 ml/kg), as two infusions at 10 ml/kg/hr, after exclusion of heart failure. Dopamine at dose 1-5 µg/kg/minute may improve renal blood flow.
  - If no response, induce diuresis with furosemide 2 mg/kg IV.
  - If no response, do an abdominal ultrasonography to define renal, urethral and bladder anatomy.

Central venous pressure (CVP)

- CVP measures the right ventricular preload and is an important parameter in assessing the fluid balance, and measuring the appropriateness of fluid therapy.

- The umbilical vein catheter may be used for CVP monitoring. It should be placed at the level of the right atrium (0.5-1 cm above the diaphragm) with placement confirmed by chest x-ray film. Central venous access can be also obtained via the internal jugular vein.
- It is difficult to establish 'normal' values for CVP. Levels between 4-6 mmHg are generally taken as normal; however, the range is 2-8 mmHg.
- Low CVP:
  - In the ventilated infant with respiratory distress, a CVP of zero is likely to be associated with hypovolemia and inadequate right ventricular preload.
  - In term infants with heart failure and pulmonary hypertension, a value of 3 mmHg may also indicate inadequate preload.
- High CVP:
  - A high CVP may be due to fluid/volume overload or congestive heart failure.
  - It may be also observed secondary to raised intrathoracic pressure (as in case of pneumothorax).

Management

- Prerenal oliguria should respond to increased cardiac output.
- Postrenal obstruction requires urologic consultation.
- Intrinsic renal failure**:**
  - Monitor: daily weight, input, output, BUN, creatinine and electrolytes.
  - Restrict fluid intake to IWL (500 ml/m^2/day, or 30 ml/kg/day) plus urine output and other measured losses.
  - Correct metabolic acidosis with IV $NaHCO_3$ only if pH <7.2 (unless the infant has PPHN).
  - Withhold potassium supplementation unless hypokalemia develops.
  - Medications**:**
    - Discontinue nephrotoxic drugs (e.g., aminoglycosides, indomethacin, and amphotericin B) and choose drugs with minimal or no renal toxicity, if possible.
    - Adjust dosage and interval of administration of drugs with renal elimination (e.g., antibiotics and digoxin) according to the degree of renal dysfunction. Monitoring serum drug levels will provide a guide for dose adjustments.
  - Peritoneal or hemodialysis may be indicated.

Chapter 17

Disorders of Glucose Homeostasis

Disorders of Glucose Homeostasis

Hypoglycemia

Glucose is a primary metabolite of the fetus and newborn. During intrauterine life, the fetus relies on the placenta for a constant supply. At birth, the infant is abruptly removed from that environment and hormonal and metabolic changes occur that facilitate adaptation to extrauterine life and the regulation of glucose homeostasis. During this transition, newborn glucose levels fall to a low point in the first 1-2 hrs of life, and then increase and stabilize at a mean of 70 mg/dl by 3-4 hrs of life.

Hypoglycemia is usually defined as a serum glucose value of <45 mg/dl in a term or preterm neonate. Hypoglycemia is one of the most important indicators of stress and disease in the infant. Untreated hypoglycemia can result in permanent neurological damage or death. Every neonatal care unit must be prepared to detect and treat hypoglycemia.

Most cases of neonatal hypoglycemia are transient, respond readily to treatment and have excellent prognosis, whereas, persistent hypoglycemia is more likely to be associated with endocrine and metabolic conditions and possibly neurologic sequelae.

Mechanisms and Causes of Hypoglycemia

Depleted stores and decreased production of glucose

- IUGR or SGA
- Preterm or post-term neonates
- Inadequate caloric intake
- Delayed onset of feeding

Increased glucose utilization (Hyperinsulinism)

- Infants of diabetic mothers
- LGA infants
- Erythroblastosis fetalis (e.g., severe Rh-isoimmunization)
- Abrupt cessation of high glucose intake
- Malpositioned umbilical artery catheter used to infuse glucose in high concentration into the celiac and superior mesenteric arteries
- Beckwith-Weidemann syndrome (macrosomia, mild microcephaly, omphalocele, macroglossia, hypoglycemia and visceromegaly)
- Islet cell hyperplasia
- Insulin producing tumors (e.g., nesidioblastosis)
- After exchange transfusion with blood containing high-glucose concentration
- Maternal drugs:
  - Tocolytic therapy with β-sympathomimetic agents (e.g., terbutaline)
  - Intrapartum glucose infusion

Increased glucose utilization and/or decreased production

Perinatal stress

- Hypothermia or cold stress
- Sepsis
- Perinatal asphyxia
- Respiratory distress
- Shock

Polycythemia

Maternal therapy

- Beta blockers (e.g., labetalol or propranolol)
- Steroids

Endocrine deficiency

- Adrenal insufficiency (e.g., adrenal hemorrhage, congenital adrenal hyperplasia)
- Hypothalamic hormone deficiencies
- Congenital hypopituitarism
- Hypothyroidism
- Congenital glucagon deficiency

Inborn errors of metabolism

(Refer to Chapter 38)

- Defects in carbohydrate metabolism (e.g., galactosemia, or glycogen storage diseases)
- Defects in aminoacid metabolism (e.g., tyrosinemia)
- Defects in fatty acids metabolism (e.g., defects in carnitine metabolism)

Miscellaneous

- Congenital heart diseases

Clinical Manifestations

Unfortunately, signs of hypoglycemia are non-specific and can be similar to signs of many other problems. Moreover, some infants may be asymptomatic. Therefore, serum glucose levels should always be evaluated and treated in high risk infants in which hypoglycemia is anticipated or when there are any of the following manifestations:

- Jitteriness, tremors, irritability
- Seizures, coma
- Apnea
- Cyanosis
- Lethargy and poor feeding

- Weak or high-pitched crying
- Hypothermia
- Respiratory distress

N.B.: These clinical signs should be alleviated with concomitant correction of plasma glucose levels.

Management

To prevent brain damage, prompt identification and treatment of the infant with hypoglycemia are essential. Bedside glucose monitoring is appropriate for initial screening and detection. If hypoglycemia is observed, the result should be confirmed by a serum laboratory value.

Management of neonatal hypoglycemia should include; anticipation of the neonates at high risk, correction of hypoglycemia, and investigation and treatment of the cause of hypoglycemia.

A suggested guideline for management of neonates with hypoglycemia is shown in **(Figure 17-1)**.

Prevention of neonatal hypoglycemia

- Dry the infant and avoid hypothermia at all stages and encourage skin to skin contact.
- Early enteral feeding is the single most important preventive measure. Feeding should be initiated early (within 1 hour of age) and frequently thereafter (at least 8 feeds per day).
- Infants at risk of hypoglycemia should have serial blood glucose monitoring starting from the first 1-2 hrs of life, and should not be allowed to wait for more than 3 hrs between feedings. Blood glucose values should be monitored until they are taking full feedings and have three normal pre-feeding readings above 45 mg/dl.
- Breast fed infants not able to suck adequately, can be fed expressed breast milk or formula. For tube fed infants, feed hourly to start off, with increasing the interval between feeds, if blood glucose remains >45 mg/dl and the infant tolerates feedings.
- If the infant is unable to tolerate nipple or tube feedings, a maintenance IV therapy with glucose 10% should be initiated and glucose levels monitored.

N.B: Glucose concentration in whole blood is 10-15% lower than in the plasma.

Treatment of neonatal hypoglycemia

Symptomatic infant

- If clinically symptomatic, and if initial measurement was done by strips, draw confirmatory laboratory specimen.
- Concurrently, administer glucose bolus of 200 mg/kg (2 ml/kg of glucose 10%) over 1 minute and begin IV glucose administration at a rate of 6-8 mg/kg/minute.
- Check serum glucose after 30 minutes and hourly until stable to determine if additional therapy is needed. If blood glucose is still <45 mg/dl, increase glucose infusion rate (GIR) by 1-2 mg/kg/minute. Additional bolus infusion of 2 ml/kg glucose 10% may be needed.

- Rarely, some infants with hyperinsulinemia will require a GIR of 12-15 mg/kg/minute.
- GIR can be calculated from the following formula:

$$\text{GIR(mg/kg/min)} = \frac{\text{Fluid rate (ml/hr)} \times \text{Dextrose concentration}}{6 \times \text{Weight (kg)}}$$

- A central venous catheter is needed, if glucose concentration >12.5% is required.
- Begin breast milk or formula feeding by gavage/orally when clinically appropriate.
- Once the infant's glucose levels have been stable for 12 hrs, IV glucose may be tapered **gradually** by 1-2 mg/kg/minute, depending on maintenance of glucose levels higher than 45 mg/dl. Wean IV slowly while feedings are advanced and stop once GIR <4 mg/kg/minute.

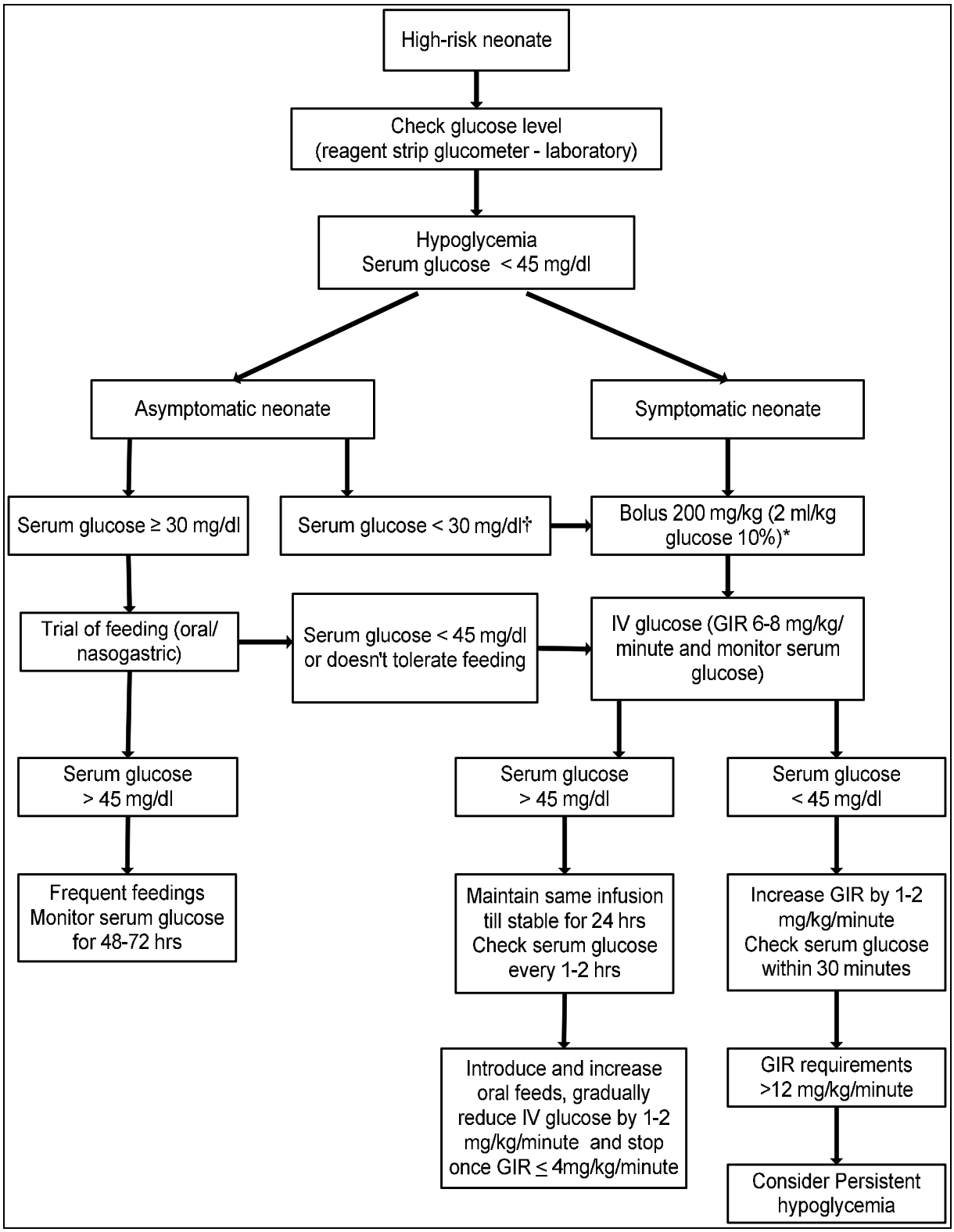
Adjunctive therapy

This is rarely needed. However, in case of persistent hypoglycemia, a pediatric endocrinologist should be consulted.

- Glucagon (0.03-0.3 mg/kg IM), is rarely used as an emergency measure to increase plasma glucose concentration. Its effect is transient and has to be followed by IV glucose infusion to maintain a normal blood glucose level.
- Hydrocortisone 10 mg/kg/day IV in two divided doses, if the infant remains hypoglycemic despite receiving GIR >12 mg/kg/minute.

Asymptomatic infant

- If clinically asymptomatic, draw confirmatory laboratory specimen if initial measurement was done by strips.
- Concurrently, if blood glucose is 30-45 mg/dl, initiate breastfeeding or age-appropriate formula by gavage/orally at appropriate intervals with close monitoring.
  - Check serum glucose 30-60 minutes after initiation of feeding and then before feeding to confirm euglycemia.
  - If serum glucose is still <45 mg/dl or the infant is unable to feed, begin IV glucose administration at 6-8 mg/kg/minute.
- If blood glucose is <30 mg/dl, administer bolus of 200 mg/kg (2 ml/kg of glucose 10%), infuse glucose 10% IV at 6-8 mg/kg/minute and recheck serum glucose within 30 minutes.
- Gradually increase feedings and decrease parenteral fluid administration while confirming maintenance of euglycemia.



* Additional bolus infusion may be needed.
†Feeding could be started while searching for an IV line
GIR; Glucose infusion rate

Figure (17-1): Management of neonatal hypoglycemia

Persistent Hypoglycemia

When hypoglycemia is refractory and severe or if the need for large glucose infusions lasts over one week, evaluation of some of the rare causes of hypoglycemia should be considered. Endocrine consultation may be helpful.

Causes

Hyperinsulinism

- Beckwith-Weidemann syndrome
- Persistent hyperinsulinemic hypoglycemia of infancy (PHHI)
  - Two types:
    - Focal adenomatous hyperplasia
    - Diffuse abnormality of the islets
  - Laboratory tests:
    - Insulin level is inappropriately elevated for the simultaneous low blood glucose concentration.
    - Decreased levels of free fatty acids, and ketone bodies in blood.
    - A robust rise in blood glucose after 1 mg of glucagon IM.

Endocrine deficiency

(Refer to causes of hypoglycemia)

Inborn errors of metabolism

(Refer to causes of hypoglycemia)

Investigations

- A sample is drawn to determine insulin level at the time of low blood glucose will document inappropriate insulin secretion in case of hyperinsulinemia.
- If insulin level is normal for the blood glucose level, other causes of persistent hypoglycemia should be considered:
  - Serum: Growth Hormone, Cortisol, ACTH, T_4, TSH, Glucagon, plasma aminoacids
  - Urine: ketones, reducing substances, aminoacids, organic acids

Treatment

- Treat the cause.
- In case of hyperinsulinemia:
  - Medical management: diazoxide.
  - Surgical management: selective resection of focal lesions or subtotal pancreatectomy in diffuse forms.

Hyperglycemia

Definition

Hyperglycemia is defined as whole blood glucose concentrations over 125 mg/dl or plasma glucose over 145 mg/dl.

Etiology

- Exogenous parenteral glucose
- Drugs: steroids, theophylline, phenytoin, lipid infusion
- ELBW infants: in 40-80% of ELBW infants. The cause is not completely understood, but is often related to insulin resistance
- Sepsis
- Stress (e.g., mechanical ventilation)
- Surgical procedures
- Neonatal diabetes mellitus; a rare condition, presents with marked glucosuria, hyperglycemia, polyuria, severe dehydration, acidosis, mild ketonuria and failure to thrive

Prevention

- Careful adjustment of the GIR, and frequent monitoring blood glucose levels and urine for glucosuria.
- ELBW infants should start with an IV glucose concentration not more than 5-7.5%.

Treatment

- Parenteral glucose intake is reduced to 4-6 mg/kg/minute by adjusting the concentration or the rate (or both) of glucose infusion with monitoring of blood glucose level. Hypotonic fluids (solutions < glucose 5%) should be avoided.
- If general condition of the infant allows, feeding can be started, as feeding can promote the secretion of hormones that promote insulin secretion.
- Insulin infusion can be used, if blood glucose is >200-250 mg/dl despite efforts to lower GIR or when prolonged restriction of parenterally administered glucose would substantially decrease the required total caloric intake.
- Preparation of insulin infusion:
  - The standard dilution is 15 unit regular human insulin added to 150 ml glucose 10% or normal saline (final concentration is 0.1 unit/ml).
  - Flush the IV tubing with a minimum of 25 ml of this insulin solution.
- Administration:
  - Continuous insulin infusion:
    - Rate: 0.01-0.2 unit/kg/hr (= 0.1-2 ml/kg/hr)

- Monitoring: check blood glucose every 30 minutes until stable and adjust infusion rate:
  - If blood glucose remains >180 mg/dl, titrate in increments of 0.01 unit/kg/hr.
  - If hypoglycemia occurs, discontinue insulin infusion and give IV bolus of glucose 10% at 2 ml/kg × 1 dose.
- Insulin can be given as intermittent dose, if infusion is not available, at a dose of 0.1-0.2 unit/kg subcutaneous every 6-12 hrs.

- Monitor for rebound hyperglycemia.

Complications

- Urinary loss of glucose and osmotic diuresis, dehydration and hyperosmolarity (may increase the risk of intraventricular hemorrhage).
- Increased mortalities, sepsis and retinopathy of prematurity have been reported in ELBW infants with hyperglycemia.

Chapter 18

Infant of a Diabetic Mother

Infant of a Diabetic Mother (IDM)

Good control of maternal diabetes is the key factor in determining fetal outcome. Recent data indicates that perinatal morbidity and mortality rates in the offspring of women with diabetes mellitus have improved with dietary management and insulin therapy.

Incidence

- Insulin dependent diabetes occurs in 0.5% of all pregnancies.
- 1-3% of women exhibit biochemical abnormalities during pregnancy consistent with gestational diabetes.

Pathophysiology

Macrosomia

- Macrosomia is a term used to describe a newborn with excessive birth weight. Fetal macrosomia has been defined as birth weight of ≥4,000 gm or greater than 90th centile for gestational age.
- Delivery of an infant weighing >4,500 gm occurs 10 times more often in women who have diabetes than in women who have normal glucose tolerance.
- Macrosomia seen in an infant of a diabetic mother is due to the maternal hyperglycemia fetal hyperinsulinemia pathway. Insulin acts as the primary anabolic hormone of fetal growth and development, resulting in visceromegaly, especially of heart and liver, and macrosomia. In the presence of excess substrate, such as glucose, fat synthesis and deposition increases during the third trimester. Fetal macrosomia is reflected by increased body fat, muscle mass, and organomegaly, but not by an increased size of the brain or kidney.
- It may be linked to increased incidence of cesarean section or shoulder dystocia and birth trauma.

Small for gestational age (SGA)

- Mothers with renal, retinal or cardiac diseases are more likely to have small for gestational age or premature infants, poor fetal outcome, fetal distress or fetal death.

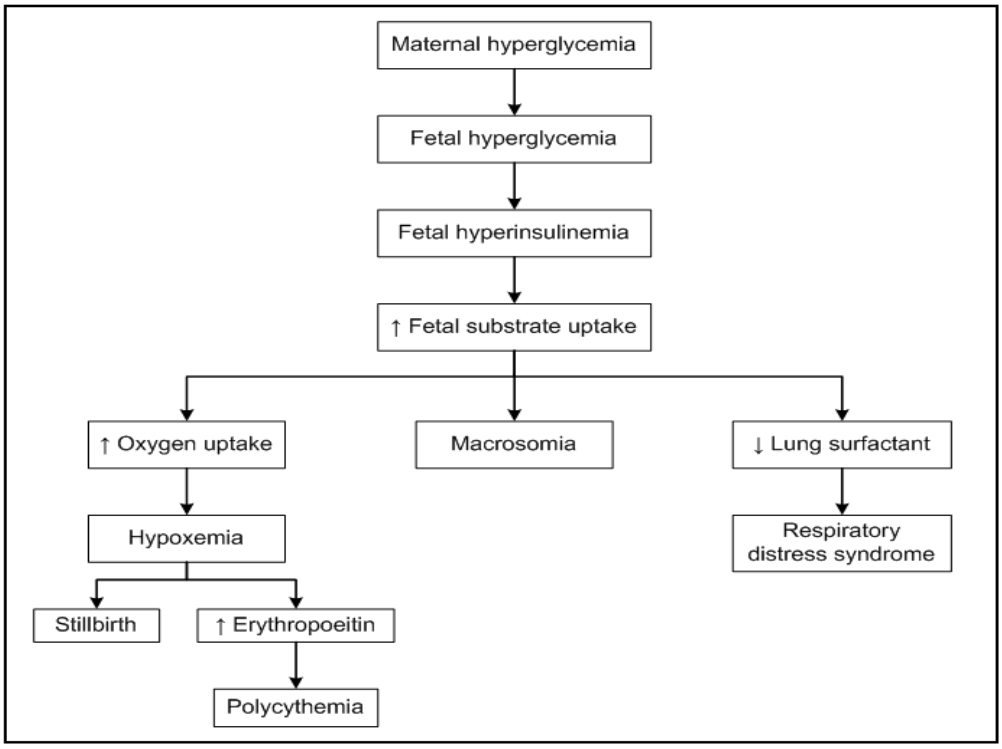


Figure (18-1): Pathogenic events in infants of diabetic mothers

Specific Disorders Frequently Encountered in IDMs

Metabolic disorders

Hypoglycemia

- Serum glucose level <45 mg/dl in a preterm or term infant.
- Immediately after birth there is a significant decrease in plasma glucose concentration, reaching a nadir between 30 and 90 minutes and followed by a spontaneous recovery in the majority of infants. However, in some infants the plasma glucose level remains persistently low, necessitating intervention.
- It occurs in 30-40% of IDMs.
- The onset is frequently within 1-2 hrs of age.
- Pathophysiology:
  - Maternal hyperglycemia resulting in fetal hyperglycemia, which stimulates the fetal pancreas, resulting in islet cell hypertrophy and beta cell hyperplasia with increased insulin availability. At birth, the transplacental glucose supply is terminated, and because of high concentrations of plasma insulin, blood glucose levels fall.
  - Other factors:
    - Inadequate glycogen stores in SGA infants (may present later 12-24 hrs of age)
    - Deceased catecholamine and glucagon secretion and diminished hepatic glucose production

Hypocalcemia

- It occurs in up to 50% of IDMs.

- Unlike hypoglycemia, hypocalcemia becomes apparent between 48 and 72 hrs after birth.
- It has been related to the severity and duration of maternal diabetes. It may be potentiated by prematurity and asphyxia.
- Pathophysiology:
  - Mechanisms are probably delayed in the usual postnatal rise of parathyroid hormone, persistently high levels of calcitonin, and possibly alterations in vitamin D metabolism.

Hypomagnesemia

- Serum magnesium <1.5 mg/dl has been found in as many as 33% of IDMs.
- It is usually transient.
- Its pathophysiologic significance remains uncertain.

Morphological and functional problems

Birth injuries

Mostly due to macrosomia, they include:

- Fractured clavicle
- Erb's palsy
- Phrenic nerve palsy

Congenital malformations

- The congenital malformation rate in IDMs varies from 5-10%. This rate represents a two to three fold higher rate of anomalies when compared with the normal population.
- This high risk may be due to an increased supply of substrate leading to an oxidative stress on the developing fetus, which in turn generates excess free oxygen radical formation that might be teratogenic.
- Poor diabetic control in the first trimester is associated with a higher percentage of malformations.
- Congenital anomalies have become the most common cause of perinatal loss in women with pregestational diabetes. They include:
  - Cardiac malformations (e.g., transposition of great arteries and ventricular septal defects)
  - Neurological defects (e.g., open meningomyelocele, holoprosencephaly, and anencephaly)
  - Skeletal defects (e.g., caudal agenesis or dysplasia syndrome, consisting of agenesis or hypoplasia of the femora with agenesis of the lower vertebrae and sacrum)
  - Renal defects (e.g., agenesis)
  - Gastrointestinal tract defects (e.g., small left colon syndrome or situs inversus)

N.B.: Caudal dysplasia (sacral agenesis), although this lesion is most specific for diabetes, it is not the most frequent anomaly in IDMs.

Perinatal asphyxia

- Perinatal asphyxia occurs in up to 25% of IDMs.
- It results from prematurity, cesarean delivery, intrauterine hypoxia caused by maternal vascular disease or macrosomia.

Cardiorespiratory disorders

Hyaline membrane disease (HMD)

- Due to premature delivery, delayed maturation of pulmonary surfactant production (hyperinsulinism antagonizes the action of cortisol), or delivery by elective cesarean section.

Other causes of respiratory distress

- Transient tachypnea of the newborn
- Hypertrophic cardiomyopathy:
  - Transient subaortic stenosis resulting from ventricular septal hypertrophy.
  - Secondary to increased fat and glycogen depositions in the myocardium.
  - Possibly leading to congestive heart failure.
  - Resolution of symptoms by 2 weeks and resolution of septal hypertrophy by 4 months.

Hematological disorders

Polycythemia and hyperviscosity

- Occurs in 20-30% of IDMs.
- The cause is unclear but may be related to:
  - Increased levels of erythropoietin.
  - Increased red blood cell production, secondary to fetal hypoxia in mothers with vascular disease.
  - Intrauterine placental transfusion resulting from acute hypoxia during labor and delivery.

Hyperbilirubinemia

- Secondary to prematurity, hypoglycemia and polycythemia, decreased life span of the red cells, increased enterohepatic circulation of bilirubin as a result of poor feeding, and decreased hepatic conjugation due to immaturity of the enzymes.

Renal venous thrombosis

- Rare complication which, most likely, is caused by hyperviscosity, hypotension, and disseminated intravascular coagulation.
- It may present with hematuria and an abdominal mass diagnosed by abdominal ultrasound.

Poor feeding

- It is a major problem in IDMs; they may take several days to establish nipple feedings.

- It is a major reason for prolonged hospital stays and parent-infant separation.

Clinical Manifestations

At birth

- The IDMs tend to have puffy, plethoric faces. They are tremulous and hyperexcitable. These infants may be large or small for gestational age.

After birth

- Infant may develop hypoglycemia.
- Infant may be lethargic with poor feeding, apnea, or jitteriness in the first 6-12 hrs after birth.
- Infant may show signs of respiratory distress.
- Cardiac disease may be present. It is diagnosed by an enlarged cardiothymic ratio on a chest x-ray film or by physical evidence of heart failure.
- Congenital anomalies may be noted on physical examination.

Diagnosis

Laboratory studies

- Glucose levels (blood-serum):
  - Checked by dextrostix at delivery and at 1, 2, 3, 6, 12, 24, 36, and 48 hrs of age.
  - Readings less than 45 mg/dl by dextrostix should be verified by serum glucose measurements.
- Serum calcium levels:
  - Check on admission and repeat if infant is jittery or appears sick.
  - If serum calcium levels are low, serum magnesium levels should be obtained.
- Hematocrit:
  - Check at 1 and 24 hrs of age.
- Serum bilirubin levels:
  - Check as indicated by physical examination.
- Other tests:
  - Check arterial blood gas levels.
  - Obtain complete blood cell count (CBC), cultures and gram stain, as clinically indicated.

Radiological studies

- These studies are not necessary unless there is evidence of cardiac, respiratory, or skeletal problems.
- Echocardiography is indicated if hypertrophic cardiomyopathy, or cardiac mal-formations suspected.

Management

Delivery should take place in a hospital, where the newborn can be carefully monitored.

Metabolic management

Hypoglycemia

- Asymptomatic infants if clinically well and normoglycemic:
  - Early feeding should be commenced as soon as the infant is stable. First feed within 30 minutes of delivery and thereafter at least 3 hourly. Breastfeeding is preferable; however, formula feeds can be given.
  - If any question arises about an infant's ability to tolerate oral feeding, the feeding should be discontinued and glucose given by peripheral intravenous infusion at a rate of 6-8 mg/kg/minute.
- Hypoglycemia should be treated, even in asymptomatic infants, by frequent feeding and/or intravenous infusion of glucose **(Refer to Chapter 17).**

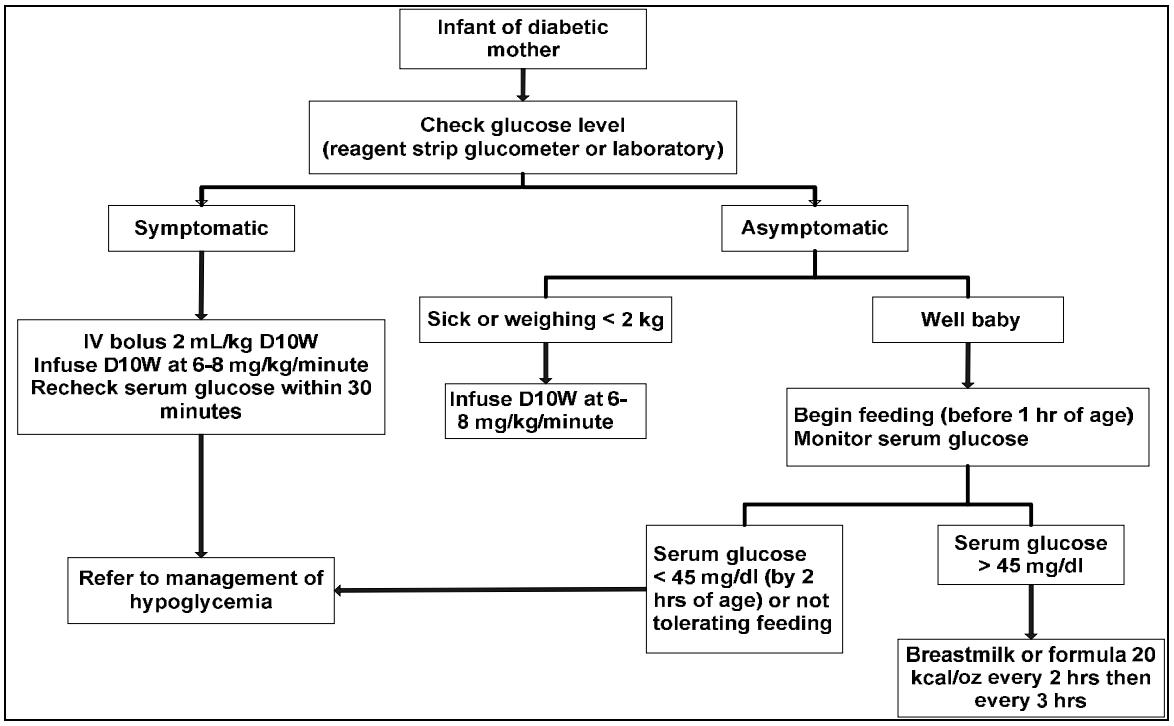


Figure (18-2): Approach for prevention and management of hypoglycemia in IDM

Hypocalcemia

- Initial dose 100-200 mg/kg/dose (1-2 ml/kg/dose) IV calcium gluconate 10% administered slowly over 10 minutes. Monitor for bradycardia and signs of extravasation.
- A maintenance dose is given by continuous IV infusion, 2-8 ml/kg/day.
- It usually responds in 3-4 days.

Hypomagnesemia

- Clinical manifestations of hypomagnesemia such as seizures should be treated promptly with parenteral magnesium. Asymptomatic cases should be also corrected, as magnesium can alter important cellular functions and may lead secondarily to hypocalcemia that is only corrected when the magnesium disturbance is corrected.

- Give magnesium sulfate (50% solution)
  - Dose: 0.05-0.1 ml/kg (0.2-0.4 mEq/kg,), given IM or slow IV infusion over 30 minutes.
  - Repeated doses may be required every 6-12 hrs until serum magnesium level is normal or symptoms resolve.
  - Concomitant oral magnesium replacement can be started if the infant is tolerating oral fluids. Magnesium sulfate (50% solution) can be given at a dose of 0.2 ml/kg/day.
- Serum magnesium levels should be measured daily or more frequently as clinically indicated until values are stable.
- Infants receiving IV magnesium therapy should receive continuous cardiorespiratory monitoring.
- Possible complications of IV infusion: hypotension, flushing, depressed cardiac function, and CNS and respiratory depression.

Cardiorespiratory support

Hyaline membrane disease

(Refer to Chapter 22)

Cardiomyopathy

- Oxygen and furosemide are often needed. In severe cases treat with propranolol.
- Inotropic agents (e.g., digoxin) worsen the obstruction and are contraindicated.

Perinatal asphyxia

(Refer to Chapter 29)

Hematological therapy

Hyperbilirubinemia

- Monitor serum bilirubin levels.
- Phototherapy and exchange transfusion, when needed.

Polycythemia

(Refer to Chapter 34)

Management of macrosomia and birth injuries

(Refer to Chapter 32)

Prognosis

- Less morbidity and mortality occur with adequate control during the diabetic pregnancy.
- The subsequent incidence of diabetes mellitus in infants of diabetic mothers is increased in comparison to that of the general population.
- Physical development is normal but obesity in childhood may occur.

Chapter 19

Breastfeeding

Breastfeeding

Breastfeeding is an unequalled way of providing ideal food for the healthy growth and development of infants.

WHO and UNICEF Recommendations for optimal infant feeding as set out in the **Global Strategy for Infant and Young Child Feeding** are:

- Exclusive breastfeeding for 6 months: means that an infant receives only breast milk, and no other liquids or solids, not even water, with the exception of oral rehydration solution, drops or syrups consisting of vitamins, minerals supplements or medicines.
- Nutritionally adequate and safe complementary feeding starting from the age of 6 months with continued breastfeeding up to 2 years of age or beyond.

Breastfeeding of the Well Newborn

To empower women to breastfeeding, the following instructions should be thoroughly explained to the mothers:

- Initiate immediate skin to skin contact and early breastfeeding
- Avoid giving the infant prelacteals (e.g., glucose, anise)
- Ensure correct positioning and latching on
- Provide feeding on demand
- The infant should empty the breast
- Night feeds are very important
- Avoid bottles and pacifiers
- Avoid supplements before 6 months

Immediate skin to skin contact (SSC) and early breastfeeding

- Mother and infant should be together, skin to skin, immediately after birth as well as later.
- Immediate skin to skin contact is indicated for all newborns not requiring resuscitation (about 90% of newborns). The infant should be dried off on the mother; the head is dried before the body. Wet towels should be immediately replaced by dry ones. Most infants will cough the secretions on their own without the need for suctioning. The infant is placed on the mother's body with the head between the two breasts and the mother supporting the infant's body with her arms. The infant uses the stepping-crawling motion to approach the breast, nuzzle and nurses on his own (this is called self attachment), and the infant usually self attaches within 30-60 minutes. Nobody should be pushing the infant; only the mother may make some attempts to help the infant to be directed to the breast.
- Hospital routines, such as weighing the infant, instilling eye drops and giving vitamin K injection should not take precedence.
- It is better to do cesarean section using epidural or spinal anesthesia and the infant is put immediately on his mother even while she is getting stitched up.
- It is not recommended to separate mothers and infants unless medically indicated. The infant should be kept in the mother's room (rooming in), or better in the same bed (co-bedding).

N.B.: Infants who are kept skin to skin with the mother immediately after birth are more likely to latch on without any help, are more likely to latch on well, and are more likely to exclusively breastfeed longer.

Avoid giving the infant prelacteals (e.g., glucose, anise)

- It's not judicious to use prelacteals as this interferes with early breastfeeding and in addition some infants refuse to latch on the breast after taking the prelacteals.
- Colostrum provides important immune protection to an infant when he/she is first exposed to the micro-organisms in the environment, and epidermal growth factor helps to prepare the lining of the gut to receive the nutrients in milk.

Correct positioning and latching-on

Correct positioning and latching-on is the cornerstone of successful breastfeeding.

Proper positioning

- The mother needs to be relaxed and comfortable. In the first few weeks the mother can put the infant on a pillow, so as not to lean forward.
  - The infant should be straight and supported by the mother's arm.
  - The infant's body should be close to and facing the mother's body.
- If the mother doesn't put the infant correctly on the breast, the infant will not be able to latch correctly. As a result, the infant and mother will experience improper withdrawal of milk, improper weight gain, introduction of formula feeds and inevitable decrease in milk production. In addition, improper latch rapidly traumatizes the mother's nipple causing her sore nipples.
- The commonly used positions are: cradle hold, cross cradle hold, football hold, and side-lying position.

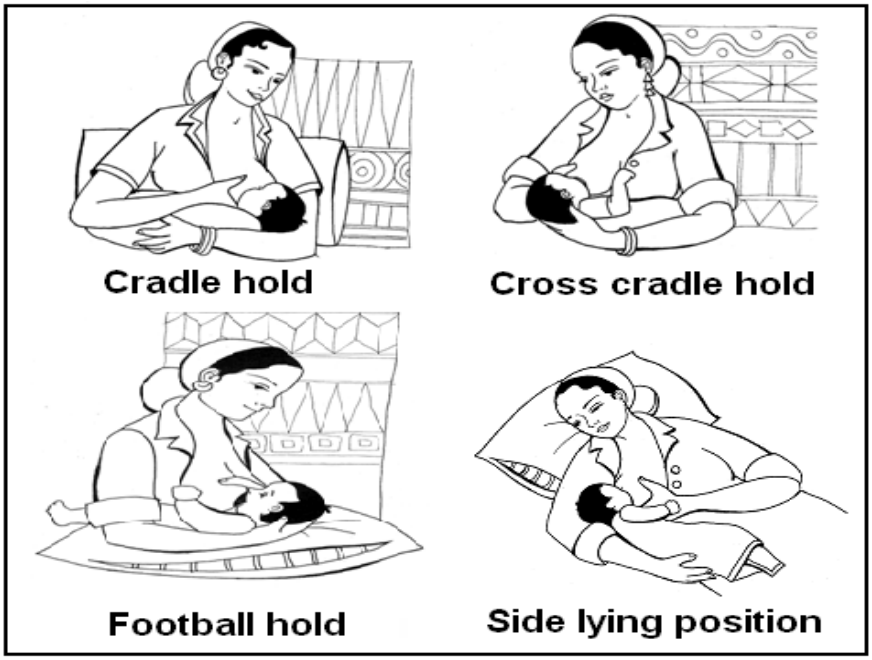


Figure (19-1): Commonly used breastfeeding positions

Positioning the twins

- Twins can breastfeed simultaneously. Simultaneous nursing is associated with higher milk production. Also, the good suckler can stimulate the milk let down for a weak suckler on the other breast.
- Twins can be positioned as illustrated in **(Figure 19-2)**.

Figure (19-2): Breastfeeding twins

Breast support

To support the breast the mother should put the thumb above and the other 4 fingers below the breast (C-hold) to allow the maximum amount of breast tissue in the infant's mouth. It is not mandatory to hold breast but it is preferable especially in the first few weeks (till there is good fit) or if the breast's size is large.

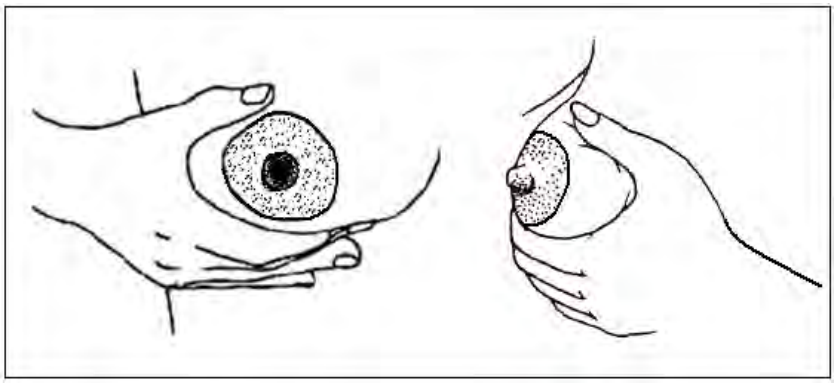


Figure (19-3): Breast support (the "C" hold)

Proper Latching

- Adjust the infant to face the breast with his nose opposite the nipple.
- The mother should touch the infant's nose or upper lip with the nipple till the infant opens his mouth widely, and then rapidly direct the infant to the breast. This will allow the infant to take a good part of the breast with more areola visible above the infant's mouth than below the mouth.
- All of these signs should be present if the attachment is good:
  - Infant's mouth is wide open.
  - Infant's chin is touching the breast.
  - Infant's nose is lightly resting on breast.
  - Infant's upper and lower lips turned outward.

- The cheeks should look full.
- More areola is visible above the infant's mouth than below the mouth.
- The infant suckles effectively with slow deep sucks, sometimes pausing.

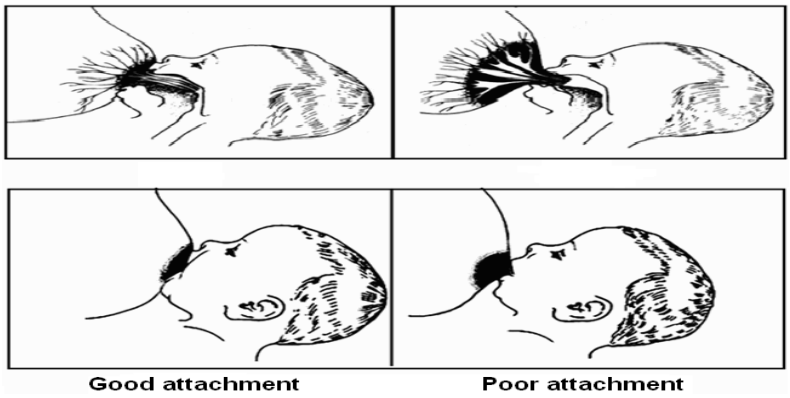


Figure (19-4): Proper latching

Feeding on demand

The infant should be allowed to feed on demand with no scheduling. Usually in the first few weeks, infants need to nurse often and fully. The more the infant suckles, the more prolactin and oxytocin produced.

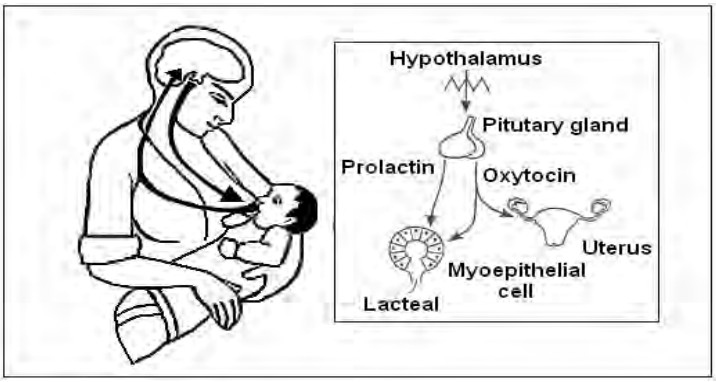


Figure (19-5): Prolactin and oxytocin reflexes

When infants are hungry, they express the following feeding cues:

- Turning the head and opening the mouth with searching movements (rooting)
- Mouthing movements of lips and tongue
- Bringing hand to mouth, sucking on a fist or fingers
- Moving legs or arms
- Head bobbing

N.B.: Crying is a late hunger cue and sometimes when infants are left to cry, they get disorganized on the breast or might sleep or fret at the breast instead of nursing.

The infant should empty the breast

The infant should empty the breast before taking the other breast to benefit from the hind milk which is high in fat that promotes good physical and mental growth. In the first few days, infants might finish one breast per feed.

Encourage night feeds

The mother should not skip the night feeds as prolactin reaches higher levels in response to suckling by night. The mother should feed the infant when he/she wakes up. However the mother should wake up the infant in the early days after delivery as most infants tend to be sleepy. The infant should be allowed to take one long sleep stretch of about 4-5 hrs and otherwise he/she should be awakened maximum every 3 hrs to breastfeed.

Avoid bottles and pacifiers

Bottles

The mechanism of bottle feeding is different from that of breastfeeding. Most infants become confused if exposed to bottles in the early weeks of life; some infants become confused after one bottle feed and some after few bottles.

Pacifiers

Pacifiers are not recommended as they affect the latch and growth of the infant. The wet rubber is a rich source of infection to the infant and the mother. Some infants refuse the breast after taking a pacifier.

Avoid supplements before 6 months

Water

Exclusively breastfed infants don't need water in the first six months even in the hot weather. Breast milk contains enough water (87%).

Herbals

Herbals are nutritionally deficient.

Formula feeds

Formulas expose the infant to the hazards of the highly allergenic cow's milk. In early months of life, the intestine is "leaky", and allows the foreign proteins to pass freely, reaching the infant's immune system, and modifying it in an undesirable way.

Formula feeds are injudiciously introduced in the following situations

Inappropriate weight gain

If the growth of the infant is inappropriate, the concept of "helping" him/her with formula feeds, whether supplementary or complementary is usually unjustified. There is usually a problem in the breastfeeding practice that should be targeted early rather than complicating the situation with decreasing the demand and thus the supply of the breast milk.

Neonatal jaundice

Increasing breastfeeding rather than the introduction of supplements is preferred to flush the bilirubin. Colostrum is a laxative which increases the intestinal motility thus decreasing bilirubin absorption in the enterohepatic circulation and increasing bilirubin loss in stools.

In cases of suspected breast milk jaundice, there is no rationale to discontinue breastfeeding as the hazards of exposing the infant to formula and the mother to engorgement greatly outweighs the reported hazards of bilirubin in breast milk jaundice.

Twins

Exclusive breastfeeding of twins is not a remote possibility as some people think. Since the quantity of milk production is totally a process of "demand and supply", when two infants are put on the breast, the supply is doubled.

Assessment of the Breast Milk Supply

- Adequate weight gain: the healthy infant loses 5-7% of his/her birth weight after delivery, and then the weight is usually regained within 2 weeks. Once gaining weight; the average newborn weight gain is 25-35 gm/day,
- Wetting 6 heavy diapers every 24 hrs, and
- Expelling 2 or more bowel movements every 24 hrs.

False Alarms of Insufficient Milk

Lots of mothers assume wrongly that they have low breast milk supply in the following situations:

- The infant feeds frequently or for a long time (usually noticed during the growth spurts at 3 weeks, 6 weeks and 3 months).
- The infant seems hungry shortly after feeding.
- The mother's breasts seem softer.
- Infant accepts bottle after feeding.
- The mother cannot express a lot of milk.
- The mother doesn't feel the let down.
- Fussy infant.

Breastfeeding of the Hospitalized Ill Infant

The mother of the hospitalized ill infant can uniquely provide him with:

Breast milk

In the NICU, breast milk can spare health, lives and money. It has the following extra advantages:

GIT benefits

Infants fed breast milk have faster gastric emptying than formula fed. There are components of human milk that may promote GI maturation (growth factors, hormones and amino acids), thus the incidence of NEC is 6-10 times more common in formula fed than in breastfed infants.

Neurodevelopmental benefits

The unique composition of fat in breast milk optimizes brain growth. This is specifically important for preterm infants and neuro-compromized neonates.

Immune benefits

Breast milk contains enormous immunological factors which can directly target the pathogens and also enhances the infant's own immune system. The anti-infective properties of the milk of the preterm are higher than that of the full term.

Better growth

Breastfed infants grow faster with faster maturity of the organs and shorter hospital stay.

Skin to skin contact

This makes his/her body functions well. It can be used for infants who are on CPAP or even ventilators **(Refer to Chapter 39).**

Milk Expression

As long as the mother expresses her milk, she will continue to produce milk. However, infant's suckling is a much potent stimulant for milk production than milk expression. Assure the mother that the amount of expressed milk increases by practice.

Frequency of milk expression

- If the infant does not nurse immediately postpartum, the mother should begin pumping within 6 hrs of the infant's birth. Starting early makes a difference for future milk production. It is important to get at least eight good nursing and/or pumping sessions per 24 hrs. The mother should pump at least once during the night. Avoid going longer than 5-6 hrs without pumping during the first few months.
- The mother should empty the breast as thoroughly as possible at each session (even if the infant will not take it all). The mother should keep pumping the breast gently for 2-5 minutes after the last drops of milk just to stimulate milk production.

Stimulation of the milk let down (oxytocin reflex)

- The mother should sit comfortably and relax. Skin to skin contact before or during milk expression greatly facilitates milk flow.
- The mother can use warm compresses or warm shower.
- The mother should be informed to:
  - Stimulate the nipples by gentle rubbing and pulling.
  - Gently massage, stroke and shake of the breast.
  - Interrupt milk expression several times to massage the breasts.

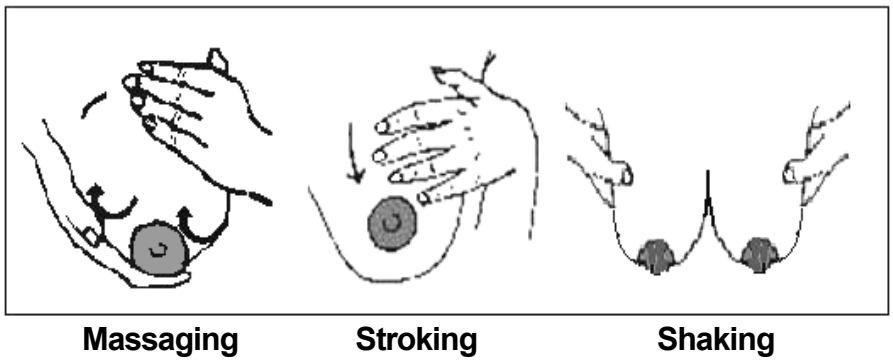


Figure (19-6): Stimulation of breast-milk let down

- Other factors which can stimulate the oxytocin reflex:
  - Infant may be nursing on the other side to stimulate the let down.
  - If the infant is not present, the mother can put his/her picture, smell his/her clothes or think of him/her.

- If milk supply starts to decrease, consider the use of galactagogues, such as fenugreek, fennel, metoclopramide (30-45 mg/day in 3-4 divided doses for 7-14 days then taper over 5-7 days) or domperidone (10-20 mg 3-4 times/days for 3-8 weeks).

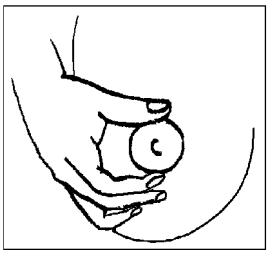
N.B.: Stimulating the milk let down should be done whether the mother will express by hand or will use a pump.

Methods of milk expression

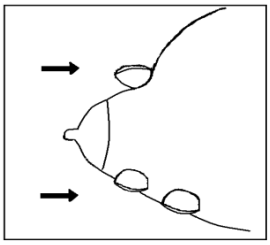
Hand expression

It is more comfortable, natural, convenient, always available and free. Inform the mother to:

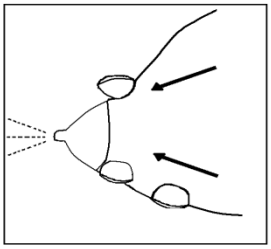
- Wash hands thoroughly.
- Hold the container under the nipple and areola.
- Position the thumb and first two fingers about 1 to 1 ½ inches behind the nipple.
- Place the thumb above the nipple and the other fingers below, in a 12 O'clock and 6 O'clock position.



- Push the breast up and backwards straight into the chest wall.



- Roll the thumb and fingers forwards. The mother shouldn't slide her fingers over the skin but should slide the fingers and the skin as one unit over the underlying ducts.



- Rotate the thumb and fingers position to milk the other ducts.

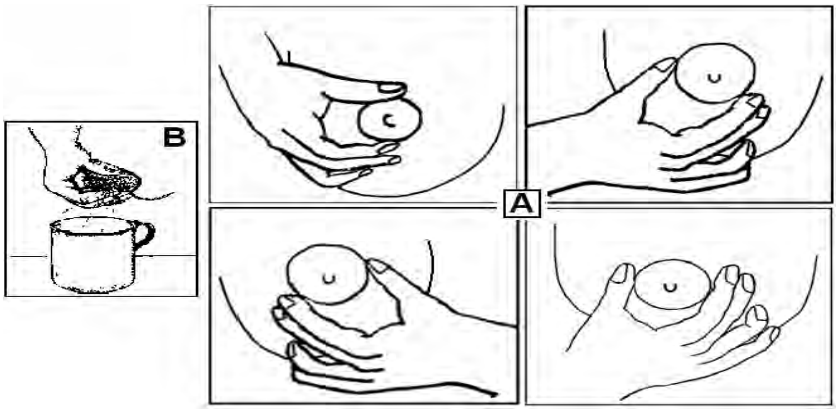


Figure (19-7): Hand expression of breast milk

A) Thumb and fingers positions for breast milk expression, B) milk let down

N.B.: The flow of milk will vary. During the first few minutes it may drip out slowly, and then squirt forcefully after there is a milk ejection. This pattern will repeat several times while expressing each breast. Switch the breasts when milk flow lessens.

Mechanical expression (breast pumps)

Breast pumps should be sterilized once a day in boiling water then wash with soap and hot water for subsequent use.

Manual breast pumps

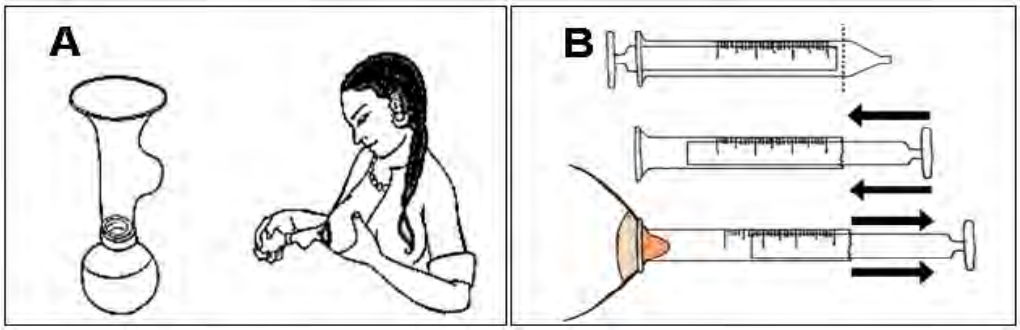


Figure (19-8): Manual breast pump

A) Rubber bulb, B) Syringe breast pump

- Rubber bulb (bicycle horn) is not recommended as it allows bacterial contamination. It also lacks pressure control, renders low milk yields, and could cause pain or damage to the nipples.
- Syringe breast pumps: cut the end of a big syringe (50 ml) near the nozzle with a sharp knife. The piston is removed from the blunt end and reintroduced through the newly cut sharp end. The mother puts the blunt end over her areola and does rapid to and fro movements with the piston. The pressure should be adjusted to maintain a good flow without pain.
- Many other types of manual pumps are available in the market.

Battery operated, electric breast pumps

- They are effective but expensive.

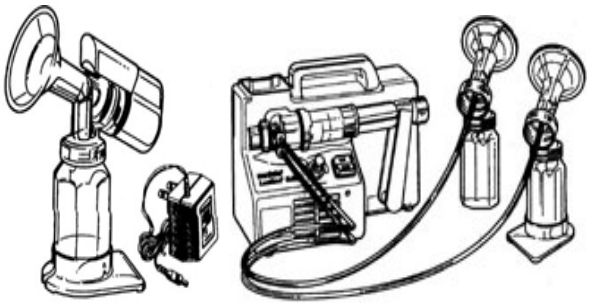


Figure (19-9): Electric breast pumps

Transporting the expressed breast milk

Fresh, refrigerated or frozen milk can be packed in an insulated cooler in ice or blue ice (for up to 24 hrs). If the frozen milk is thawed during transportation it should be used and not refrozen. For this reason, it is usually better to wait to freeze the milk once it has reached its final destination.

Storage of the expressed breast milk

Choice of containers

Glass is usually considered the best choice for freezing milk because the components of milk are better preserved in glass. Second choice would be **hard**, clear plastic containers.

Storage guidelines

Milk storage guidelines are different for premature or hospitalized infants, as these infants are more at risk for infection **(Table 19-1).**

Table (19-1): Storage guidelines of the expressed breast milk

Freshly expressed milk: refrigerate, as soon as possible, if not using within 4 hours.	
• Room temperature (24-26ºC)	4 hours
Refrigerated milk: store at back; do not store in-door	
• Refrigerator (fresh milk)	48 hours
• Refrigerator (thawed milk)	24 hours
Frozen milk: store at back; do not store in door; do not refreeze	
• Freezer compartment inside refrigerator door	Not recommended
• Freezer compartment with separate door	3 months
• Deep freeze (not attached to refrigerator)	6 months

Precautions

- Store in amounts equal to what the infant will take in one feed.
- Label each container with name, date, time, and amount.
- Refrigerate or freeze immediately after expressing. Milk that is in the refrigerator may be frozen within 48 hrs.

- Serve the milk to the infant warm by putting it under running warm water or in a bowel of warm water. Excessive heat modifies or destroys enzymes and proteins. Never use a microwave oven to defrost or warm milk.
- The fresher the better, however colostrums should be provided to the infant whenever the infant starts feeds. The mother can take her pump kit to the hospital to pump fresh milk for infant's next feeding. The longer the milk is stored, the more it loses in nutrient and immunological content.
- The cream will rise to the top of the milk during storage. Gently swirl milk (do not shake) to mix before offering to the infant.
- Thawing Milk:
  - Thaw frozen milk by (slow defrost) overnight in refrigerator.
  - Defrost the total amount, as butterfat separates during the freezing process.
  - Once thawed, breast milk should be used within 24 hrs.
- If infant does not finish milk, the unused warmed milk should be discarded at the end of the feeding.

Methods of giving the expressed breast milk to the infant

Nasogastric tube

Lipids can adhere to the lumen of the feeding tube, the greatest lipid loss occurs with continuous slow infusions. If infusion pumps are used, the syringe should be tilted upwards at 25-45 degree angle, thus the lipids rise to the top of the syringe and are infused first.

Cup feeding

It has provided a safe alternative method of feeding preterm and low birth weight infants until they are strong and/or mature enough to be fully breast-fed.

Cup feeding can be initiated when the infant starts swallowing. Infants with neurologic problems are also often able to sip or lap milk from a cup. It should not be given to any newborn that is likely to aspirate (poor gag reflex, generally lethargic, marked neurologic deficits).

Advantages of cup feeding

- It reduces the need for nasal and oral gastric tubes.
- It enables parents to resume feeding of their infant at the earliest possible time.
- The infant paces his own intake both in time and quantity.
- It requires little energy expenditure for the infant.
- It stimulates appropriate tongue and jaw movements that facilitate breastfeeding later.
- It stimulates the production of saliva and lingual lipases resulting in more efficient digestion.
- Antibacterial factors in breast milk may have a protective effect, even in the infant's mouth.

Procedure for cup feeding

- Wrap the infant, so the cup will not be knocked.

- Support the infant in an upright sitting position.
- Fill the 30 ml medicine cup at least half full with breast milk.
- Place the rim of the cup at the outer corners of the upper lip, resting gently on the lower lip with the tongue inside the cup.
- Tip the cup, so the milk is just touching the infant's lips. Do not pour the milk into the infant's mouth.
- The infant usually laps the milk, or may sip it.
- Allow time for the infant to swallow.
- Leave the cup in position during the feed; that is, while the infant rests, do not move the cup from this position.
- Stop to burp the infant from time to time.

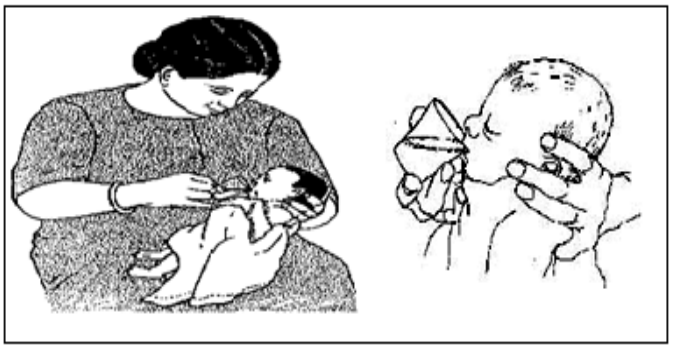


Figure (19-10): Cup feeding

Dropper/syringe

Make sure that it is directed to the side of the mouth, not backwards in the mouth to avoid choking. Push 0.25-0.5 ml and wait till the infant swallows. Burp the infant when he refuses to swallow. Use one syringe for each feed.

Nursing supplementer (lactational aid)

The manufactured lactational aid consists of a milk container hung on the mother's neck. Two thin tubes come out of this container; which are taped each to the mother’s breast so that the tip of the tube is on the tip of the nipple. The infant takes both the areola and the tube bringing milk in his mouth. The infant benefits from the good flow of milk without so much effort. Meanwhile, the mother benefits from each suck to stimulate her milk production.

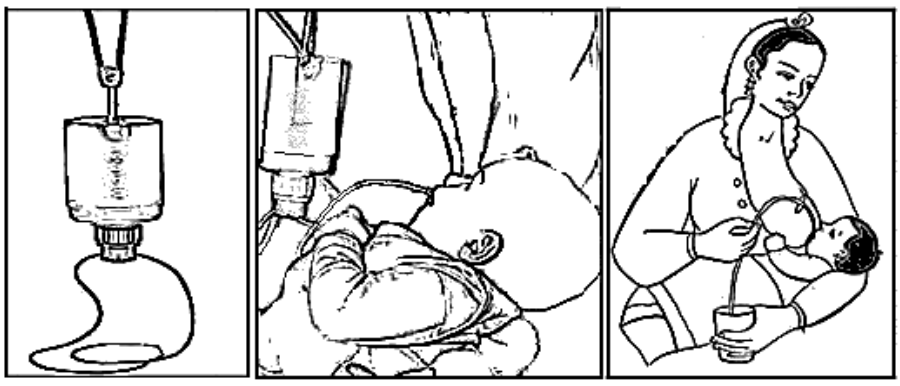


Figure (19-11): Lactational aid

To mimic the manufactured lactational aid, milk can be put in a cup and a nasogastric tube (ryle's tube) of an appropriate size can be dropped in it with the other end attached to the mother's breast.

Finger feeding

The thin tubing of the lactational aid is taped on the finger. It can be used to prime the infant before transferring him to the breast. It shouldn't be applied for a long time as some infants get used to it.

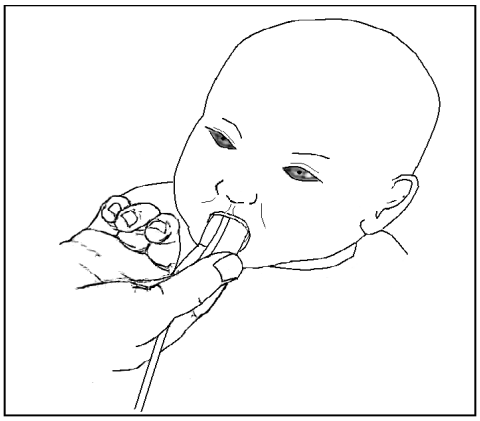


Figure (19-12): Finger feeding

Bottle feeding

It should be avoided, as many infants can refuse the breast.

Transition to the Breast

To facilitate transition to the breast:

- If suckling-swallowing is not yet well developed (occurs at 32-34 weeks' gestation), practice non-nutritive sucking (NNS) by making the infant suckle on a drained breast or on a partially drained breast.
- Apply frequent skin to skin contact especially before feeding.

Breastfeeding after Infant's Discharge

- **The mother:** should be well trained about the correct positioning and latching on.
- **The infant:** preterm infants are characterized by sleepiness, minimal hunger cues, weak suckling, inability to open the mouth widely, lack of coordination between suckling, swallowing, and breathing, and easily tiring due to a low muscle tone.
- Ask the mother to give direct breastfeeding, and if not adequate, to continue by providing expressed breast milk.
- Providing feeding on demand (maximum every 2 hrs) might be useful till cue based feeding develops, usually at their corrected term age.
- Apply kangaroo mother care as long as possible.
- When pumping during the night, milk yield tends to be better if mother pumps when she naturally awakens (to go to the bathroom or because her breasts are uncomfortably full) than if set an alarm in order to pump.
- The mother can add newly expressed milk to refrigerated milk but not to frozen milk.

The Baby Friendly Hospital Initiative

The Baby-Friendly Hospital Initiative (BFHI) launched in 1991, is a global program sponsored by the World Health Organization (WHO) and The United Nations International Children's Emergency Fund (UNICEF) to encourage and recognize hospitals and birthing centers that offer an optimal level of care for lactation.

The ten steps to successful breastfeeding

1. Have a written breastfeeding policy that is routinely communicated to all health care staff.
2. Train all health care staff in skills necessary to implement this policy.
3. Inform all pregnant women about the benefits and management of breastfeeding.
4. Place babies in skin-to-skin contact with their mother immediately following birth and allow them to remain skin-to-skin with their mother, without interruption, until the completion of the first breastfeeding. Encourage mothers to recognize when their babies are ready to breastfeed, offering help if needed.
5. Show mothers how to breastfeed, and how to maintain lactation even if they should be separated from their babies.
6. Give newborn babies no food or drink other than breast milk, unless medically indicated.
7. Practice rooming-in (allow mothers and babies to remain together), 24 hrs a day.
8. Encourage breastfeeding on cue.
9. Give no artificial teats or pacifiers (also called dummies or soothers) to breastfeeding babies.
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or clinic. Assessment of early post-discharge follow-up and referral system.

The International Code of Marketing of Breast Milk Substitutes

- The International Code of Marketing of Breast-Milk Substitutes is included in the Baby Friendly Hospital Initiative. The “Code” underlines the minimum requirements for the protection, promotion and support of breastfeeding by suggesting regulations on the marketing practices of those companies producing breast milk substitutes, feeding bottles, teats/nipples, and related equipment.
- The “Code” covers all breast milk substitutes. These are products which are marketed in a way which suggests they should replace breastfeeding, even if the product is not suitable for that purpose. This may include: baby formulas, follow-on formulas, baby foods, teas, and juices. The “Code” requires companies producing such products to abide by the following regulations:
  - No advertising of products under the scope of the code to the public.
  - No free milk substitute samples for mothers.
  - No promotion of products in health care facilities, including the distribution of free or low-cost supplies.
  - No words or pictures idealizing artificial feeding, including pictures of babies on products.

- Information to health workers should be scientific and factual.
- All information on artificial feeding, including the labels, should explain the benefits of breastfeeding and all costs and hazards associated with artificial feeding.

Acceptable Medical Reasons for the Use of Breast Milk Substitutes *(WHO, 2009)*

Infant conditions

Infants who should not receive breast milk or any other milk except specialized formula

- Infants with classic galactosemia: a special galactose-free formula is needed.
- Infants with maple syrup urine disease: a special formula free of leucine, isoleucine and valine is needed.
- Infants with phenylketonuria: a special phenylalanine-free formula is needed (some breastfeeding is possible, under careful monitoring).

Infants for whom breast milk remains the best feeding option but may need other food in addition to breast milk for a limited period

- Infants born weighing less than 1500 gm (VLBW infants)
- Infants born at less than 32 weeks of gestation (very preterm)
- Newborn infants who are at risk of hypoglycaemia due to impaired metabolic adaptation or increased glucose demand (e.g., preterm and SGA infants or infants who have experienced significant intrapartum hypoxic/ischemic stress, those who are ill and those whose mothers are diabetic), if their blood glucose fails to respond to optimal breastfeeding or breast milk feeding

Maternal conditions

Mothers who are affected by any of the conditions mentioned below should receive treatment according to standard guidelines.

Maternal conditions that may justify permanent avoidance of breastfeeding

- HIV infection: if replacement feeding is **A**cceptable, **F**easible, **A**ffordable, **S**ustainable and **S**afe (AFASS). Otherwise, exclusive breastfeeding for the first six months is recommended. Mixed feeding is not recommended.

Maternal conditions that may justify temporary avoidance of breastfeeding

- Severe illness that prevents a mother from caring for her infant, for example sepsis.
- Herpes simplex virus type 1 (HSV-1): direct contact between lesions on the mother's breasts and the infant's mouth should be avoided until all active lesions have resolved.
- Maternal medication:
  - Sedating psychotherapeutic drugs, anti-epileptic drugs and opioids and their combinations may cause side effects such as drowsiness and respiratory depression and are better avoided if a safer alternative is available.

- Radioactive iodine-131 is better avoided, given that safer alternatives are available, a mother can resume breastfeeding about two months after receiving this substance.
- Excessive use of topical iodine or iodophors (e.g., povidone-iodine), especially on open wounds or mucous membranes, can result in thyroid suppression or electrolyte abnormalities in the breastfed infant and should be avoided.
- Cytotoxic chemotherapy requires that a mother stops breastfeeding during therapy.

Maternal conditions during which breastfeeding can still continue, although health problems may be of concern

- Breast abscess: breastfeeding should continue on the unaffected breast; feeding from the affected breast can resume once treatment has started.
- Hepatitis B: infants should be given hepatitis B vaccine, within the first 48 hours or as soon as possible thereafter.
- Hepatitis C.
- Mastitis: if breastfeeding is very painful, milk must be removed by expression to prevent progression of the condition.
- Tuberculosis: mother and baby should be managed according to national tuberculosis guidelines.
- Substance use:
  - Maternal use of nicotine, alcohol, ecstasy, amphetamines, cocaine and related stimulants has been demonstrated to have harmful effects on breastfed babies.
  - Alcohol, opioids, benzodiazepines and cannabis can cause sedation in both the mother and the baby. Mothers should be encouraged not to use these substances, and given opportunities and support to abstain.

Chapter 20

Nutrition of At-Risk Infant

Nutrition of At-Risk Infant

Enteral Nutrition

Nutritional support can be accomplished enterally, parenterally, or with a combination of both methods. Whenever it is safe and tolerable, enteral feeding is the natural and preferred route of nutrition as the structural and functional integrity of the GI tract is dependent upon the provision of enteral feeding.

Providing appropriate nutritional support remains a significant challenge in infants with health problems. Preterm infants, especially those with extremely low birthweights (<1,000 gm), require special attention because of several problems, some of them unique to these small infants. These problems include immaturity of bowel function, inability to suck and swallow and high risk of illnesses that may interfere with adequate enteral feeding (e.g., NEC, RDS and PDA).

A change in feeding pattern is often an early sign of a problem in a neonate. Most seriously ill neonates do not feed well and often will not tolerate feeding. These neonates must be managed carefully with IV fluids or parenteral nutrition (PN) until stabilization.

When to Start Feeding?

- Start feeding as soon as it is medically possible.
- Evaluate the ability to feed the baby daily.
- In general, enteral feeding for preterm infants is started in the first 3 days of life with the objective of reaching full enteral feeding in 2-3 weeks. For the stable, larger premature neonate (>1,500 gm), the first feeding may be given within the first 24 hrs of life.

Contraindications for Early Feeding

- Significant hypoxic/asphyxic event or acidosis
  - Perinatal depression, indicated by an Apgar score of 3-5 at 5 minutes, or seizures.
  - Neonates who have experienced shock or asphyxia may have an ischemic injury to the intestines that will require 2-3 days or more for recovery before small feedings can be attempted.
- Severe hypotension and hemodynamic instability, (i.e. the use of pressor agents).
- Severe respiratory distress: infants with sustained respiratory rates >60 /minute should not be fed orally; they should be maintained with either gavage feedings for respiratory rates between 60-80/minute, and NPO with IV fluids for more severe tachypnea.
- Symptomatic sepsis.
- Suspected or confirmed NEC.
- Evidence of intestinal obstruction/perforation or paralytic ileus.
- Presence of symptomatic PDA.
- Treatment with indomethacin for PDA (controversial).

Indications for Feeding

- Presence of bowel sounds
- Lack of abdominal distension
- Stable blood pressure
- Stable electrolytes (as electrolyte abnormalities affect gastric motility)
- Stable respiratory status

Initiating and Advancing Enteral Feeds

Trophic feeding (non-nutritive feeding)

Trophic feeding, also known as minimal enteral nutrition (MEN), gut-priming or hypocaloric feeding, refers to the practice of feeding very small amounts of enteral nourishment for the purpose of induction of gut maturation (trophic effect on the gut mucosa), rather than nutrient delivery.

Early initiation of enteral feedings is not associated with increased incidence of NEC. However, rapid advancement of feeds and use of hyperosmotic formulas have been associated with NEC.

Indications

- Premature infants with extremely low birth weights (<1,000 gm).
- Infants recovering from NEC.
- Infants who have been NPO for an extended period of time.

N.B.: Mechanical ventilation or the presence of UAC (per se) is not a contraindication for initiation of trophic feedings.

Contraindications

See contraindications for feeding

Strategy

- Minimal enteral nutrition should be started after ensuring hemodynamic stability in preterm neonates. This is usually possible by day 2 to 3 of life.
- Use colostrum/breast milk or full strength term or preterm formulas (20 kcal/oz); begin at a volume of one ml every 6 hrs for 2 days, then one ml every 4 hrs for another 2 days, and then advance slowly to reach 10-20 ml/kg/day divided into equal aliquots and administered by gavage feeding every 3-6 hrs as slow bolus feeds.
- Trophic feeds should be used until the infant becomes clinically stable enough for feeding advancement.
- The transition to nutritive enteral feedings then can proceed slowly, with continuous assessment of feeding tolerance (see later) to avoid complications such as NEC.

N.B.: Expressed breast milk (EBM) is the preferred milk for MEN.

Example

Day of life # 1-2	NPO
Day of life # 3-4	1 ml every 6 hrs
Day of life # 5-6	1 ml every 4 hrs
Thereafter	Advance slowly to reach 10-20 ml/kg/day divided into equal aliquots every 3-6 hrs

Monitoring

The infant should be monitored for any evidence of feeding intolerance including abdominal girth, gastric residuals or clinical signs of NEC.

Advantages

- Improve GI motility
- Promote GI hormones and enzyme secretion
- Improve feeding tolerance
- Allow earlier progression to full enteral feedings
- Reduce days on parenteral nutrition
- Reduce incidence of sepsis
- Lower incidence of cholestasis
- Improve bone mineralization
- Improve growth and weight gain

Standard feeding advancement (nutritive feeding)

Goal

- The goal of nutritive feeding is to supply the required nutrients and calories to achieve the expected weight gain. Matching intrauterine growth rate is the ultimate goal.
- Neonates lose almost 10% of their birthweights within the first week of life. Following this drop in weight, the expected daily weight gain varies from 20-30 gm/day according to the neonate's gestational age. For the average-growth of a preterm infant, expected weight gain is approximately 15-20 gm/kg/day.

Energy

- Caloric requirements for the healthy term infant average 110 (100-120) kcal/kg/day.
- Preterm infants have limited total body energy stores, so providing adequate early energy resources is more crucial than for full-term infants. Enteral intakes of 120-130 kcal/kg/day have been recommended.
- Infants with severe and/or prolonged illness (e.g., sepsis, BPD) have higher energy requirements (up to 130-150 kcal/kg/day).

Strategy

- In general, if bolus feedings are tolerated without emesis or residuals, infants weighing <1,200 gm are fed every 2 hrs and those weighing more are fed every 3 hrs.
- The recommended volume goal for feeding is 140-160 ml/kg/day. As enteral volumes are increased, the rate of any IV fluid is reduced accordingly, so that the total daily fluid volume remains the same.
- Weight-specific guidelines are based on birth weight and gestational age (GA):
  - Weight: <1,200 gm; GA <30 weeks.
    - Volume: 1-2 ml/ kg every 2 hrs, and advance by 10-20 ml/kg/day.
    - Type: EBM, term or preterm formulas (20 kcal/oz). Once full feedings of 20 kcal/oz are tolerated, consider preterm formulas (24 kcal/oz), or adding human milk fortifier (HMF) to breast milk (if available).
  - Weight: 1,200-1,500 gm; GA <32 weeks
    - Volume: 1-2 ml/kg every 3 hrs, and advance by 10-20 ml/kg/day.
    - Type: EBM, term or preterm formulas (20 kcal/oz). Once full feedings of 20 kcal/oz are tolerated, consider preterm formulas (24 kcal/oz) or adding HMF to breast milk (if available).
  - Weight: 1,500-2,000 gm; GA 32-36 weeks
    - Volume: 2.5-5 ml/kg every 3 hrs, and advance by 10-20 ml/kg/day as tolerated.
    - Type: breast milk or preterm formulas.
  - Weight: 2,000-2,500 gm; GA >36 weeks.
    - Volume: 5 ml/kg every 3 hrs, and advance by 10-20 ml/kg/day as tolerated.
    - Type: breast milk or term formula.

Another suggested enteral feeding strategy for stable, growing preterm infants is presented in **(Table 20-1)**; this should be individualized based on the infant's clinical status/severity.

Table (20-1): Suggested guidelines for feeding the preterm infants

Day of life	Type of milk	Volume	Frequency	Increases
Body weight <1,000 gm				
3-9	EBM, term, or preterm formula* (20 kcal/oz)	1-2 ml/kg	6-12 hrs	None
10-16	EBM, term, or preterm formula* (20 kcal/oz)	2 ml/kg	2 hrs	15 ml/kg/day
17-19	EBM, term, or preterm formula* (20 kcal/oz)	8-9 ml/kg	2 hrs	20 ml/kg/day
20-21	Fortified EBM* or preterm formula (24 kcal/oz)	12-13 ml/kg	2 hrs	For increasing weight
22-23	Fortified EBM* or preterm formula (24 kcal/oz)	12-13 ml/kg	2 hrs	For increasing weight
Body weight 1,001-1,200 gm				
2-6	EBM, term, or preterm formula* (20 kcal/oz)	3-5 ml/kg	6 hrs	None
7-11	EBM, term, or preterm formula* (20 kcal/oz)	2 ml/kg	2 hrs	20 ml/kg/day
12-14	EBM, term, or preterm formula (20 kcal/oz)	8-9 ml/kg	2 hrs	20 ml/kg/day
15	Fortified EBM* or preterm formula (24 kcal/oz)	12-13 ml/kg	2 hrs	For increasing weight
17	Fortified EBM* or preterm formula (24 kcal/oz)	12-13 ml/kg	2 hrs	For increasing weight
Body weight 1,201-1,500 gm				
2-6	EBM, term, or preterm formula* (20 kcal/oz)	3-5 ml/kg	6 hrs	None
7-11	EBM, term, or preterm formula* (20 kcal/oz)	2 ml/kg	3 hrs	20 ml/kg/day
12-14	EBM, term, or preterm formula* (20 kcal/oz)	8-9 ml/kg	3 hrs	20 ml/kg/day
15	EBM, term, or preterm formula* (20 kcal/oz)	12-13 ml/kg	3 hrs	For increasing weight
17	Fortified EBM* or preterm formula (24 kcal/oz)	12-13 ml/kg	3 hrs	For increasing weight
Body weight 1,501-2,000 gm				
1-3	EBM, term, or preterm formula* (20 kcal/oz)	5 ml/kg	6 hrs	None
4-5	EBM, term, or preterm formula* (20 kcal/oz)	3 ml/kg	3 hrs	None
6-9	EBM, term, or preterm formula* (20 kcal/oz)	3 ml/kg	3 hrs	20 ml/kg/day
10-12	Fortified EBM* or preterm formula (24 kcal/oz)	12-14 ml/kg	3 hrs	20 ml/kg/day
13	Fortified EBM* or preterm formula (24 kcal/oz)	18-20 ml/kg	3 hrs	For increasing weight

*Means to be used if available, EBM: Expressed breast milk.

Composition of Enteral Feedings

Breast milk

- The importance of breast milk in the management of preterm infants is well recognized and has been reported to improve host defenses, digestion and absorption of nutrients, gastrointestinal function, neurodevelopmental outcomes, and enhanced maternal psychological well-being. GI effects of feeding breast milk include enhanced intestinal lactase activity, more rapid gastric emptying, and a decrease in intestinal permeability early in life, compared with preterm formula.
- The ideal enteral diet for almost all term newborn infants is breast milk (20 kcal/oz) providing sufficient energy, protein, fat, carbohydrate, micronutrients, and water for normal growth.
- Whenever available, the mother's own preterm breast milk is the milk of choice for her preterm infant. Compared with term breast milk, preterm breast milk has higher levels of energy, lipids, protein, nitrogen, fatty acids, some vitamins, and minerals (such as sodium, chloride, and magnesium). In addition, preterm breast milk has higher levels of immune factors, including cells, immunoglobulins, and other anti-inflammatory elements than term breast milk.
- Hindmilk feeding; the lipid and caloric content of hindmilk is greater than that of foremilk. Some researchers recommend that the hindmilk fraction of expressed breast milk to be predominantly used for feeding of preterm VLBW infants.
- Human milk fortifier (HMF) is added to the breast milk to increase energy, protein, and essential minerals (calcium, phosphorus, zinc, and cupper) to a level that is more appropriate for preterm infants.
  - HMF is used in premature infants with birth weights <1,500 gm and should be considered in those with birth weights <2,000 gm.
  - The addition of HMF is started once preterm infants are tolerating 100 ml/kg/day of breast milk and continued for up to the time of discharge or at a weight of 2,000 gm.
  - Example:
    - Fortify with 1 packet HMF, to each 50 ml breast milk when baby receives 100 ml/kg (22 kcal/oz)
    - Fortify with 1 packet HMF, to each 25 ml breast milk when baby receives 150 ml/kg (24 kcal/oz)
  - The fortified breast milk is prepared daily and stored at refrigerator temperature. For ELBW infants, the milk should be stored in small aliquots for thawing or warming of small feeding volumes in order to minimize wasting the maternal milk supply.

Formulas

- Cow's milk-derived formulas have been designed to mimic human milk, to provide biologically available protein mixtures with appropriate protein/energy ratio for normal growth.
  - Term formulas (20 kcal/oz) are adequate to meet the needs of term infants with an intact gastrointestinal tract and 'normal' fluid requirements.

- Preterm formulas
  - Designed to meet the nutritional and physiologic needs of preterm infants, they contain a higher calcium and phosphorus ratio, increased protein, vitamins, electrolytes and caloric content sufficient for the growth of the premature infant.
  - Preterm formulas are available in 2 preparations:
    - 20 kcal/oz formulas; and
    - 24 kcal/oz formulas
  - They are indicated in preterm infants <1,800-2,000 gm.
  - Start with preterm formula (20 kcal/oz) and advance to preterm formula (24 cal/oz), as tolerated, at 100 ml/kg of volume. This volume is then maintained for approximately 24 hrs before the advanced schedule is resumed.
  - Preterm formulas are given until the infants weigh 2,000-2,500 gm.
  - At discharge, premature infants are usually fed either breast milk or term formula (20 kcal/oz). Preterm post-discharge formula [transitional formula (22 kcal/oz), if available] may lead to better nutritional outcomes, probably because of its higher energy, calcium, and phosphate content. Supplementation may be used until 9-12 months corrected age.

- Specialized formulas have been designed for a variety of congenital and neonatal disorders (e.g., milk protein allergy, malabsorption syndromes, and several inborn errors of metabolism). Soy derived formulas are not appropriate for preterm infants because of the poorer quality of protein and lower calcium and zinc accretion rates seen with these formulas.
- Caloric-enhanced feedings: when feeding volumes cannot be tolerated or fluid intake must be limited (e.g., infants with BPD, or renal failure), caloric delivery and nutritional support can be maintained by increasing the caloric density of feedings. This can be done by adding HMF, glucose polymers, microlipids, corn oil, or medium chain triglycerides (MCT) oil to the formula or milk as tolerated (not to exceed maximum caloric density of 30 kcal/oz).

Routes of Feeding

Nasogastric/orogastric feedings

Nasogasteric tubes are used more than orogasteric tubes since orogasteric tube is more difficult to secure.

Indications

Can be used in infants who are unable to nipple feed, such as:

- Premature infants 32-34 weeks' gestation according to the ability to coordinate suck-swallow-breathe pattern
- Infants with neurological impairment (e.g., hypotonia, or encephalopathy)

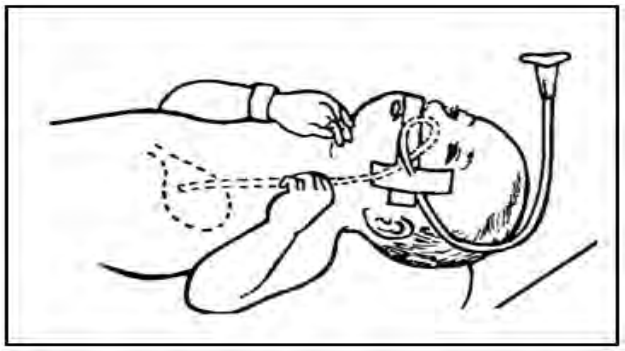


Figure (20-1): Nasogasteric feeding

- Maxillofacial abnormalities
- Infants with respiratory distress

Procedure

- Use a polyethylene orogastric or nasogastric tube (6Fr or 8Fr).
- Turn the infant's head to the side and measure the length from the xiphoid to the ear lobe and then to the nose.
- Mark that length on the feeding tube using a small piece of tape.
- Pass the tube through the nose or mouth with the neck in the flexed position.
- Inject air through the tube while auscultating the stomach for bubbling; then gently aspirate the stomach content. If you cannot hear any bubbling, tube may be in the trachea. Therefore, do not feed infant until you are certain that tube is in stomach.

Transpyloric feedings

Indications

- Infants at increased risk of aspiration (e.g., severe reflux or delayed gastric emptying).
- May be routinely used in extremely low birth weight (ELBW) infants (<1,000 gm).

Procedure

- Insert orogastric tube as described above.
- Measure transpyloric tube 10 cm longer than the orogastric tube.
- Turn patient onto the right side (with left hip up).
- Insert air through the orogastric tube to distend the stomach.
  - 10 ml for infants <1,000 gm.
  - 15-20 ml for infants >1,000 gm.
- Insert the transpyloric tube.
- Wait 10-20 minutes with the neonate on right side and aspirate through the transpyloric tube gently.
- The transpyloric tube is considered to be in a good position if:
  - Aspirate is bilious
  - Aspirate is alkaline

- No air is aspirated

- If it is not in a good position, leave the transpyloric tube open and the orogastric tube closed for up to 4 hrs or until there is a bilious return.
- If unsuccessful within 4 hrs, repeat the entire procedure.

N.B.: Transpyloric tube has to be flexible so that it will not stiffen in the jejunum (silastic or polyurethane tubes are suitable).

Methods of Feeding

Gavage (bolus) feeding

- Premature infants weighing >1,000 gm can generally tolerate gavage feedings up to full feeds.
- Feeding is to be introduced by over 10-20 minutes (by gravity), not to be injected by a syringe.
- Feeding is introduced every 2-3 hrs.
- Measure the gastric residual before each feed.

Continuous drip feeding

- This is indicated in infants with severe gastroesophageal reflux and ELBW neonates (<1,000 gm) and in transpyloric method.
- Use an automated pump.
- The pump rate is set at the desired hourly rate.

Gavage vs. continuous feeding

- Gavage feeding is more physiologic and can promote better gut growth than continuous feeding. Continuous feeding results in better energy retention and growth rate.
- It is advisable to reserve continuous feeds for premature infants with ELBW (<1,000 gm) and those with gastroesophageal reflux.
- It is advisable to start with bolus feedings divided every 2-3 hrs. If feeding intolerance occurs, the time over which a feeding is given is to be lengthened by using syringe pump for 30-120 minutes.
- With gastric feeds, we can use gavage or continuous techniques. However, with transpyloric feeds, we use only continuous technique.

Transition to breast/bottle feedings

Infants who are 34 weeks' gestation and who have coordinated suck-swallow-breathe patterns and respiratory rate <60/minute are candidates for breast/bottle feeds.

- Oral feedings should begin slowly at one feeding per day, then increase as tolerated to once every 8 hrs, then once every third feeding, then every other feeding, and finally to full nipple feedings. Too rapid change to oral feeding may result in weight loss, primarily because the infants tires with feeding and is unable to take in a sufficient amount of food.

- Scheduling oral feedings for parent visits enables them to actively participate in their infant's care.
- Non-nutritive sucking (NNS) may facilitate the tube-to-oral feeding transition. Preterm infants who practice "non-nutritive sucking" on their mothers' emptied breasts or a pacifier during gavage tube feeds gain more weight, have faster gut transit-time, better state organization, and can be released from the hospital earlier.

Supplements

- Premature infants fed expressed breast milk without human milk fortifier should be started on a multivitamin supplement as soon as they are receiving full enteral nutrition.
- Premature infants receiving expressed breast milk with human milk fortifier or standard premature infant formulas do not routinely require additional vitamin supplements.
- Vitamin E supplementation (12 IU/kg/day) is recommended for preterm infants.
- Iron supplementation:
  - Start supplementation of infants at 4 weeks of age once they are tolerating **full enteral** volumes of 24 kcal/oz feedings.
  - Give supplemental dose: 2-4 mg/kg/day for breast milk fed preterm infants for a total of 12 months. If they are fed a premature infant formula, supplementation will depend on the amount of iron in the formula.
- If HMF is unavailable, calcium and phosphorous are needed for premature infants receiving exclusive breast milk feeds. Serum calcium, phosphorus, and alkaline phosphatase levels may be checked regularly to determine any need for supplementation.
- After discharge supplementation should include
  - Vitamin D: the American Academy of Pediatrics (AAP) recommends 200 IU vitamin D per day for all breast milk-fed infants beginning during the first 2 months of life (up to 400 IU/day). This 200 IU can be provided by continuing a daily dose of 0.5 ml of the standard infant multivitamin.
  - Iron, as previously described **(Table 20-2).**

Table (20-2): Post discharge multivitamins and iron supplementation for preterm infants

If infant is primarily on:	What supplements are recommended?	When can the supplements be stopped?
Breast milk	0.5 ml daily (Infant Multivitamin with Iron)	Continue until 12 months of age
Iron-fortified formula	0.5 ml daily (Infant Multivitamin without Iron)	Stop when intake reaches about 500-750 ml

Nutritional Assessment of Enterally-fed Preterm infants

Parameters that should be assessed in enterally-fed preterm infants are listed in **(Table 20-3)**

Table (20-3): Nutrition assessment of the enterally fed preterm infant

Parameter	Frequency of Measurement
Fluid intake (ml/kg/day) • Enteral intake • Parenteral intake	Daily
Nutritional caloric intake (kcal/kg/day)	Daily
Anthropometry	
• Weight (gm) • Length (cm) • Head circumference (cm)	Daily at the same time Weekly Weekly
Biochemical monitoring	
• Serum electrolytes	Twice weekly, then every 2weeks*
• Albumin, BUN	Twice weekly, then every 2 weeks
• Calcium, phosphorus	Twice weekly, then every 2 weeks
• Alkaline Phosphatase	Twice weekly, then every 2 weeks
• Hemoglobin, hematocrit	Weekly
• Reticulocytes	Weekly
Other assessments	
• Renal ultrasound	At 2 months of age (to evaluate for nephrocalcinosis)

*If infant is receiving breast milk or diuretics, BUN: blood urea nitrogen
From: Schanler RJ. Enteral Nutrition for the High-Risk Neonate. In Avery's Disease of the Newborn, 8th Ed. Taeusch HW, Ballard RA, Gleason CA (eds). Philadelphia, Elsevier Saunders, 2005; (68): 1056.

Assessment of Feeding Tolerance

Infants on enteral feeds should have parameters evaluated listed in **(Table 20-4)**.

Table (20-4): Assessment of feeding tolerance

Parameter	Frequency of Measurement
Abdominal girth	Before each feeding
Gastric residual	Before each feeding
Vomiting	Every 8 hrs
Stools	
• Reducing substances	Every 8 hrs
• Heme-guaiac test	Daily
• Consistency	Each stool

Feeding intolerance

Stop enteral feeds if any of the following signs are present:

- Clinical picture of NEC.
- Acute onset of high residuals: >30% of a feed or more than a 1 hr volume, if on continuous feeding.
- Bilious (or greenish) gastric residual.
- Vomiting of the entire feed or vomiting associated with other signs of illness.
- Acute increase of abdominal girth (>2 cm).
- Watery stool with reducing substances greater than 0.5%.
- GI bleeding or heme-positive stool.

Residuals

- Interventions: decrease feeding volumes, slowing the rate of instillation, or slowing the rate of feeding advance.
- The presence of bile or blood in the gastric aspirate warrants further investigation and consideration of NEC **(Refer to Chapter 33).**

Emesis

- Interventions: allowing the feeding to flow more slowly by the use of smaller gavage tube, instilling the feeding over a longer period of time, decreasing feeding volumes and maintaining a prone position.
- Feeding should be stopped if infection, obstruction, metabolic disorders, or increased intracranial pressure are suspected.

Abdominal distention

- Interventions: if the abdomen remains soft and non tender, maintaining a prone position and gentle rectal stimulation with a glycerin suppository help to relieve gas and enable stooling.
- Persistent abdominal distention, pain with palpation, and discoloration of the overlying skin are signs of NEC. An abdominal x-ray examination is indicated in these patients. Abdominal girth is measured every 4-8 hrs to document increased distention.

Watery diarrhea

- Stool culture for bacterial or viral pathogens and stool Clinitest should be performed if the infant also appears ill or if there is blood in the stool.
- In lactose malabsorption, short-term use of a non-lactose containing formula or hydrolysate formula should result in return to normal stools.

Blood in stools

- Discontinue feedings; consider obtaining clotting studies and abdominal radiograph.

Apnea and/or bradycardia

- Interventions to decrease vagal stimulation include changing to an indwelling gavage tube, decreasing feeding volume, and feeding more slowly.

N.B.: If there is any doubt about how well an infant is tolerating feedings, it is best to hold feedings, evaluate the infant and discuss the case with a senior staff member.

The algorithm demonstrated in **(Figure 20-2)**, can be helpful in the management of feeding intolerance.

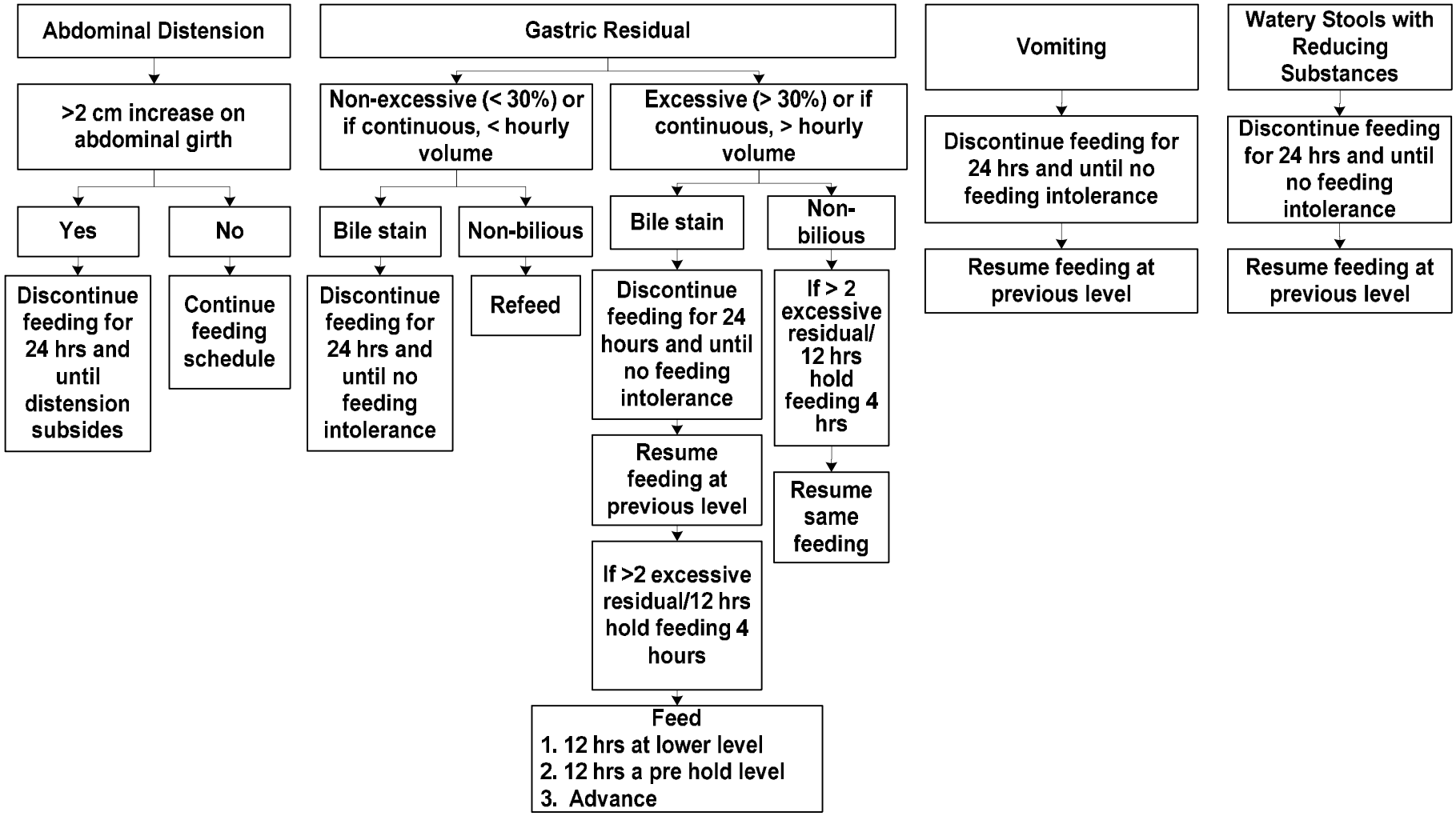


Figure (20-2): Management of feeding intolerance

Parenteral Nutrition in the Newborn

Parenteral nutrition (PN) is a means of providing, either partially or completely, the nutritional requirements for the infant's growth including water, carbohydrate, proteins, fats, electrolytes, vitamins and trace elements. The initial goal of PN is to provide sufficient energy and aminoacids to prevent catabolism and to achieve positive nitrogen balance.

Indications

PN should be considered in neonates who are not on significant enteral feeds for more than 3-5 days or are anticipated to be receiving less than 50% of total energy requirement by day 7 of life.

- Infants with birth weights <1,500 gm: this is often done in conjunction with slowly advancing enteral feeding.
- Infants with birth weights >1,500 gm and for whom significant enteral intake is not expected for >3 days:
  - Infants diagnosed with NEC
  - Post-surgical infants who are unable to feed for an extended period
  - Infants diagnosed with congenital GI anomalies (e.g., gastroschisis, omphalocele, TEF, intestinal atresia, malrotation)

Routes of Administration

- Parenteral solutions may be infused through a peripheral vein or a central vein, usually the superior or inferior vena cava.
- With peripheral PN, the caloric intake is limited because the fluid osmolarity should not exceed 900 mOsm/L resulting in limited carbohydrate (dextrose <12.5%) and amino acids (<3%) concentrations.
- Central PN allows the use of hypertonic solutions but with a higher risk of complications, particularly catheter related sepsis.
- In general central PN is warranted under the following conditions:
  - Nutritional needs exceed the capabilities of peripheral PN (e.g. ELBW)
  - An extended period (>7 days) of inability to take enteral feeding (e.g. NEC and some post operative infants)

Components of Parenteral Nutrition

Fluid volume

(Refer to the fluids and electrolytes section Chapter 15) for the daily fluid requirements at different days of life.

Calories

- Energy must be supplied to cover two major components: energy expenditure and growth.
- Parenteral energy requirements are about 20% less than those required for enteral nutrition because there is no energy lost in the stools.

- The ultimate goal for the daily caloric intake is 90-100 kcal/kg/day for VLBW infants and 105-115 kcal/kg/day for ELBW infants. A parenteral intake of 80-90 kcal/kg/day is most often sufficient for term infants.
- The calories in PN solutions are provided primarily by carbohydrates and fats.
- A non-protein caloric balance between carbohydrates and lipids of 60:40 is required to minimize excess energy expenditure.
- The ideal distribution of calories should be 50-55% carbohydrates, 10-15% proteins (should not exceed 15% of the total caloric intake), and 30-35% fats (should not exceed 50% of the total caloric intake).

Table (20-5): Recommendations for parenteral energy intake for ELBW and VLBW infants

ELBW infants (kcal/kg/day)			VLBW infants (kcal/kg/day)		
Day 0*	**Transition****	**Growing**	**Day 0***	**Transition****	**Growing**
40-50	75-82	105-115	40-50	70-80	90-100

*Recommended caloric intake on the first day of life.
** Period of transition to physiologic and metabolic stability; for most premature neonates, this occurs between 2-7 days.

From: Poindexter B, Denne SC. Parenteral Nutrition. In: Avery's Disease of the Newborn, 8th Ed. Taeusch HW, Ballard RA, Gleason CA (eds). Philadelphia, Elsevier Saunders, 2005; (69): 1062.

Glucose

- Each gram provides 3.4 kcal.
- Glucose infusions rate are expressed in terms of mg of glucose/kg/minute.
- Glucose should be provided to maintain normal plasma glucose levels and to meet the demand for glucose use. This may be achieved with initial glucose infusion rates of 4-6 mg/kg/minute in full term infants, and 4-8 mg/kg/minute in preterm infants (as preterm infants have higher brain-to-body weight and higher total energy needs).
- Advance in daily increments of 1-2 mg/kg/minute to a maximum of 11-12 mg/kg/minute.
- Do not infuse a concentration higher than D12.5W in a peripheral IV line. Use a central line for higher concentrations (up to D25W).
- Extremely preterm infants are frequently glucose intolerant because of relative insulin hypoactivity and poor peripheral glucose utilization; they frequently develop hyperglycemia and glucosuria.
- If hyperglycemia develops, decrease the glucose infusion rate. Insulin (beginning at 0.05 unit/kg/hr) may be required in ELBW infants with persistent hyperglycemia.

N.B.: Do not provide glucose at a rate <3 mg/kg/minute as this is the basal need in premature infants.

Lipids

- Intravenous lipids (Intralipid or Liposyn II) are made up of triglycerides (TG), phospholipids from egg yolk, and glycerol.

- IV lipids are important not only to prevent essential fatty acids (linoleic and linolenic acids) deficiency but also as a significant source of non-protein energy.
- Lipid emulsions are available as either 10% or 20% emulsions. The 20% emulsions are preferred (lower phopholipid concentration resulting in lower plasma levels of TG and cholesterol).
- Each gram lipid provides 9.1 kcal (each ml of lipid emulsion 20% provides 2 kcal/ml).
- Lipids can be started as early as the first day of life. Start with 0.5-1 gm/kg/day and gradually advance by 0.5-1 gm/kg/day, as tolerated, to a maximum of 3 gm/kg/day while monitoring and maintaining normal serum triglyceride levels.
- Administer slowly over 24 hrs via a separate syringe pump and the rate should not exceed 0.12 gm/kg/hr for optimal clearance. Syringes may be changed every 12 hrs to avoid sepsis.
- Limiting IV lipid infusions in infants with sepsis and severe lung disease is often recommended.
- Neonates with hyperbilirubinemia who are on phototherapy often have IV lipid intake restricted to <2 gm/kg/day (especially if bilirubin levels are rising while on photo-therapy).
- Monitor serum triglyceride level and adjust infusion rate to maintain triglyceride level less than 150-200 mg/dl. Levels should be <150 mg/dl when the infant is jaundiced.

Protein

- Crystalline amino acid solutions provide the nitrogen source in PN.
- Each gram provides 4.0 kcal.
- Most newborn infants can be safely started on at least 1.5-2 gm/kg/day, as soon as possible, after birth (in the first 24 hrs) and advanced by 1 gm/kg/day to a target of 3.5 gm/kg/day for infants weighing <1,500 gm (up to 4 gm/kg/day in ELBW infants) and 3 gm/kg/day for infants weighing >1,500 gm.
- If sufficient amounts of non-protein energy are not provided, amino acids are catabolised for energy production. Maintain a non-protein calorie-to-protein ratio of at least 25-30:1 (i.e., Protein/Energy ratio: 3-4 gm/100 kcal).
- Very unstable preterm infants and those with renal insufficiency or shock may need to advance more slowly.
- Monitor BUN: a rising BUN (prerenal azotemia) indicates that the infant is not clearing nitrogen waste; the rate of amino acid infusion should not be increased.

Electrolytes

- Sodium and potassium concentrations are adjusted daily based on individual requirements **(Refer to Chapter 15).**
- Parenteral nutrition solutions require the addition of anions, either as acetate or chloride. Acetate is metabolized to bicarbonate in the body and is added to adjust acid-base status. In general, excess anions should be provided as acetate to prevent hyperchloremic metabolic acidosis.

- Calcium and phosphorus solubility in PN depends on temperature, type and concentration of amino acid, glucose concentration, pH, type of calcium salt, sequence of addition of calcium and phosphorus to the solution, the calcium-to-phosphorus ratio, and the presence of lipid. It is recommended to use PN solutions containing 50-60 mg/dl of elemental calcium and 40-47 mg/dl of phosphorus. A calcium-to-phosphorus ratio of 1.7:1 by weight (1.3:1 by molar ratio) appears to be optimal for bone mineralization.
- Recommended daily intake of electrolytes and minerals for term and preterm infants are listed in **(Table 20-6),** and **(Table 20-7)**.

Table (20-6): Infant daily requirements of electrolytes and minerals

Nutrient	Daily Requirements
Sodium (sodium chloride)	3-4 mEq/kg
Potassium (potassium phosphate or potassium chloride)	2-3 mEq/kg
Calcium (elemental)	50-100 mg/kg depending on size of the infant
Phosphorus (potassium phosphate or sodium phosphate)	1.5-2 mmol/kg (1 mmol of phosphorus = 31 mg)
Magnesium (magnesium sulfate)	0.25-0.5 mEq/kg (1mEq magnesium = 12.15 mg)
Chloride	3-7 mEq/kg

Adapted from: Georgieff MK. Nutrition. In Avery's Neonatology, 6th Ed. McDonald MG, Seshia MK, Mullett MD (eds). London, Lippincott Williams and Wilkins, 2005; (22): 395

Table (20-7): Suggested daily parenteral intakes of electrolytes and minerals for ELBW and VLBW infants

Components (units/kg/day)	Day 0*	Transition**	Growing
Na (mEq) • ELBW infants • VLBW infants	 0-1 0-1	 2-4 2-4	 3-7 3-5
K (mEq)	0	0-2	2-3
Chloride (mEq)	0-1	2-4	3-7
Calcium (mg)	20-60	60	60-80
Phosphorus (mg)	0	45-60	45-60
Magnesium (mg)	0	3-7.2	3-7.2

*Recommended intake on the first day of life.
** Two to seven days of life.

Adapted from: Poindexter B, Denne SC. Parenteral Nutrition. In: Avery's Disease of the Newborn, 8th Ed. Taeusch HW, Ballard RA, Gleason CA (eds). Philadelphia, Elsevier Saunders, 2005; (69): 1062.

Vitamins

- Water- and fat-soluble vitamins are added as a pediatric multi-vitamin solution.
- Pediatric multivitamin preparation is delivered at a standard dosage of 2 ml/kg per day (maximum, 5 ml) in preterm infants and 5 ml in term infants.
- Vitamin A (5,000 IU IM/3 times/week for the first 4 weeks) in ELBW infants who receive respiratory support at age 24 hrs is recommended.

Trace elements

- Zinc is recommended from day one of PN, whereas the other trace elements are generally provided after two weeks.
- Several pediatric trace metal solutions are available that contain zinc, copper, magnesium, and chromium in varying proportions (administered at 0.2 ml/kg per day) and selenium 1.5 µg/dl. Additional zinc is usually needed in preterm infants.
- In infants with cholestasis (direct bilirubin >3 mg/dl), copper and manganese should be discontinued.
- Chromium and selenium should be used with caution and in smaller amounts in the presence of renal dysfunction.
- Parenteral iron is recommended **only** when preterm infants are exclusively nourished by parenteral solutions for the first 2 months of life.

Precautions

- The 3-in-1 PN solutions (glucose, amino acid and lipid mixed in single bag) should not be used for the following reasons:
  - The pH of lipid emulsions is more basic (decreases calcium and phosphorus solubility).
  - 3-in-1 solutions require larger micron filter or no filter (risk for sepsis).
- The continuity of a central line should not be broken for blood drawing or blood transfusion because of the risk of infection.
- Add heparin (0.5-1 unit/ml of solution) to all central lines.
- Medications should not be given in the same line with PN solutions. If necessary PN catheter may be flushed with sterile water or normal saline before infusing medication.
- Because of toxic products of lipid peroxidation, lipid emulsions should be protected from both ambient and phototherapy lights (by wrapping lipid syringes and tubing in aluminum foil).

Potential Complications Associated With PN

Catheter related complications

- Sepsis, local skin infection, sloughs, thrombosis, and chylothorax.
- The most common bacterial pathogens are *staphylococcus epidermidis* and *aureus*. Fungal infections (by *Candida albicans*) can also occur.

Cholestasis

- Hepatic dysfunction is an important complication of long term PN and is manifested primarily as cholestatic jaundice.
- The precise cause is unknown and most likely multifactorial.
- Risk factors include: prematurity, duration of PN administration, duration of fasting, infection, and possible relationship between certain amino acids and hepatic dysfunction.
- Management:
  - Normal bile flow usually returns when PN is stopped and enteral feeding is begun.
  - Start minimal enteral feedings in combination with PN in infants with TPN-associated cholestasis who require continued PN.

Metabolic abnormalities

- Hyperglycemia or hypoglycemia
- Azotemia, hyperammonemia and hyperchloremic metabolic acidosis may occur if aminoacid intakes exceed 4 gm/kg/day.

Metabolic bone disease

- The incidence has been reduced by the use of earlier enteral feedings and central PN, with higher calcium and phosphorus ratios.

Metabolic complications related to lipid emulsion

- Hyperlipidemia and hypertriglyceridemia:
  - Tends to be inversely related to gestational age and postnatal age.
  - Management: decrease lipid infusion to maintain serum triglyceride levels <150-200 mg/dl.
    - Discontinue lipid infusion if serum triglyceride level is >300 mg/dl.
    - Decrease lipid infusion if serum triglyceride >200 mg/dl, and <300 mg/dl.

N.B.: Do not withhold lipids completely for >48-72 hrs (0.5 gm/kg/day will prevent fatty acid deficiency).

- Indirect hyperbilirubinemia: free fatty acids may displace bilirubin from albumin binding sites.
- Sepsis: PN decreases lipoprotein lipase activity. During sepsis episode limit lipid infusion to 2 gm/kg/day if triglyceride level is >150 mg/dl.
- Chronic lung disease may be developed.

Monitoring Infants on Parenteral Nutrition

All infants receiving PN are monitored according to the schedule indicated in **(Table 20-8).**

Table (20-8): Monitoring of infants receiving parenteral nutrition

Parameter	Frequency of measurement
Weight Length Head circumference	Daily Weekly Weekly
Blood gases	Daily until stable, then twice weekly
Serum electrolytes (Na, K)	Daily until stable, then twice weekly
Blood glucose level	1st week: every 6 hrs the first 2 days, then every 12 hrs After the 1st week: daily
BUN and serum creatinine	Weekly
Serum calcium, phosphorus, magnesium and alkaline phosphatase	Weekly
Total and direct bilirubin, ALT, AST	Weekly
Total protein and albumin	Weekly
Serum triglycerides	Weekly
Hematocrit	Weekly
Urine • Volume • Specific gravity and glucose	 Daily First week: each urine sample, then once per shift

BUN; Blood urea nitrogen, ALT; Alanine transaminase, AST; Aspartate transaminase

Advancing to Oral Feedings

The routine expression of breast milk until oral feedings are established is important to help the mother maintain an adequate milk supply. In case of prematurity the change to breast and/or nipple feeding can be started and gradually advanced as soon as the infant exhibits sucking and swallowing reflexes adequate for oral feeding without fatigue or apnea.

Weaning of TPN

Parenteral nutrition, once initiated, probably should be continued until enteral feedings supply approximately 100-110 kcal/kg/day.

Example

Preterm baby: weight 2,000 gm; day 3 of life, started TPN after 24 hrs of life, Prescribe TPN with calculation of GIR and energy.

Requirements

- Total Fluid Intake = 110 ml/kg/day
- Amino Acids = 3 gm/kg/day = 6 gm
- Lipid = 2 gm/kg/day = 4 gm
- Na = 3 mEq/kg/day = 6 mEq
- K = 2 mEq/kg/day = 4 mEq
- Ca = 45 mg elemental/kg/day (4.5 ml/kg/day) = 9 ml
- Vitamins and Trace elements = 1 ml/100 ml of solution = 2 ml

Prescription

- Total Fluid Intake will be 220 ml composed of
  - 20 ml of intralipid 20%
  - Remaining 200 ml composed of:
    - 60 ml aminovenous 10%
    - 40 ml of NaCl 0.9%
    - 2 ml of KCl
    - 9 ml of calcium gluconate
    - 2 ml of soluvit
    - 2 ml vitalipid
    - 2 ml trace elements
    - 83 ml of glucose 20%

Calculations

Total energy intake =

Lipid (2 gm/kg/d × 9 kcal/gm) = 18 Kcal/kg/d

+

Protein (3 gm/kg/d × 4 kcal/gm) = 12 Kcal/kg/d

+

Glucose 83 ml glucose 20% gives 16.6 gm / day (8.3 gm/kg/day × 3.4 Kcal/gm) = 28.2 kcal/kg/day

Total Calories given = 18 + 12 + 28.2 = 58.2 kcal/kg/d

$$\text{GIR} = \frac{3.5 \times 20}{2 \times 6} = 5.8 \text{ mg/kg/minute}$$

Chapter 21

Hyperbilirubinemia

Hyperbilirubinemia

Hyperbilirubinemia is an elevation of serum bilirubin concentration >2 mg/dl. It is presented in one of two forms in the neonate: unconjugated hyperbilirubinemia or conjugated hyperbilirubinemia.

The most prevalent and easily identified symptom of both types is jaundice, which is defined as a yellowish discoloration of skin and mucous membranes. In neonates, clinical jaundice is diagnosed if the total serum bilirubin is ≥7 mg/dl.

Incidence

- 25-50% of all full-term neonates.
- 80% of premature neonates.

Bilirubin Metabolism

Source

Bilirubin is the breakdown product of heme-containing proteins in the reticulo-endothelial system. The major heme-containing protein is the RBC hemoglobin. It is the source of 75% of all bilirubin production. One gram of hemoglobin produces 34 mg bilirubin.

The other 25% of bilirubin is called early-labeled bilirubin which is derived from hemoglobin released by ineffective erythropoiesis in the bone marrow, from other hem-containing tissue proteins (e.g., myoglobin, cytochrome and catalase) and from free heme.

Transport

Unconjugated bilirubin (UCB) is nonpolar and insoluble in water. UCB released into the circulatory system is rapidly bound to albumin. Bilirubin bound to albumin does not pass the blood brain barrier.

Uptake

The bilirubin (dissociated from albumin) crosses the hepatocyte plasma membrane and is bound mainly to cytoplasmic ligandin (Y protein and other binding proteins).

Conjugation

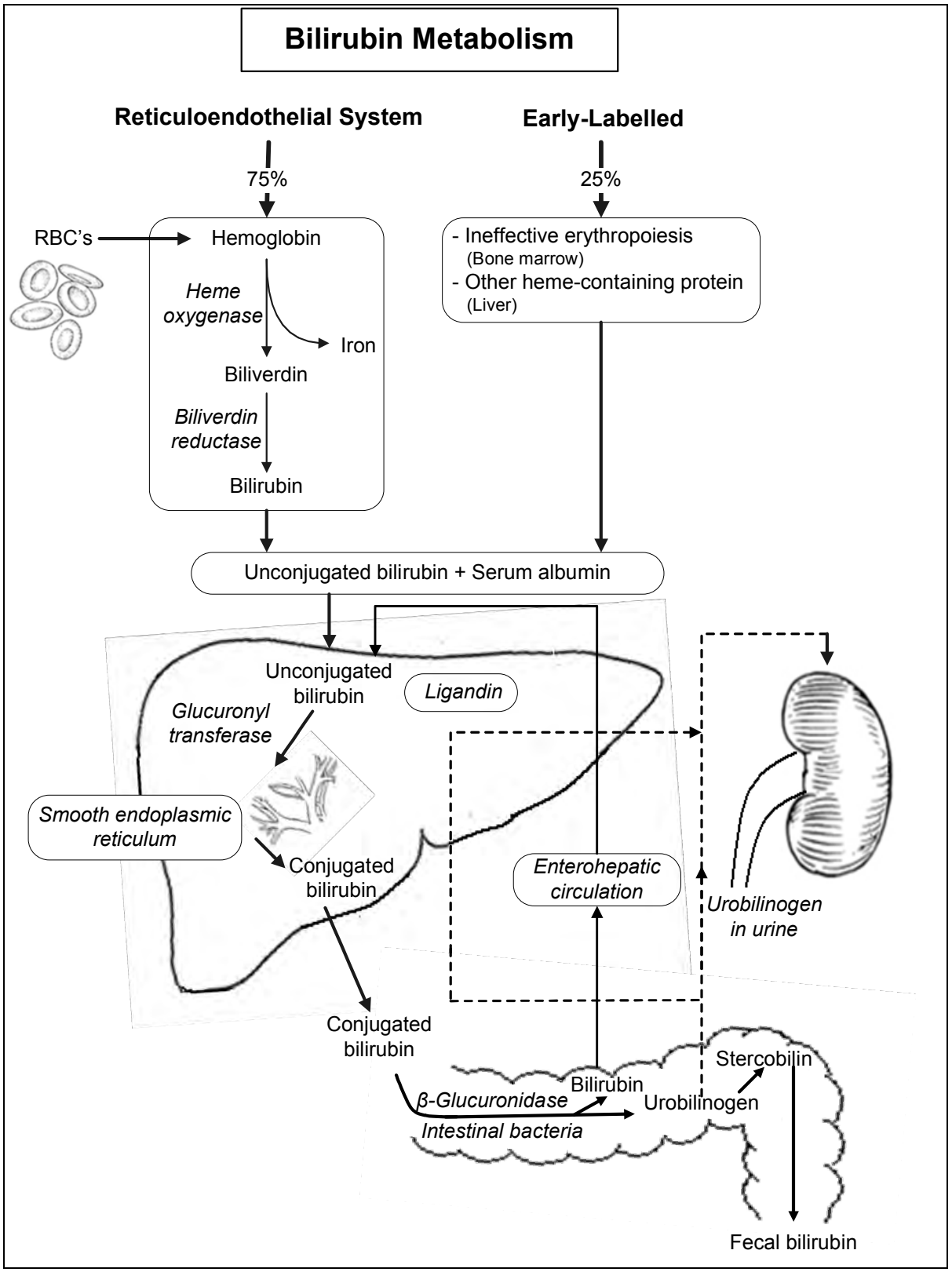
Unconjugated bilirubin (UCB) is converted to the polar, water soluble conjugated bilirubin (CB) in the smooth endoplasmic reticulum by uridine diphosphate glucuronyl transferase (UDPG-T) enzyme. CB is excreted into bile canaliculi against a concentration gradient.

Excretion

Conjugated bilirubin (CB) in the biliary tree enters the gastrointestinal (GI) tract and is then eliminated from the body in the stool. CB is not normally reabsorbed from the bowel unless it is converted back to unconjugated bilirubin (UCB) by intestinal enzyme ß- glucoronidase.

The process by which bilirubin is reabsorbed from the GI tract and delivered back to the liver for reconjugation is called enterohepatic circulation.

Intestinal bacteria can prevent enterohepatic circulation of bilirubin by converting CB to urobilinoids which are not substrates for ß-glucoronidase.



RBC: Red blood cell

Figure (21-1): Neonatal bilirubin metabolism

Unconjugated Hyperbilirubinemia

Definition

It is defined as an elevation of unconjugated serum bilirubin.

Etiology

Increased bilirubin production

- Hemolytic diseases:
  - Isoimmune hemolytic disease (Rh, ABO, and other blood group incompatibilities)
  - Nonimmune (G6PD deficiency, spherocytosis, and α-thalassemia)
- Extravasated blood (cephalhematoma, extensive bruises)
- Polycythemia
- Sepsis

Defective bilirubin uptake by the liver

- Gilbert syndrome (both defective hepatic uptake of bilirubin and decreased hepatic UDPG-T activity)

Defective conjugation of bilirubin

- Crigler-Najjar syndrome (types I and II)
- Gilbert syndrome
- Transient familial neonatal hyperbilirubinemia (Lucey-Driscoll Syndrome)
- Hypothyroidism

Increased enterohepatic circulation

- Pyloric stenosis
- Bowel obstruction (meconium ileus and/or meconium plug)
- Delayed passage of meconium (delayed feeding and hypothyroidism)

Uncertain mechanism

- Breast milk jaundice

Table (21-1): Risk factors for development of severe hyperbilirubinemia in infants of 35 or more weeks' gestation *(*in approximate order of importance*)*

Major risk factors

- Predischarge TSB or TcB levels in the high-risk zone **(Figure 21-2)**
- Jaundice observed in the first 24 hrs
- Blood group incompatibility with positive direct antiglobulin test, other known hemolytic disease (G6PD deficiency) elevated ETCOc
- Gestational age 35-36 weeks
- Previous sibling received phototherapy
- Cephalhematoma or significant bruising
- Exclusive breastfeeding, particularly if nursing is not going well and weight loss is excessive
- East Asian race

Minor risk factors

- Predischarge TSB or TcB levels in the high intermediate-risk zone **(Figure 21-2)**
- Gestational age 37-38 weeks
- Jaundice observed before discharge
- Previous sibling with jaundice
- Macrosomic infant of a diabetic mother
- Maternal age ≥25 years
- Male gender

Decreased risk (these factors are associated with decreased risk of significant jaundice, listed in order of decreasing importance)

- TSB or TcB levels in the low-risk zone **(Figure 21-2)**
- Gestational age ≥41 weeks
- Exclusive bottle feeding
- Black race*
- Discharge from hospital after 72 hrs

* Race as defined by mother's description

TSB: total serum bilirubin, TcB: transcutaneous bilirubin, G6PD: glucose-6-phosphate dehydrogenase, ETCOc: end tidal carbon monoxide

(Reprinted with permission from the Subcommittee on hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004; 114:297-316).

Physiologic Hyperbilirubinemia

Traditionally, a distinction has been made between benign physiologic jaundice and hyper-bilirubinemia, which is either pathologic in origin or severe enough to consider deserving further evaluation and intervention. This later entity has been called "non-physiologic" as frequently no disease is identified as being causative or consequent.

In almost every newborn infant, the elevation of serum unconjugated bilirubin develops during the first week of life and resolves spontaneously. This form is referred to as physiological jaundice. This normal jaundice is attributed to:

- Increased bilirubin load because of the larger RBC volume and the shorter RBC life span, and increased enterohepatic circulation of bilirubin
- Defective bilirubin uptake as a result of decreased concentration of bilirubin binding protein (ligandin)
- Defective conjugation because of reduced UDPG-T activity
- Impaired hepatic excretion into bile
- Overall impairment/immaturity of neonatal liver function

The clinical course of physiologic jaundice is divided into two phases:

- Phase I includes the first 5 days of life in term infants and is characterized by a rapid increase in TSB levels for 3 or 4 days after which the level begins to decline.
- Phase II is characterized by stable, but elevated TSB levels lasting about 2 weeks. After phase II, TSB levels become comparable with adult levels.

In full term healthy infants, jaundice becomes visible on the 2^{nd}-3^{rd} day, usually peaking between the 2^{nd} and 4th days at 5-6 mg/dl, and usually disappearing by 6^{th} to 8^{th} days of life. However, it may last up to the 14^{th} day with a maximum total serum bilirubin level of <12 mg/dl.

In preterm infants, physiologic jaundice is more severe with mean peak TSB concentrations reaching 10-12 mg/dl by the 5^{th} day of life. This delay primarily reflects the delay in maturation of hepatic UDPG-T activity. Because mean peak UCB concentrations of 10-12 mg/dl may be associated with acute bilirubin encephalopathy in certain high-risk, LBW neonates, all degrees of visible jaundice in premature neonates should be monitored closely and investigated fully. In both term and preterm infants, levels <2 mg/dl may not be seen until 1 month of age.

All newborns, especially babies who are at high risk for developing high levels of bilirubin **(Table 21-1)** should be followed closely using the "Hour-specific bilirubin nomogram"**(Figure 21-2)**.

N.B.: Most experts consider the 95^{th} percentile of maximal TSB concentration in healthy mature newborn is 12.4 mg/dl for formula-fed infants and 14.8 mg/dl for breastfed infants.

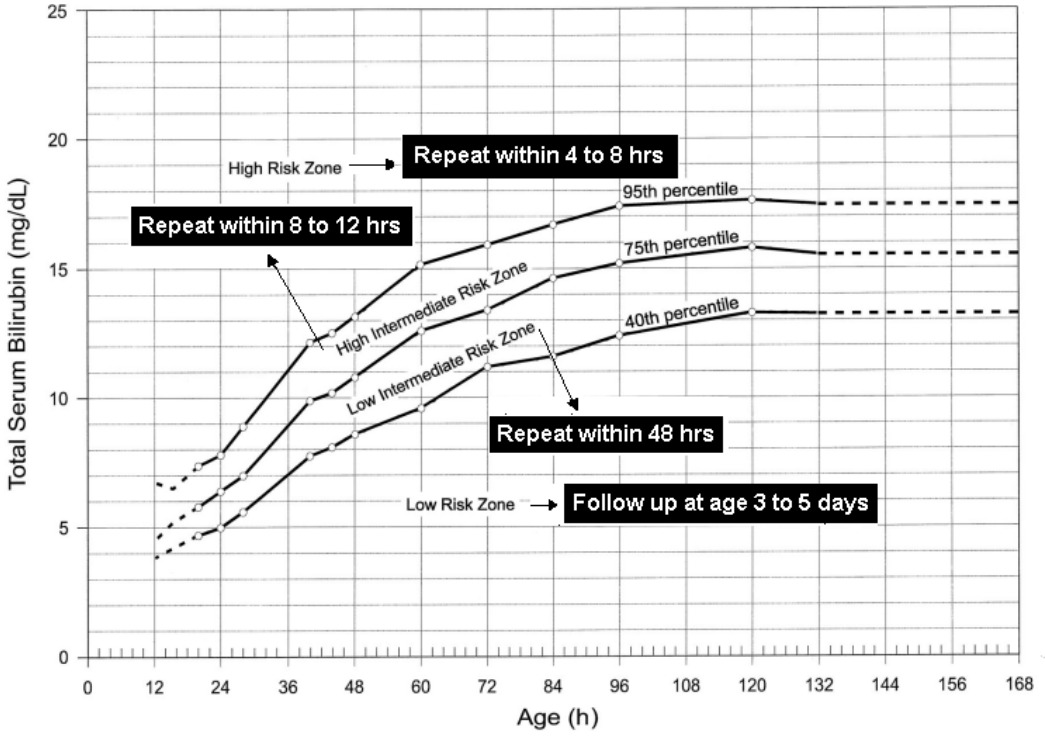


Figure (21-2): Hour-specific bilirubin nomogram

Risk designation of term and near-term well newborns based on their hour-specific serum bilirubin values. The high-risk zone is designated by the 95th percentile track. The intermediate-risk zone is subdivided to upper- and lower-risk zones by the 75th percentile track. The low-risk zone has been electively and statistically defined by the 40th percentile track.

(From Bhutani VK, Johnson L. A proposal to prevent severe neonatal hyperbilirubinemia and kernicterus. Journal of Perinatology, 2009; 29: S61-S67). Reprinted with permission

Nonphysiologic Hyperbilirubinemia

Non-physiologic jaundice may not be easily distinguished from physiologic jaundice. This should be suspected when the criteria of physiological jaundice are not fulfilled.

Criteria

- Clinical jaundice in the first 24 hrs of life
- TSB concentration increasing by more than 0.2 mg/dl/hr or 5mg/dl/day
- TSB concentration exceeding the 95th percentile for age in hours
- Direct serum bilirubin exceeding 2 mg/dl
- Clinical jaundice persisting after 8 days in full term infants and >14 in preterm infants
- Signs of underlying illness in any infant (vomiting, lethargy, poor feeding, excessive weight loss, apnea, tachypnea, or temperature instability)

Jaundice Associated with Breastfeeding

Breastfeeding jaundice (not-enough breast milk jaundice)

- An early-onset, accentuated unconjugated hyperbilirubinemia occurs in the first week of life in breastfed infants who normally have higher bilirubin levels after the 3rd day of life as compared to formula fed infants. The differences are usually not clinically significant.

- The main factor thought to be responsible for breast feeding jaundice is a decreased intake of milk that leads to increased enterohepatic circulation.

Breast milk jaundice (late onset)

- Occurs in 2-4% of term neonates.
- It is rarely a serious condition and should be considered if the following criteria present:
  - By day 4, the bilirubin level continues to rise instead of decreasing. The bilirubin level may reach 20-30 mg/dl by 14 days of age. If breastfeeding is continued, the levels will stay elevated and then fall slowly at 2 weeks of age, returning to normal by 4-12 weeks.
  - Stopping breast milk leads to a rapid fall in serum bilirubin within 48 hrs. Resumption of breastfeeding increases bilirubin levels slightly but usually below previous levels. Although this is currently the only definitive diagnostic test, it is not routinely recommended.
- These infants have good weight gain, normal liver function tests and no evidence of hemolysis.
- The mechanism of breast milk jaundice is not entirely clear but it is thought to be a result of an unidentified factor in breast milk that interferes with bilirubin metabolism, with also an increased enterohepatic circulation because of the presence of glucuronidase enzyme in some breast milk.
- Breast milk jaundice may recur in 70% of future pregnancies.

Diagnosis of Unconjugated Hyperbilirubinemia

History

- Day of onset of jaundice
- Maternal blood group and Rh
- Family history of jaundice, anemia, splenectomy
- Family history of liver disease
- Previous sibling with jaundice or anemia
- Maternal disease (diabetes mellitus or immune disorder)
- Maternal drug intake e.g., sulfonamides, aspirin, antimalarials
- Perinatal history: traumatic delivery, birth trauma, delayed cord clamping, asphyxia
- Postnatal history: vomiting, infrequent stooling, delayed breastfeeding
- The infant is breastfed or formula-fed

Examination

Observe in good daylight. Jaundice progresses in cephalocaudal direction (highest bilirubin levels are associated with jaundice below knees and in the hands) **(Table 21-2).**

Table (21-2): Progression of skin involvement by jaundice in a neonate

Clinical Extent	Grade
none	0
limited to the head and neck	1
involves the (chest and upper abdomen) and/or back	2
involves the abdomen below the umbilicus to the knees	3
involves the legs below the knees and/or upper and lower arms	4
involves hands and/or feet	5

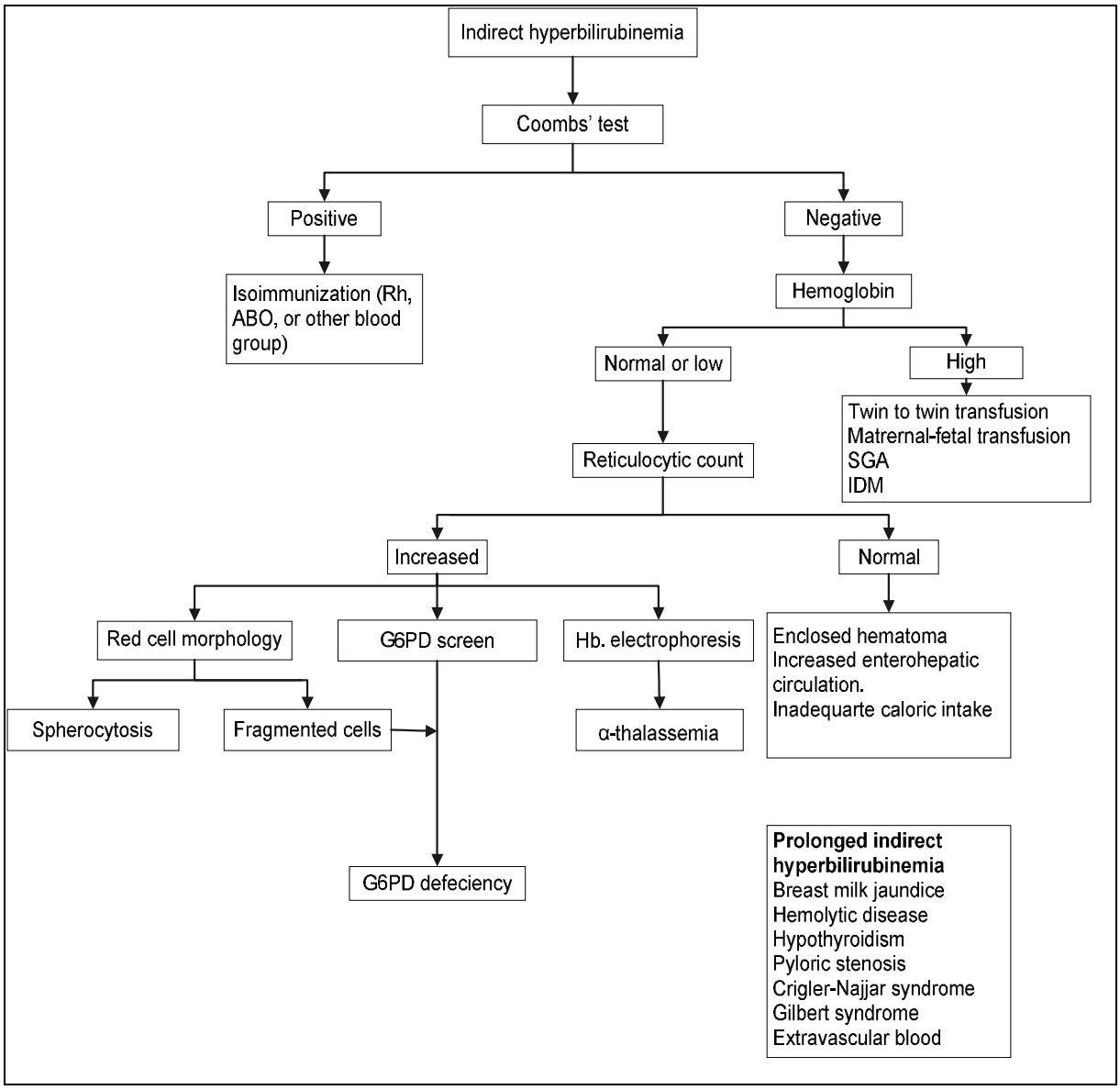
(From: Kramer LI. Advancement of dermal icterus in the jaundiced newborn. Am J Dis Child. 1969; 118: 454-45).

Infants with jaundice should be examined for the following physical findings:

- Prematurity
- Small for gestational age (SGA)
- Microcephaly: congenital infection
- Extravasated blood (e.g., cephalhematoma or bruises)
- Pallor, plethora, petechiae
- Hepatosplenomegaly: hemolytic anemia or infection
- Signs of hypothyroidism (large anterior fontanelle, delayed passage of meconium, hypothermia, poor tone, mottled skin, and poor feeding)
- Signs of neonatal sepsis **(Refer to Chapter 28)**
- Color of jaundice:
  - Orange yellow = unconjugated
  - Olive green = increased conjugated
- Signs of bilirubin encephalopathy (kernicterus)

Laboratory investigations

- Serum bilirubin total and direct (visual inspection is not a reliable measure of serum bilirubin)
- Blood group and Rh of the infant and the mother
- Coomb's test
- Complete blood count (Hb, Hct, WBC total, and differential, red cell morphology)
- Reticulocytic count



IDM: Infant of a diabetic mother, SGA: Small for gestational age, G6PD: Glucose-6-phosphate dehydrogenase, Hb: Hemoglobin

Figure (21-3): Diagnostic approach to neonatal indirect hyperbilirubinemia

Prediction of Non-Physiologic Hyperbilirubinemia

- A screening TSB collected predischarge from the newborn nursery and plotted on an "hour specific bilirubin nomogram" **(Figure 21-2)**.
- Transcutaneous bilirubin (TcB), in infants >30 weeks' gestation, can be used as a screening tool to identify infants at high risk of severe hyperbilirubinemia by plotting values on an (hour specific bilirubin nomogram). If the TcB is >8, check TSB.

N.B.: TcB monitoring is not reliable after initiation of phototherapy.

- Post-discharge follow-up is essential for early recognition of problems related to hyperbilirubinemia and disease progression. The timing of follow-up depends on the age at discharge and the presence of risk factors. In some cases, follow-up within 24 hrs is necessary **(Table 21-3)** and **(Figure 21-2)**.

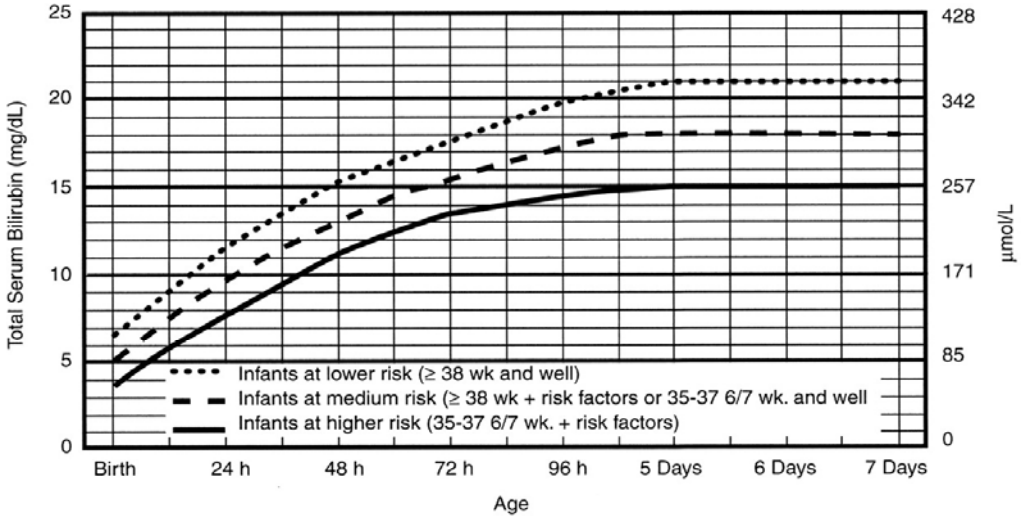
Table (21-3): Timing of post-discharge follow-up

Infant discharge	Should be seen by age
Before age 24 hrs Between 24 and <47.9 hrs Between 48 and 72 hrs	72 hrs 96 hrs 120 hrs
Some newborns discharged before 48 hrs, may require two follow-up visits (the first between 24-72 hrs and the second between 72-120 hrs). Clinical judgment should be used in determining follow-up. Earlier or more frequent follow-up should be provided for those who have risk factors for hyperbilirubinemia **(Table 21-1)**, whereas those discharged with few or no risk factors can be seen after longer intervals. Reprinted with permission from the Subcommittee on hyperbilirubinemia. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation. Pediatrics 2004;114:297-316.	

- End tidal carbon monoxide (ETCOc) may give an idea about the underlying pathology contributing to hyperbilirubinemia (hemolysis versus conjugation defect) as carbon monoxide is produced during bilirubin metabolism.

Management of Unconjugated Hyperbilirubinemia

- Increase feeds in volume and calories, and avoid routine supplementation with water or glucose water.
- Stop those drugs that interfere with bilirubin metabolism.
- Correct hypoxia, infection and acidosis.
- Three methods of treatment are commonly used to decrease the level of unconjugated bilirubin: exchange transfusion, phototherapy, and pharmacologic therapy.
- Refer to **(Figures 21-4 and 21-5)** and **(Tables 21-4 and 21-5)** for treatment option guidelines.



- Use total bilirubin. Do not subtract direct reacting or conjugated bilirubin.
- Risk factors = isoimmune hemolytic disease, G6PD deficiency, asphyxia, significant lethargy, temperature instability, sepsis, acidosis, or albumin < 3.0g/dL (if measured)
- For well infants 35-37 6/7 wk can adjust TSB levels for intervention around the medium risk line. It is an option to intervene at lower TSB levels for infants closer to 35 wks and at higher TSB levels for those closer to 37 6/7 wk.
- It is an option to provide conventional phototherapy in hospital or at home at TSB levels 2-3 mg/dL (35-50mmol/L) below those shown but home phototherapy should not be used in any infant with risk factors.

Figure (21-4): Guidelines for phototherapy in hospitalized infants of 35 or more weeks' gestation

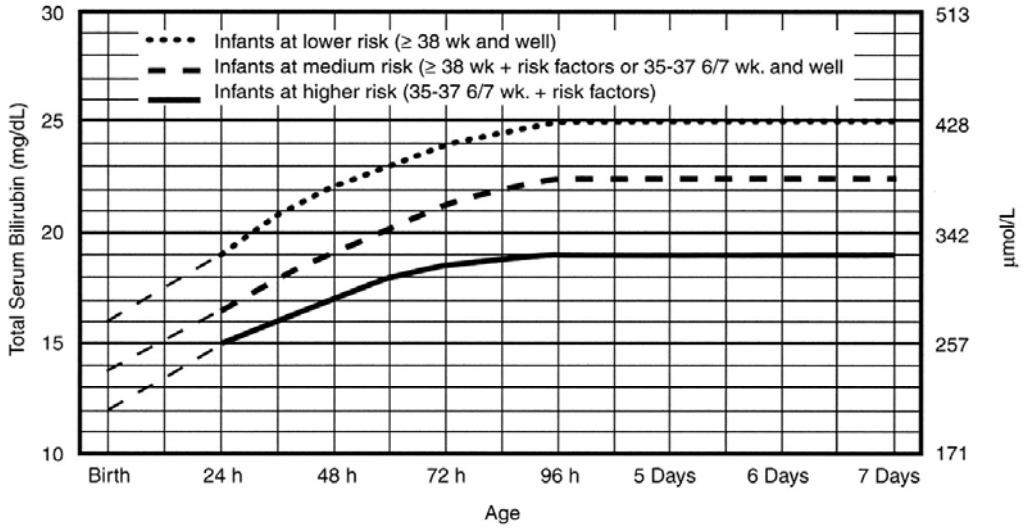


Figure (21-5): Guidelines for exchange transfusion in hospitalized infants of 35 or more weeks' gestation

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Table (21-4): Management of hyperbilirubinemia in healthy and sick premature infants (<37 weeks' gestation)

Weight	Healthy Infants: Total Serum Bilirubin Level (mg/dl)		Sick Infants: Total Serum Bilirubin Level (mg/dl)	
	Phototherapy	Exchange Transfusion	Phototherapy	Exchange Transfusion
≤ 1,000 gm*	5-7	10-12	4-6	8-10
1,001-1,500 gm	7-10	12-15	6-8	10-12
1,501-2,000 gm	10-12	16-18	8-10	14-16
2,001-2,500 gm	12-15	18-20	10-12	16-18

For infants <1,000 gm; prophylactic phototherapy may be started within the first 24 hrs.

N.B.: Bilirubin levels refer to the total bilirubin. Direct bilirubin is not subtracted from the total unless it constitutes >50% of the total bilirubin.

Table (21-5): Bilirubin/albumin (B/A) ratio at which exchange transfusion should be considered

Risk Category	B/A ratio TSB (mg/dl)/Albumin (gm/dl)
Infants ≥38 0/7 weeks	8.0
Infants 35 0/7 -36 6/7 weeks and well, or infants ≥38 0/7 weeks if higher risk or isoimmune hemolytic disease or G6PD deficiency	7.2
Infants 35 0/7-37 6/7 weeks if higher risk or isoimmune hemolytic disease or G6PD deficiency	6.8

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- The bilirubin/albumin (B/A) ratio can be used together with, but not in lieu of the TSB level as an additional factor in determining the need for exchange transfusion.
- Serum albumin level and the B/A ratio are factors that can be considered in the decision to initiate phototherapy **(Figure 21-4)** or perform an exchange transfusion **(Figure 21-5).** Elevations of unbound bilirubin have been associated with kernicterus in sick preterm newborns.
- The ratio of bilirubin (mg/dl) to albumin (gm/dl) does correlate with measured unbound bilirubin in newborns and can be used as an approximate surrogate for the measurement of unbound bilirubin. It is therefore a clinical option to use the B/A ratio together with, but not in place of, the TSB level as an additional factor in determining the need for exchange transfusion **(Figure 21-5).**

Phototherapy

- Phototherapy is the treatment of disease by exposure to light.
- Indications:
  - Phototherapy should be initiated according to the guidelines in **(Figure 21-4)** and **(Table 21-4).**
  - When bilirubin level approaches the toxic range, although it has not reached levels requiring exchange transfusion.
  - Prophylactic phototherapy may be indicated for ELBW infants and severely bruised infants.
  - It is initiated during the wait for exchange transfusion.
- A blue light with a wave length of 425-475 nm is the most efficient.
- Photochemical reactions:
  - Photo-isomerization (reversible): occurs in the extravascular space of the skin, the natural UCB is converted to less toxic polar isomer that diffuses into the blood and is excreted by in bile without conjugation.
  - Structural isomerization (irreversible): UCB is converted to lumirubin which is excreted in bile and urine without conjugation.

- Photo-oxidation (least important): produces polar bilirubin products that are excreted in urine.

- Technique:
  - The infant should be undressed except for a diaper and eye patches. Eye patches must be in place but should not be too tight or occlude the nares.
  - The lamp should be 5-8 cm over the incubator and 45 cm above the infant.
  - Effectiveness of phototherapy is related to the amount of irradiation to which the skin is exposed. Phototherapy is given continuously and the infant should be turned every 2 hrs **(Figure 21-6).**
  - Maintain a neutral thermal environment (NTE); the infant's temperature should be carefully monitored and servo-controlled.
  - Infants should be weighed daily (twice daily in small infants). The infant's fluid balance must also be carefully monitored and dehydration prevented by determining the infant's fluid requirements and replacing the calculated insensible water loss (increase fluid therapy by 20%).

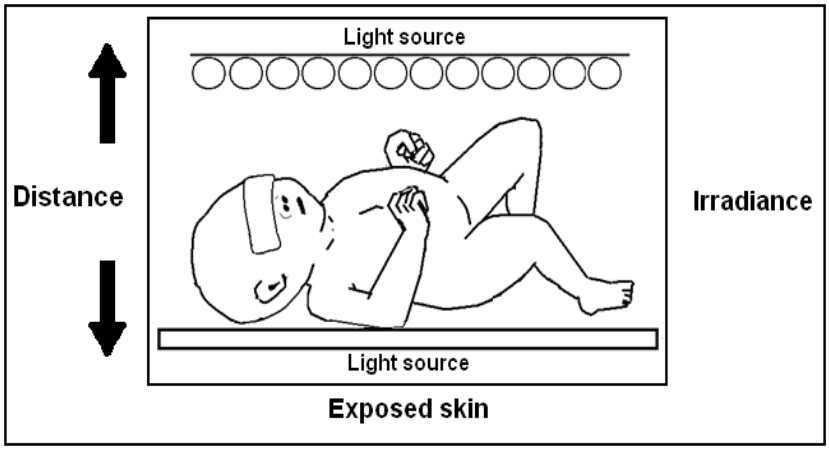


Figure (21-6): Factors determining the efficacy of phototherapy

- Monitoring: the frequency of TSB measurements depends upon the initial TSB value.
  - When infant is admitted with TSB values exceeding the 95th percentile for hour-specific TSB levels, the TSB measurement should be repeated 2-3 hrs after initiation of phototherapy to assess the response.
  - When phototherapy is started for a rising TSB, TSB should be measured after 4-6 hrs, and then within 8-12 hours, if TSB continues to fall.
  - If, despite intensive phototherapy, the TSB is at or approaches the threshold for exchange transfusion, blood should be sent for immediate typing and cross-matching.
- Once started, the skin color cannot be taken as a guide to the level of hyperbilirubinemia.
- Side effects:
  - Hyperthermia and dehydration due to increased insensible water loss
  - Watery diarrhea
  - Hypocalcemia

- Retinal damage
- Erythema
- Bronze baby syndrome, if used in infants with direct hyperbilirubinemia
- Potential genetic damage, mutations
- Upsets of maternal infant interaction

- Discontinuation:
  - Phototherapy is stopped when the following criteria are met:
    - The bilirubin level is low enough to eliminate the risk of kernicterus
    - The infant is old enough to handle the bilirubin load
  - TSB should be measured 18-24 hrs after phototherapy is terminated

Exchange transfusion

(Refer to Chapter 44)

- There are many factors involved in deciding the exact bilirubin level at which to initiate the exchange transfusion. The overall state (sick or well), birth weight, gestational age and age of the infant are all important considerations.
- This procedure removes bilirubin and hemolytic antibodies and corrects anemia.
- **Refer to (Figure 21-5), (Table 21-4), and (Table 21-5)** for indications for exchange transfusion.
- A double blood volume exchange is done (2 × 80-85 ml × body weight in kg).
- Type of blood for exchange transfusion: fresh citrated blood is to be used
  - In neonates with Rh-incompatibility, use Rh-negative blood that has been cross-matched with the mother's blood if prepared before delivery. It may be also cross matched with the infant if the blood is obtained after delivery.
  - In neonates with ABO incompatibility, use O positive or O negative group, (low-titer anti-A and anti-B blood) that has been cross-matched with both the infant's and mother's blood.
  - In other isoimmune hemolytic disease, the blood should be cross matched with the mother's blood.
  - In other cases, use the infant's group after cross-matching with the infant's blood.
- Albumin transfusion (1 gm of albumin, 1 hr before exchange transfusion): may be useful to improve the yield of bilirubin removal if bilirubin levels are >20 mg/dl and serum albumin levels are <3 gm/dl. Fluid volume and cardiovascular status must be carefully considered before giving albumin.

Pharmacologic agents

Intravenous Immunoglobulin (IVIG)

- IVIG (500-1,000 mg/kg IV over 2-4 hrs) can reduce the need for exchange transfusion in infants with isoimmune hemolytic disease.

- The mechanism is uncertain, but IVIG is thought to inhibit hemolysis by occupying the Fc receptors of reticuloendothelial cells, preventing them from taking up and lysing antibody-coated RBC's.
- IVIG is recommended if the TSB is rising despite intensive phototherapy or is within 2-3 mg/dl of the threshold for exchange transfusion. The dose may be repeated in 12 hrs if necessary.

Phenobarbital

- Phenobarbital increases the conjugation and excretion of bilirubin. Phenobarbital is **NOT** used to treat indirect neonatal hyperbilirubinemia, except in Crigler-Najjar syndrome type II.
- It causes lethargy and poor feeding and needs 3-4 days to take effect.

Bilirubin Encephalopathy (Kernicterus)

Definition

Kernicterus is a pathologic term and refers to yellow staining of the brain with evidence of brain damage. It is due to the deposition of UCB in the brain (mainly, the basal ganglia and cranial nerve nuclei). Cell injury, yellow staining, neuronal loss and glial replacement can occur with subsequent neurological damage. In small, sick preterm infants, even a bilirubin level in a low range may cause kernicterus.

Factors influencing risk of kernicterus

Reduced albumin binding capacity

Prematurity, asphyxia, acidosis, hypoalbuminemia and infections

Competition for binding sites

Displacement of bilirubin from its albumin binding sites by drugs (e.g., synthetic vitamin K, sulfonamide, salicylates, gentamicin, aminophylline, furosemide and digoxin), or free fatty acids secondary to hypoglycemia, starvation, or hypothermia

Increased susceptibility to bilirubin toxicity

Asphyxia and hypoglycemia

Clinical manifestations

The development of bilirubin encephalopathy is dependent on the level of indirect bilirubin, duration of exposure to elevated levels, the cause of jaundice, and the infant's well-being.

Acute bilirubin encephalopathy

It is the clinical manifestation of bilirubin toxicity seen in the neonatal period. It can be divided into three phases:

- Early phase: hypotonia, lethargy, high-pitched cry, and poor suckling
- Intermediate phase: hypertonia of extensor muscles (with opisthotonus, oculogyric crises and retrocollis), irritability, seizures, fever. Neonatal mortality is high at this stage. All infants who survive this stage develop chronic bilirubin encephalopathy (clinical diagnosis of kernicterus).

- Advanced phase: pronounced opisthotonus (although hypotonia replaces hypertonia after about 1 week of age), shrill cry, apnea, seizures, coma and death.

Chronic bilirubin encephalopathy (Kernicterus)

It is marked by athetosis, deafness, limitation of upward gaze, dental dysplasia and intellectual deficits.

N.B.: Level at which kernicterus can occur is variable and no specific bilirubin level is definitely safe or toxic.

Management

- If bilirubin toxicity is suspected, treatment is an immediate exchange transfusion, preceded by phototherapy until the exchange starts.
- Exchange transfusion should always be done in cases with clinically established kernicterus in order to minimize further brain damage.

N.B.: Hearing screen or Auditory Evoked Potential should be done for every infant with TSB level approaching exchange transfusion prior to discharge.

Conjugated Hyperbilirubinemia

Conjugated hyperbilirubinemia is a sign of hepatobiliary dysfunction. Conjugated hyperbilirubinemia is defined as an increased level of direct bilirubin >15% of the total serum bilirubin.

Etiology

Anatomic abnormalities

- Extrahepatic biliary atresia
- Choledochal cyst
- Others: spontaneous perforation of common bile duct, and cholelithiasis

Neonatal hepatitis/cholestasis

Idiopathic neonatal hepatitis

- It is defined as intrahepatic cholestasis in which the characteristic giant-cell hepatitis lesion is present on liver biopsy but for which no cause is identified.

Infections

- Viral: CMV, rubella and hepatotropic viruses (e.g., HBV)
- Bacterial: sepsis (especially gram negative organisms) and urinary tract infection

Familial intrahepatic cholestatic syndromes

- Alagille syndrome (arteriohepatic dysplasia)
- Nonsyndromic paucity of the interlobular bile ducts
- Progressive familial intrahepatic cholestasis (several types)

Metabolic disorders

- Disorders of carbohydrate metabolism (e.g., Galactosemia)
- Disorders of amino acid metabolism (e.g., Tyrosinemia)
- Disorders of lipid metabolism (e.g., Niemann-Pick disease)
- Disorders of bile acid synthesis
- Peroxisomal disorders (e.g., Zellweger's syndrome “cerebrohepatorenal syndrome”)
- Mitochondrial hepatopathies
- Miscellaneous metabolic disorders
  - α_1-Antitrypsin deficiency
  - Cystic fibrosis
  - Neonatal hemochromatosis

Cholestasis-associated TPN

- It usually does not occur until the infant has been on TPN for >2 weeks. It occurs more commonly in sick premature infants.

Miscellaneous

- Vascular disorders of the liver
- Drug hepatotoxicity
- Inspissated bile syndrome seen in any severe hemolytic disease
- Ischemia
- Chromosomal e.g., trisomy 21

Clinical Manifestations

History

A detailed history should be obtained including;

- Prenatal (to evaluate for intrauterine infection or hemolytic disease)
- Postnatal (feeding history as well as the presence of any acholic stools)
- History of prematurity and prolonged use of hyperalimentation
- Family history of neonatal hyperbilirubinemia, prematurity or SGA or a family history of splenectomy or liver disease suggesting metabolic disease.

Examination

- Olive green jaundice
- Clay-colored stools
- Dark urine
- Bleeding tendency
- Abdominal distention with hepatosplenomegaly, ascites, and portal hypertension
- Failure to thrive
- Pruritus
- The presence of nonhepatic findings will provide helpful clues to specific diagnosis, such as the following:
  - Signs of sepsis
  - Galactosemia: failure to thrive, vomiting, cataracts, and Gram-negative bacterial sepsis (e.g., *E. coli*)
  - Congenital infections: IUGR, microcephaly, chorioretinitis, and intracranial calcifications.
  - Unusual features: Alagille syndrome, characterized by a cholestasis, cardiovascular findings (pulmonary artery stenosis), butterfly vertebrae, ocular findings (posterior embryotoxon).

Investigations

- Serum bilirubin (total and direct)
- Liver function tests including gamma-glutamyl transpeptidase (GGT)

- Sepsis work up
- TORCH screening
- Abdominal ultrasound
- Metabolic screening
- Liver biopsy
- Hepatobiliary scan

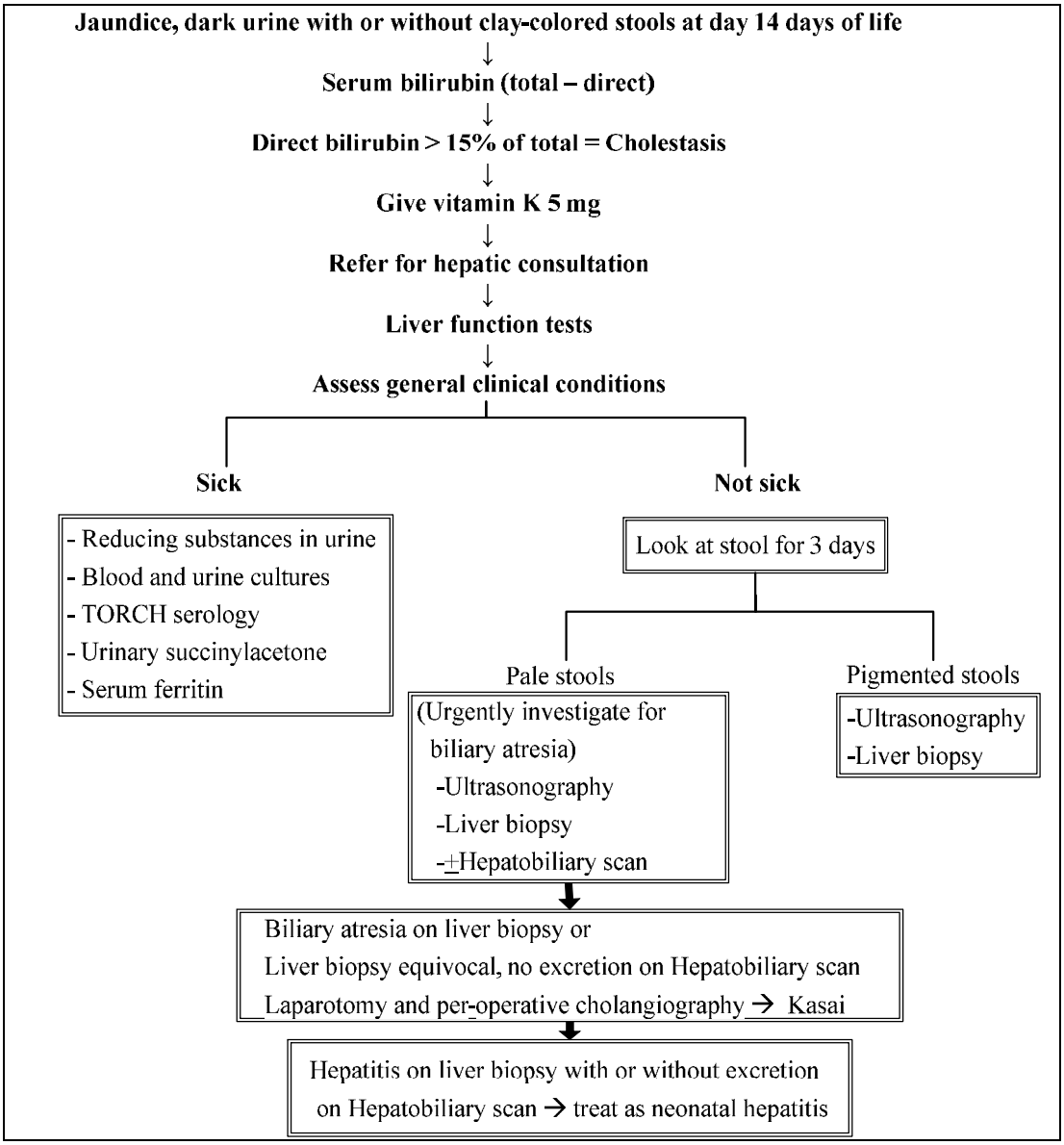


Figure (21-7): An approach to neonatal cholestasis

Management

The key to managing conjugated hyperbilirubinemia is identifying and managing the underlying pathological process causing the elevated serum bilirubin level.

Supportive management

Promotion of bile flow and prevention of malnutrition, vitamin deficiencies, and bleeding are the goals.

- Formulas containing medium-chain triglycerides (Portagen and Pregestimil)
- Supplementation with fat soluble vitamins (A, D, E, and K). Extra-vitamin K supplementation may be necessary if a bleeding tendency develops.
- Choleretic bile acids: ursodeoxycholic acid (15 mg/kg/day, in 2 divided doses)

Treatment of the cause

- Extrahepatic biliary atresia: Kasai portoenterostomy should be done to establish biliary drainage before 8 weeks of age.
- Metabolic causes such as galactosemia and tyrosinemia require specific dietary modification.
- Infectious causes and a few of the congenital infections can be readily treated with the appropriate antimicrobial therapy.
- Stop TPN completely or use partial parenteral nutrition with some enteral feedings.

N.B.: Phototherapy should not be used in cases of conjugated hyperbilirubinemia (may lead to bronze baby syndrome). If both direct and indirect bilirubin are high, exchange transfusion is probably safer than phototherapy.

Chapter 22

Neonatal Respiratory Disorders

Neonatal Respiratory Disorders

Respiratory problems are the most common difficulty seen in neonatal care units especially in preterm infants. Birth initiates a dramatic change from the intrauterine state, in which the placenta is the primary organ of respiration, to life outside the uterus, in which the lung is the organ of gas exchange.

Causes of Respiratory Distress in the Newborn

Pulmonary causes

- Transient tachypnea of the newborn (TTN)
- Respiratory distress syndrome (RDS)
- Pneumonia
- Meconium aspiration syndrome (MAS)
- Air leak syndromes
- Pulmonary hemorrhage

Extra-pulmonary causes

- Cardiac causes:
  - Congenital heart disease; cyanotic or acyanotic
  - Congestive heart failure
- Persistent pulmonary hypertension of the newborn (PPHN)
- Neurological causes (e.g., prenatal asphyxia, meningitis)
- Diaphragmatic disorders (e.g., congenital diaphragmatic hernia, diaphragmatic paralysis)
- Chest wall deformities
- Metabolic causes (e.g., hypoglycemia, hypothermia or hyperthermia)
- Disturbances of acid-base equilibrium (e.g., metabolic acidosis)
- Hematological causes (e.g., anemia, polycythemia)

Table (22-1): Evaluation of respiratory distress using Downes' score

Test	Score		
	0	**1**	**2**
Respiratory rate	<60/minute	60-80/minute	>80/minute
Retractions	No retractions	Mild retractions	Severe retractions
Cyanosis	No cyanosis	Cyanosis relieved by O_2	Cyanosis on O_2
Air entry	Good bilateral air entry	Mild decrease in air entry	No air entry
Grunting	No grunting	Audible by stethoscope	Audible with ear
Evaluation			
Total	**Diagnosis**		
<4	No respiratory distress		
4-7	Respiratory distress		
>7	Impending respiratory failure; blood gases are required		

Wood DW, Downes' JJ, Locks HI. A clinical score for the diagnosis of respiratory failure. Amer J Dis Child 1972; 123: 227-229.

Management of Neonatal Respiratory Distress

The initial approach to a neonate with respiratory distress, regardless of etiology, consists of:

- Relieving cyanosis with supplemental oxygen and providing assisted ventilation, if needed. A neonate with obvious respiratory distress needs a continuous monitoring with pulse oximetry to decide when intubation and ventilation is required.
- Obtaining a chest radiograph to assist in diagnosis and to identify complications such as pneumothorax that may require urgent treatment.
- Providing an appropriate fluid management, and a neutral thermal environment (NTE) to reduce the infant's energy and oxygen consumption. Neonates with respiratory distress may require restriction of input to be equal to urine output (1-3 ml/kg/hr) and IWL. Excessive fluid and sodium intake may increase risk of BPD and PDA.
- Correction of any metabolic abnormalities (e.g., acidosis, hypoglycemia), if present.
- Providing an adequate nutrition. In general, infants with sustained respiratory rates >60 breaths/minute should not be fed orally; these infants should be maintained on gavage feedings for respiratory rates between 60-80 breaths/minute, and NPO with IV fluids or TPN for more severe tachypnea.
- Obtaining a blood culture and beginning an antibiotic coverage with ampicillin and gentamicin while awaiting the results of the culture, in case of a preterm infant with respiratory distress or a term infant with respiratory distress that persists longer than 4-6 hrs, or if sepsis or pneumonia is suspected by history or physical examination.
- Providing an appropriate specific therapy that is directed at the underlying disorder.

Transient Tachypnea of the Newborn (TTN)

TTN (known as wet lung) is a relatively mild, self limiting disorder of near-term or term infants who display respiratory distress shortly after delivery.

Pathophysiology

Disruption or delay in clearance of fetal lung fluid from a number of conditions results in transient pulmonary edema. The increased fluid volume causes a reduction in lung compliance and increased airway resistance.

Risk factors

- Elective cesarean section delivery
- Macrosomia and infants of diabetic mothers
- Prolonged labor
- Excessive maternal sedation
- Fluid overload to the mother, especially with oxytocin infusion
- Delayed clamping of the umbilical cord

Clinical manifestations

- The infant is usually near-term or term and presents within 6 hrs after delivery with tachypnea (typically >80 breaths/minute).
- Tachypnea is accompanied by mild to moderate respiratory distress with grunting, nasal flaring, rib retraction and cyanosis.
- Auscultation usually reveals good air entry with or without crackles.
- These manifestations usually persist for 12-24 hrs, but can last up to 72 hrs in more severe cases.
- It is important to exclude other causes of respiratory distress in the first 6 hrs of life [e.g., pneumonia, congenital heart disease, RDS and brain insults accompanied by central hyperventilation such as HIE].

N.B.: Spontaneous improvement of the neonate is an important marker of TTN.

Investigations

- To rule out infection take a complete blood count (CBC) and CRP.
- Blood gas analysis may reveal varying degrees of hypoxemia, $PaCO_2$ is usually low, and if hypercarbia exists, it is usually mild. If respiratory failure occurs, another diagnosis should be considered.
- Chest x-ray **(Refer to Appendix 9)**; the typical findings in TTN are:
  - Prominent perihilar streaking (due to engorgement of periarterial lymphatics)
  - Fluid in the minor fissure
  - Prominent pulmonary vascular markings
  - Hyperinflation of the lungs, with depression of diaphragm

- Chest x-ray usually shows evidence of clearing by 12-18 hrs with complete resolution by 48-72 hrs

Management

- Follow general management of respiratory distress **(as mentioned before).**
- Physician can begin a course of antibiotic therapy, depending on the history and clinical status of the infant, and can terminate at 48-72 hrs, if cultures are negative.
- Respiratory symptoms improve as intrapulmonary fluid is mobilized, usually occurring with diuresis. However, there is no role for diuretics in management of TTN.

Prognosis

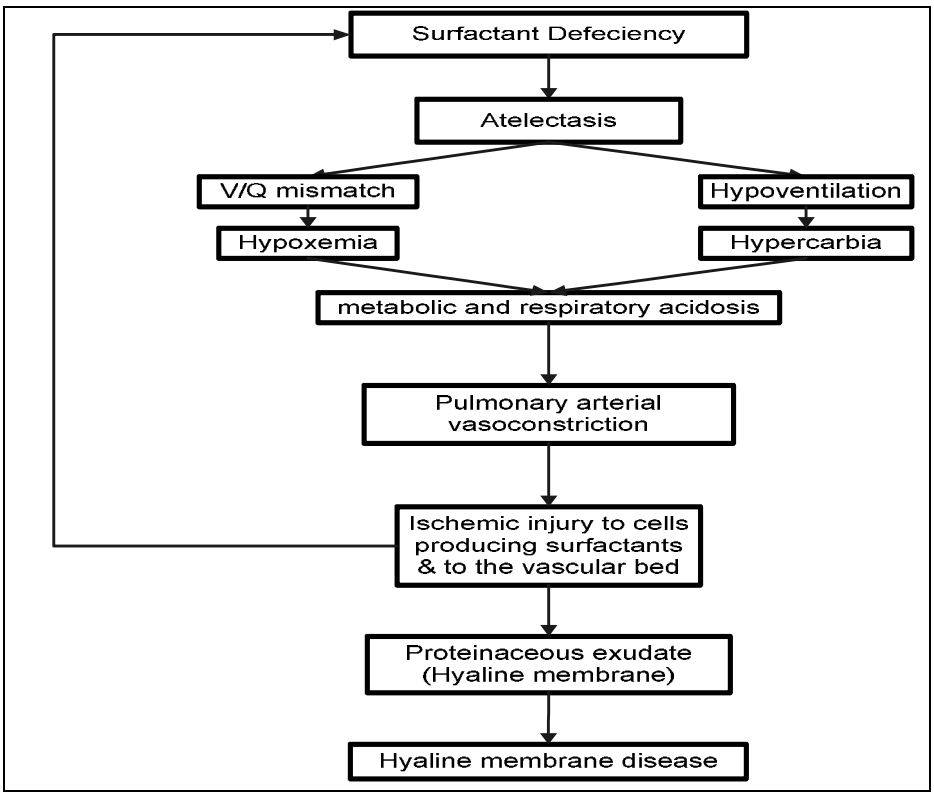
The disease is self-limiting, and there is no risk of residual pulmonary dysfunction.

Respiratory Distress Syndrome (RDS)

Respiratory distress syndrome (RDS) [also called hyaline membrane disease (HMD)] is a respiratory disease that primarily affects preterm infants; its incidence is inversely related to gestational age and birthweight. It occurs in about 15-30% of those between 32-36 weeks' gestation, in about 5% beyond 37 weeks' gestation.

Pathophysiology

The development of RDS begins with impaired or delayed surfactant synthesis and secretion followed by series of events that may progressively increase the severity of the disease for several days **(Figure 22-1)**.



V/Q mismatch: ventilation/perfusion mismatch

Figure (22-1): Series of events responsible for respiratory distress syndrome

Risk factors

Increased risk

- Prematurity
- Maternal diabetes
- Multiple births
- Elective cesarean section without labor
- Perinatal asphyxia
- Cold stress
- Genetic disorders of surfactant production and metabolism (e.g., surfactant protein B mutation, resulting in RDS like picture in full-term babies)

Decreased risk

- Chronic intrauterine stress
- Prolonged rupture of membranes
- Antenatal steroid prophylaxis

Clinical manifestations

- Manifestations of RDS usually appear within minutes of birth, although they may not be recognized for several hours in larger premature infants.
- Infants with respiratory distress syndrome present with a combination of tachypnea (>60 breaths/minute), nasal flaring, subcostal and intercostal retractions, cyanosis, and an expiratory grunting. Breath sounds may be normal or diminished and fine rales may be heard, especially over the lung bases.
- The natural course of untreated RDS is characterized by progressive worsening of cyanosis and dyspnea. Blood pressure may fall; fatigue, cyanosis, and pallor increase, and grunting decreases or disappears as the condition worsens.
- Apnea and irregular respirations are ominous signs, indicating hypoxemia and respiratory failure.
- In most cases, the symptoms and signs reach a peak within 3 days, after which improvement occurs gradually.

Investigations

- Blood gas analysis may reveal hypoxia, hypercapnia and acidosis.
- Work-up for sepsis including CBC with differential and blood culture to rule out early-onset sepsis.
- Monitor serum glucose and electrolyte levels.
- Chest x-ray: the typical radiographic features consist of a diffuse reticulogranular pattern, giving the classic ground-glass appearance, in both lung fields with super-imposed air bronchograms **(Refer to Appendix 9)**.

Management

Prevention

- Lung maturity testing: lecithin/sphingomyelin (L/S) ratio in the amniotic fluid gives an idea about degree of lung maturity. Levels of >2 is associated with low risk of RDS.
- Tocolytics (e.g., magnesium sulfate, terbutaline and indomethacin) to inhibit premature labor.
- Antenatal corticosteroid therapy:
  - They induce surfactant production and accelerate fetal lung maturation.
  - Are indicated in pregnant women 24-34 weeks' gestation at high risk of preterm delivery within the next 7 days.
  - Therapy consists of either;
    - Betamethasone 12 mg/dose IM for 2 doses, 24 hrs apart, or
    - Dexamethasone 6 mg/dose IM for 4 doses, 12 hrs apart
  - Optimal benefit begins 24 hrs after initiation of therapy and lasts seven days.
- Early surfactant therapy: prophylactic use of surfactant in preterm newborn <27 weeks' gestation.
- Early CPAP administration in the delivery room.

Treatment

- Follow general management of respiratory distress (as mentioned before).
- The method of oxygen administration depends on the severity of illness.
- CPAP is used as early as possible to prevent further atelectasis in infants with mild respiratory distress who require an FiO_2 below 0.4 to maintain target oxygen saturation and have a $paCO_2$ <55-60 mmHg. CPAP is initiated at 5-6 cmH_2O and increased to a maximum of 7-8 cmH_2O.
- Mechanical ventilation is indicated in the presence of respiratory acidosis with a $PaCO_2$ >60 mmHg, a PaO_2 <50 mmHg or oxygen saturation <90% with an FiO_2 above 0.5 or with the presence of severe frequent apnea.
- Surfactant replacement therapy: early rescue therapy within 2 hrs after birth is better than late rescue treatment when the full picture of RDS is evident.

Prognosis

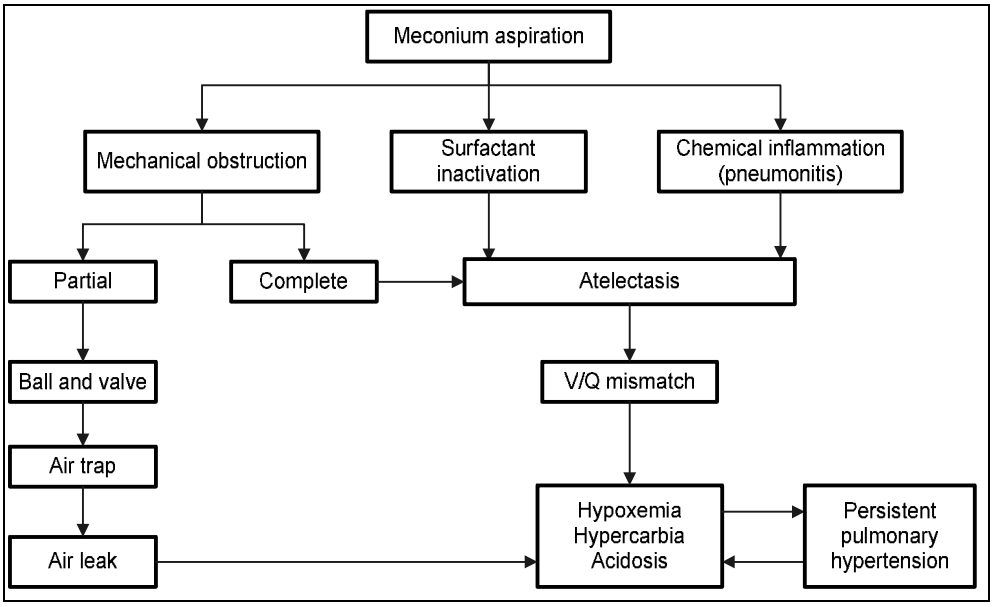
- Long term complications include bronchopulmonary dysplasia (BPD) and other complications of prematurity including neurodevelopmental impairment and retinopathy of prematurity (ROP). The risk of these complications increases with decreasing birth weight and gestational age.

Meconium Aspiration Syndrome (MAS)

Meconium staining of the amniotic fluid or fetus usually indicates fetal distress. It is found in 10-15% of births and usually occurs in term or post-term infants; meconium aspiration develops in 5% of such infants. The passage of meconium in an asphyxiated infant < 34 weeks' gestation is unusual.

Pathophysiology

Either in-utero or more often with the first breath, thick, particulate meconium is aspirated into the lungs. The aspirated meconium can cause airway obstruction and an intense inflammatory reaction.



V/Q mismatch: ventilation/perfusion mismatch

Figure (22-2): Pathophysiology meconium aspiration syndrome

Risk factors

- Post-term pregnancy
- Pre-eclampsia – eclampsia
- Maternal hypertension
- Maternal diabetes mellitus
- IUGR
- Evidences of fetal distress (e.g., non reassuring signs of fetal heart rate, abnormal biophysical profile)

Clinical manifestations

- Meconium staining of amniotic fluid is noted at birth (ranging from thin, green-stained fluid to a thick, "pea soup" consistency). The majority of infants who become ill have a history of thick, meconium-stained fluid.
- Infants often exhibit the classic signs of postmaturity with evidence of weight loss, together with meconium stained nails, skin, and umbilical cord.
- Aspiration of large amounts of thick meconium, and if not removed by endotracheal suctioning, it will result in acute large airway obstruction.
- Meconium aspiration with partial distal airway obstruction will result in respiratory distress (i.e., tachypnea, nasal flaring, intercostals retractions, prolonged expiration and cyanosis) soon after birth. Neonates with severe MAS often have an increased anterior-posterior dimension of the thorax (i.e., a "barrel" chest).

- Some infants may have mild initial respiratory distress, which becomes more severe hours after delivery, such as atelectasis and chemical pneumonitis may develop.
- Pneumothorax or pneumomediastinum or both may occur.
- Persistent pulmonary hypertension is also frequently observed in severe cases.
- Clinical manifestations of hypoxic damage to other organs may be present (e.g., seizures, oliguria).

Investigations

- CBC with differential
- Blood gas analysis
- Chest x-ray: it will show patchy infiltrates, coarse streaking of both lung fields, an increased anterior-posterior diameter, and flattening of the diaphragm **(Refer to Appendix 9)**.
- Conduct surveillance for end organ hypoxic/ischemic damage (brain, kidney, heart, and liver) including kidney function tests and cranial ultrasonography.

Management

- Prenatal management:
  - Identification of high-risk pregnancy
  - Monitoring of fetal heart rate during labor
- In the delivery room (if amniotic fluid is meconium stained):
  - Suctioning of the oropharynx by obstetricians before delivery of the shoulders is not recommended anymore because meconium aspiration occurred in-utero and suction of the oropharynx is of no value.
  - Visualization of the vocal cords, and tracheal suctioning before ambu-bagging should be done **only** if the baby is not vigorous (the term vigorous means strong respiratory effort, good muscle tone and heart rate >100 beats/minute) **(Refer to Chapter 4).**
- In the NICU:
  - Follow general management of respiratory distress (as mentioned before).
  - Follow procedures for respiratory management:
    - Empty the stomach contents to avoid further aspiration.
    - Suctioning frequently and perform chest physiotherapy.
    - Maintain antibiotic coverage (ampicillin and gentamicin).
    - Provide generous amounts of supplemental oxygen, maintaining PaO_2 at least in the range of 80-90 mmHg.
    - Consider CPAP, if FiO_2 requirements exceed 0.4; however CPAP may aggravate air trapping and must be used cautiously.
    - Mechanical ventilation is indicated in severe cases for excessive CO_2 retention ($paCO_2$ >60 mmHg) or for persistent hypoxemia (paO_2 <50 mmHg) **(Refer to Chapter 26).**

    - High frequency ventilation may be required, if the baby does not respond to mechanical ventilation.
  - Cardiovascular management:
    - Correct systemic hypotension (hypovolemia, myocardial dysfunction).
    - Lower persistent pulmonary hypertension **(Refer to Chapter 35).**
  - Other systems:
    - Manage seizures or renal problems, if present, according to the systems affected.
  - Surfactant therapy may improve oxygenation and reduce pulmonary complications especially in infants whose clinical status continue to deteriorate.

Complications

- Air leak: occurs in 15-30% of cases especially in babies on mechanical ventilation.
- Persistent pulmonary hypertension of newborn (PPHN) is associated with MAS in 1/3 of cases and contribute to mortality from this syndrome. Echocardiography should be performed in suspected cases.
- Pulmonary sequelae:
  - Pneumonia
  - Bronchopulmonary dysplasia (BPD), in 5% of cases
  - Airway reactivity

Prognosis

The mortality rate can be as high as 50%, and survivors may suffer long-term sequelae including BPD. The ultimate prognosis depends on the extent of CNS injury from asphyxia, and the presence of associated problems as pulmonary hypertension.

Air Leak Syndromes

The air leak syndromes (pneumomediastinum, pneumothorax, pulmonary interstitial emphysema and pneumopericardium) comprise a spectrum of diseases with the same underlying pathophysiology. Overdistension of alveolar sacs or terminal airways leads to disruption of airway integrity, resulting in dissection of air into the surrounding spaces.

These syndromes are most commonly seen in infants with lung diseases who are on ventilatory supports; however, they can also occur spontaneously. The more severe the lung disease, the higher the incidence of pulmonary air leak.

Risk factors

- Ventilatory support: lung overdistention from high tidal volume (volutrauma) is more injurious than high PIP (barotrauma)
- Meconium aspiration syndrome (MAS)
- Surfactant therapy without decreasing pressure support in ventilated infants
- Vigorous resuscitation
- Prematurity with stiff lungs
- Pneumonia

Types

Pneumothorax

- Pneumothorax refers to a collection of gas or air in the pleural sac resulting in collapse of the lung on the affected side. It may be seen as an isolated finding or may be associated with other forms of lung disease (particularly RDS and MAS).
- Spontaneous pneumothorax may be asymptomatic or only mildly symptomatic (i.e., tachypnea and increasing O_2 needs, progressing to classic signs of respiratory distress). If the infant is on ventilatory support, he/she will have sudden onset of clinical deterioration characterized by cyanosis, hypoxemia, hypercarbia and respiratory acidosis associated with decreased breath sounds and shifted heart sounds.
- A tension pneumothorax is a life-threatening condition caused by air in the pleural space that is under pressure. With tension pneumothorax, compression of major veins and decreased cardiac output occurs, and signs of obstructive shock will be evident. In this circumstance, urgent drainage prior to a radiograph is mandatory **(Refer to Chapter 44).**
- Chest x-ray **(Refer to Appendix 9)** may show just minimal differences in lucency of lung fields (in case of spontaneous pneumothorax) or may show jet black lung and shift of mediastinum to the opposite side (in case of tension pneumothorax).

Pulmonary interstitial emphysema (PIE)

- Pulmonary interstitial emphysema (PIE) is dissection of air into the perivascular tissues of the lung. This interstitial air can be localized or can spread to involve significant portion of the lung.
- PIE is most commonly seen in small preterm infants with significant RDS usually in the first 48 hrs of life.
- With overdistention of the alveoli, rupture may occur and there may be dissection of the air into the interstitial tissues. Air can dissect towards the hilum and the pleural surface through connective tissue surrounding the lymphatics and pulmonary vessels or through the lung interstitium. Pneumothorax and pneumomediastinum may occur.
- PIE affects pulmonary mechanics by decreasing compliance and enhancing ventilation-perfusion (V/Q) mismatch. BPD is a common sequela.
- Chest x-ray may reveal radiolucencies that are either linear or cyst-like in nature. Linear lucencies radiate from the lung hilum and the cyst-like lucencies vary from 1-4 mm in diameter.

Pneumomediastinum

- Pneumomediastinum is defined as free air or gas contained within the mediastinum, almost invariably originating from the alveolar space or the conducting airways.
- Pneumomediastinum can occur with aggressive endotracheal tube insertion or Ryle's feeding tube insertion, neonatal lung disease, mechanical ventilation, or chest surgery or other invasive procedures such as in tracheo-esophageal fistula.

Pneumopericardium

- Pneumopericardium is the least common form.

- Air accumulates in the pericardium around the heart with gradual heart compression and tamponade. Pneumopericardium should be suspected in any ventilated newborn with acute hemodynamic deterioration.

Others

- Pneumoperitoneum
- Subcutaneous emphysema
- Systemic air embolism

Clinical manifestations

- Clinical diagnosis is based on the presence of respiratory distress or sudden deterioration in the infant's clinical status with an alteration in vital signs such as cyanosis or bradycardia.
- In cases with unilateral pneumothorax, asymmetry of the thorax will be noted with hyper-resonant chest on percussion and shift of mediastinum to the opposite side.

Investigations

- Blood gas analysis may show respiratory and/or metabolic acidosis with hypoxemia.
- Chest x-ray (anterior-posterior and lateral views) is the gold standard test for diagnosis of air leak and differentiation of the type.
- With the Transillumination test**,** using a fiber-optic light source to the side of the chest, in pneumothorax cases the light will spread all over the affected side. This test is more sensitive in preterm babies as they have thin chest walls.

N.B.: Needle aspiration should be done for suspected cases of pneumothorax with deteriorating general condition until intercostal tube is inserted.

Management

- Prevention: judicious use of ventilatory support, close attention to distending pressures [Peak inspiratory pressure (PIP) and positive end expiratory pressure (PEEP)], inspiratory time and appropriate weaning of ventilatory support as the clinical condition improves.
- General management of respiratory distress (as mentioned before).
- Specific therapy:
  - Conservative therapy: close observation of the degree of respiratory distress as well as oxygen saturation, without any other intervention aiming at spontaneous resolution and absorption of air. This plan of management can be used more in spontaneous pneumothorax and non ventilated cases.
  - Decompression of air leak according to the type (intercostal tube insertion in case of pneumothorax), **(Refer to Chapter 44).**

Pneumonia

Neonatal pneumonia occurs perinatally or postnatally in about 1% of term neonates and 10% of preterm neonates. This prevalence may be as high as 28% for ventilated VLBW infants in the NICUs.

Etiology

The most often causing organisms in neonatal pneumonia, are mainly GBS, gram negative organisms (e.g. *E.Coli, Klebsiella, Pseudomonas), Staphylococcus aureus, Staphylococcus epidermidis, and Candida.* Less commonly, acquired viral infections (e.g., herpes, CMV).

Clinical manifestations

- Aspiration of bacteria in amniotic fluid leads to congenital pneumonia or a systemic bacterial infection with the manifestations becoming apparent prior to delivery (e.g., fetal distress, tachycardia), at delivery (e.g., perinatal asphyxia) or after a latent period of a few hours (e.g., respiratory distress, shock).
- Early signs and symptoms of pneumonia may be nonspecific, including poor feeding, lethargy, irritability, cyanosis, temperature instability, and the overall impression that the infant is not well.
- Respiratory distress, cyanosis, apnea, and progressive respiratory failure may become evident. In preterm infants, these signs of progressive respiratory distress may be superimposed upon RDS or BPD. If an infant is being ventilated at the time of infection, the most prominent change may be the need for an increased ventilatory support.
- Signs of pneumonia (e.g., dullness to percussion, change in breath sounds, and the presence of rales or rhonchi) are **very difficult** to appreciate in the neonates.
- Pyogenic organisms (e.g., group B-*streptococci*) will result in a fulminant infection. Onset is usually during the first hours or days of life, with rapidly progressive circulatory collapse and respiratory failure. The clinical course and radiographs of the chest may be indistinguishable from severe RDS.

Investigation

- Chest x-rays may reveal infiltrates or effusion, but if the neonate has an underlying RDS or BPD, it is very difficult to determine whether the radiographic changes represent a new process or worsening of the underlying disease.
- Workup for sepsis; CBC with differential and CRP.
- Tracheal aspiration and blood culture are useful tools in identifying the organisms.

Management

- General management of respiratory distress (as mentioned before).
- Specific therapy:
  - If the causative agent is bacterial, antibiotic therapy must be instituted (ampicillin and gentamicin IV). If the culture is positive, treatment consists of the appropriate antibiotic according to culture results for 14 days.
  - If there is a fungal infection, an antifungal agent is used **(Refer to Chapter 45).**

Apnea and Bradycardia

- Apnea is the absence of breathing for >20 seconds or a shorter pause associated with oxygen desaturation or bradycardia (<100 beats/minute). After 30-45 seconds, pallor and hypotonia are seen.
- Apnea and bradycardia are common in premature infants. In term infants, they are uncommon and are usually associated with serious disorders.

- Periodic breathing is defined as respiratory pauses <10 seconds with normal or rapid respirations between episodes. This is not associated with bradycardia.

Classification

- Apnea is traditionally classified as obstructive, central, or mixed.
  - Obstructive apnea may occur when the infant's neck is overflexed or hyperextended. It may also occur due to low pharyngeal muscle tone or to inflammation of the soft tissues, which can block the flow of air though the pharynx and vocal cords.
  - Central apnea occurs when there is a lack of respiratory effort. This may result from central nervous system (CNS) immaturity or from the effects of medications or illness resulting in absent both the airflow and chest wall motion.
  - Mixed apnea is both central and obstructive apnea.
- Clinically, apnea is classified as:
  - Idiopathic apnea of prematurity:
    - Occurs in infants who are usually <34 weeks' gestation, weighing <1,800 gm, and having no other identifiable cause.
    - The most common pattern of idiopathic apnea in preterm neonates is that of a mixed etiology (50-75%), with obstructive apnea preceding (usually) or following central apnea.
    - It usually resolves by 36-37 weeks' corrected age without long-term sequelae.
  - Pathological apnea.
    - Pathological apnea has variable etiologies listed in **(Table 22-2)**.

Table (22-2): Potential causes of pathological apnea

Neurological	IVH, perinatal asphyxia, meningitis, cerebral infarction, seizures
Respiratory	Hypoxia, airway obstruction, severe RDS, pneumonia, pneumothorax, inadequate ventilation or too early extubation
Infections	Sepsis
Gastrointestinal	NEC, gastroesophageal reflux, feeding intolerance
Metabolic	Hypoglycemia, hypocalcemia, hyponatremia or hypernatremia, hyperammonemia, acidosis, hypothermia
Cardiovascular	Hypotension, heart failure, PDA, congenital heart block
Hematological	Anemia or polycythemia
Drugs	• Prenatal exposure (transplacental transmission): narcotics, β-blockers • Postnatal exposure: sedatives, prostaglandin E_1

Clinical manifestations

- All neonates assessed as being at high risk for apneic spells (<34 weeks' GA) should be carefully monitored for at least the first week after birth.
- A thorough physical and neurological examination rules out grossly apparent abnormalities.

- Observation and documentation of apneic and bradycardic spells and any relationship to precipitating factors help to differentiate primary from secondary apnea.

Investigations

- CBC with differential
- Serum electrolyte, calcium, and glucose levels
- Blood gas analysis
- Radiologic studies: chest x-ray, abdominal x-ray, cranial sonar and a computed tomography (CT) for infants with definite signs of neurologic involvement

Management

General measures

- Begin with tactile stimulation for mild self resolving apneas.
- Give oxygen supplementation by nasal cannula (prongs) or head box. Nasal cannula flows of 0.5-2 liters/minute are capable of delivering a positive distending pressure to preterm infants.
- If no response to tactile stimulation and O_2 supplementation, bag and mask ventilation should be used during the spell.
- Avoid maneuvers that may trigger apnea (e.g., suctioning, and oral feedings), and extreme flexion or extension of the neck.
- Give packed red cell transfusion, if hematocrit <35%, with frequent and severe apneic spells.
- Follow specific therapy to treat the identified cause**,** (e.g., give antibiotics for sepsis, infuse glucose 10% for hypoglycemia, and correct electrolyte abnormalities).

Pharmacological (Xanthine) therapy

- Theophylline: start with a loading dose of 6 mg/kg/IV followed 8 hrs later by a maintenance dose of 2 mg/kg every 8 hrs. Theophylline level should be monitored; levels of 7-12 μg/ml are required.
- Caffeine citrate is safer than aminophylline and is given at a dose of 20 mg/kg as a loading dose orally or IV over 30 minutes, followed, 24 hrs later, by a maintenance dose of 5-8 mg/kg orally or IV every 24 hrs. An adequate therapeutic plasma level is 5-25 μg/ml.
- If no apneic spells have occurred for 5-7 days, treatment is generally discontinued at 34-36 weeks' gestation.
- Continue monitoring until no apnea has been detected for at least 5 days after that period.

Nasal-CPAP

- Some premature infants continue to have apnea while on theophylline therapy. A low CPAP of 4-5 cmH_2O decreases the incidence of apnea in these infants.

Mechanical ventilation

- May be required if other measures are unsuccessful.

Chapter 23

Disorders of Acid-Base Balance

Disorders of Acid Base Balance

Normal pH is essential for intact functioning of all enzymatic processes, and thus for the intact functioning of all the organ systems of the body.

Newborns are subject to many stresses that may affect their acid-base balance. Newborn infants and especially premature neonates are limited in their ability to compensate for acid-base alterations.

Definitions

pH

The negative logarithm of hydrogen ion concentration is pH = -log $\{H^+\}$, and corresponds to a pH of range of 7.35-7.45.

Acidosis

Acidosis is a downward shift in pH below 7.35. It is either metabolic acidosis or respiratory acidosis.

Metabolic acidosis

It is due to either:

- Increased amounts of nonvolatile acids (increased anion gap) or
- Decreased amounts of alkali (HCO_3^-) in ECF (normal anion gap)

Respiratory acidosis

It is due to hypoventilation and decreased excretion of volatile acid (CO_2).

Alkalosis

Alkalosis is an upward shift in pH above 7.45. It is either metabolic alkalosis or respiratory alkalosis.

- Metabolic alkalosis: due to either increased amounts of HCO_3^- in ECF.
- Respiratory alkalosis: due to hyperventilation and increased excretion of volatile acid (CO_2).

N.B.: Anion gap = Serum [Na+] – (Serum [Cl-] + Serum [HCO3-]) (normal: 8-16 mEq/L).

Acid-Base Disorders

Normal arterial blood gas values

- pH: 7.35-7.45
- $PaCO_2$: 35-45 mmHg
- HCO_3^- : 22-26 mEq/L
- Base excess/base deficit: (-4)-(+4)
- paO_2: 60-80 mmHg
- O_2 saturation 92-94%

N.B.: Venous samples ($PaCO_2$ 6-8 mmHg higher and pH slightly lower than arterial samples) can be used to assess ventilation and acid base status but not oxygenation.

Parameters used for the diagnosis of acid-base disorders

- Type: acidosis or alkalosis (by pH)
- Cause: metabolic or respiratory (by $PaCO_2$ and bicarbonate)
- Response: uncompensated or compensated
- Duration: acute or chronic
- Form: simple or mixed

Expected compensation in primary acid-base disorders

- Metabolic disturbances are compensated acutely by the pulmonary mechanism (hyperventilation in acidosis or hypoventilation in alkalosis), and chronically by appropriate renal responses.
- Respiratory disturbances are compensated by appropriate renal tubular responses (bicarbonate retention in acidosis or bicarbonate loss in alkalosis).

Table (23-1): Expected compensatory mechanisms operating in primary acid-base disorders

Acid-Base Disorder		Primary event	Compensation	Rate of compensation
Metabolic acidosis	normal anion gap	HCO_3^- Loss	↓ PCO_2	For ↓1 mEq/L in HCO_3^-→ ↓ PCO_2 by 1-1.5 mmHg
	increased anion gap	↑ acid production ↑ acid intake		
Metabolic alkalosis		↑ HCO_3^-	↑ PCO_2	For ↑1 mEq/L in HCO_3^-→ ↑ PCO_2 by 0.5-1 mmHg
Respiratory acidosis	Acute <12-24hrs	↑ PCO_2	↑ HCO_3^-	For ↑10 mmHg in PCO_2 → ↑ HCO_3^- by 1 mEq/L
	Chronic 3-5 days			For 10 mmHg ↑ in PCO_2→ ↑ HCO_3^- by 4 mEq/L
Respiratory alkalosis	Acute <12 hrs	↓ PCO_2	↓ HCO_3^-	For ↓10 mmHg in PCO_2 → ↓ HCO_3^- by 1-3 mEq/L
	Chronic 1-2 days			For ↓10 mmHg in PCO_2 → ↓ HCO_3^- by 2-5 mEq/L

Modified from: Brewer ED. Disorders of acid-base balance. Pediatr Clin North Am 37: 430-447, 1990.

The Winters' formula can be used to predict the appropriate respiratory response (decrease in PCO_2) to a metabolic acidosis: [$PaCO_2 = (1.5 \times HCo_3^-) + 8 \pm 2$].

Example: the Winters' formula predicts that a decrease in HCO_3^- to 10 mEq/L will result in a decrease of PCO_2 to 21-25 mmHg.

Forms of acid-base disorders

Simple acid-base disorders

Simple disorder occurs when only one primary acid-base abnormality and its compensatory mechanism occur.

Mixed acid-base disorders

Mixed disorders occur when a combination of simple acid-base disturbances occurs. They should be considered when the expected compensation falls out of the expected range.

Acid-base nomogram

A nomogram presented in **(Figure 23-1)** can aid in diagnosing simple and mixed acid-base disorders. If the pH, PCO_2, and HCO_3^- are measured, then a presumptive diagnosis may be made by locating the point corresponding to these values on this nomogram to determine which of the diagnostic zones it falls into. Examples:

- A newborn with pH 7.3, PCO_2 25 mmHg, and HCO_3^- 12 mEq/L will be classified as having simple metabolic acidosis.
- A newborn with pH 7.17, PCO_2 34 mmHg, and HCO_3^- 12 mEq/L will be classified as having mixed metabolic and respiratory acidosis. This could be explained by observing the acidic pH and the low serum HCO_3^- in this patient suggesting a primary metabolic acidosis. However, when the values for pH, HCO_3^-, and PCO_2 are plotted on the nomogram, the convergence point falls outside the range for a simple metabolic acidosis, suggesting the possibility of a superimposed respiratory acidosis.

N.B.: Results of blood gas analysis should be correlated to the infant's clinical status.

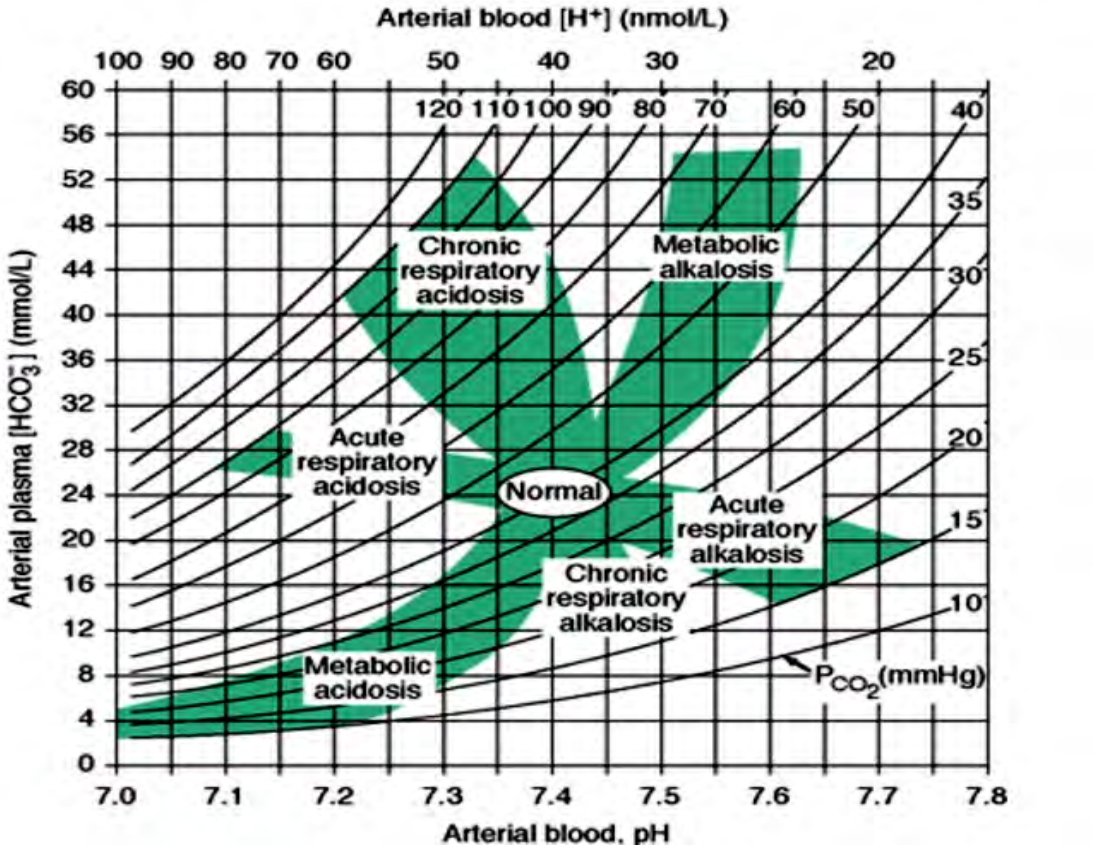


Figure (23-1): Acid-base nomogram

Depending on pH, PCO_2 and serum bicarbonate (HCO_3^- mmol/L = mEq/L). Reproduced with permission from DuBose Jr, TD. Acid base disorders. In: Brenner and Rector's The kidney, 6th Ed, Brenner BM (ed.). Philadelphia, Saunders 2000: 925-997.

Metabolic Acidosis

Etiology

Metabolic acidosis with an elevated anion gap

It indicates the accumulation of strong acids due to increased intake or production, or to decreased excretion. It is most frequently due to:

- Lactic acidosis; secondary to tissue hypoxia as seen in:
  - Asphyxia
  - Hypothermia
  - Severe respiratory distress
  - Sepsis
  - Shock
- Inborn error of metabolism as in:
  - Congenital primary lactic acidosis
  - Organic acidemias
- Renal failure
- Diabetic ketoacidosis

Metabolic acidosis with a normal anion gap

It occurs as a result of HCO_3^- loss from the extracellular space through the kidneys or GI tract. It is most frequently due to:

- Renal bicarbonate loss:
  - Bicarbonate wasting due to immaturity
  - Renal tubular acidosis
- Gastrointestinal bicarbonate loss:
  - Small bowel drainage such as ileostomy and fistula
  - Diarrhea

Complications

- Arteriolar vasoconstriction followed by dilatation
- Depression of cardiac contractility
- Systemic hypotension
- Pulmonary edema
- Arrhythmias

Management

- Correction of the underlying cause can usually be achieved by improving circulating blood volume and/or cardiac output.

- In case of significant metabolic acidosis (arterial pH <7.25), it may be useful to give exogenous sodium bicarbonate ($NaHCO_3$).
- In case of significant metabolic acidosis (arterial pH <7.25), it may be useful to give exogenous sodium bicarbonate ($NaHCO_3$).
  - Dose: **$NaHCO_3$ (mEq) = base deficit (mEq/L) × body weight (kg) × 0.3**
  - $NaHCO_3$: not given if ventilation is inadequate
  - $NaHCO_3$ (8.4% concentration): administered slowly and diluted 1:1 with glucose 5% or sterile water
  - Recommended: half of the calculated total correction dose for initial therapy to avoid overcorrection of metabolic acidosis; subsequent doses given based on the results of repeated blood gas measurements

Metabolic Alkalosis

Etiology

- Excessive loss of acid from the GI tract:
  - Continuous nasogastric aspiration
  - Persistent vomiting
- Excessive administration of $NaHCO_3$ in attempting to correct metabolic acidosis
- Other causes:
  - Hypokalemia
  - Furosemide therapy
  - Bartter syndrome

Management

- The treatment should be directly related to the cause of metabolic alkalosis.
- Associated hypovolemia and/or hypokalemia should be corrected.

Respiratory Acidosis

Etiology

It is a common problem in newborn infants. It can be due to many causes such as RDS, pneumonia, PDA, bronchopulmonary dysplasia.

Management

Improve alveolar ventilation and treat the underlying disorder. This is often provided by mechanical ventilation in sick patients.

Respiratory Alkalosis

Etiology

- Hyperventilation in spontaneously breathing newborns is due to fever, sepsis and CNS disorders.
- In NICU, the most frequent cause is hyperventilation of the intubated newborn.

Complications

Hypocapnia is associated with the development of periventricular leukomalacia and BPD in ventilated preterm infants.

Management

Specific management of the underlying process causing hyperventilation

Chapter 24

Oxygen Therapy

Oxygen Therapy

Clinicians must keep in mind that oxygen is a drug and must be used in accordance with well recognized pharmacologic principles (i.e., since it has certain toxic effects and is not completely harmless, it should be given only in lowest dosage or concentration required by the particular patient).

Oxygen is the most commonly used therapy in the neonatal intensive care units. The ultimate goal of oxygen therapy is to achieve an adequate tissue oxygenation, but without creating an oxygen toxicity or complications.

Physiological Considerations

Tissue oxygenation depends on:

- Inspired oxygen
- Gas exchange mechanisms within the lungs
- Oxygen carrying capacity of the blood (approximately 97% of oxygen transported to the tissues is carried by hemoglobin, and 3% is dissolved in plasma)
- Cardiac output
- Local tissue edema or ischemia

Equipment for Oxygen Administration

Special care neonatal units must have properly functioning equipment available for the administration of oxygen to the infant. Personnel must be trained in the use of the equipment and be able to evaluate infant's status. Refer to **(Figure 24-1) and (Figure 24-2)** for the required equipment and proper set-up.

Oxygen source

Pipe system, O_2 cylinder, or oxygen concentrator: an adequate supply of oxygen must be available at all times. Pipe system is the cheapest and more practical. Oxygen cylinders can be saved for emergencies and transport.

Oxygen flowmeter

It is connected to the oxygen source and regulates the flow of gas in liter/minute.

Humidifier

It is used to humidify the dry inspired gas. The water must be sterile because tap water contains bacterial organisms that will multiply in the warmed water causing infection of the infant. The water should be maintained at the proper level and should be changed with new sterile water every 24 hrs.

Connecting tubing and oxygen delivery equipment

It is the method that delivers the oxygen to the infant **(Figure 24-1) and (Figure 24-2)**.

Oxygen analyser

It determines the concentration of oxygen/air being delivered to the infant. The analyser must be routinely maintained and calibrated properly. Once the calibration is set, the analyser

sensor should be placed in the oxyhood near the infant's nose to best determine the concentration the infant is receiving.

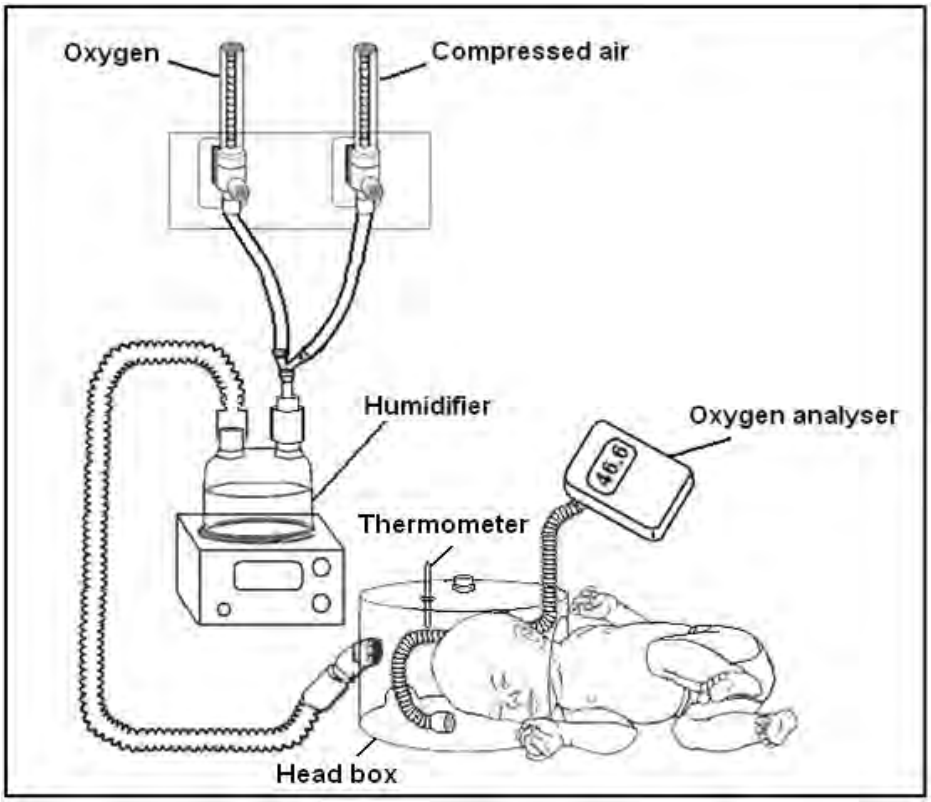


Figure (24-1): Equipment for oxygen administration

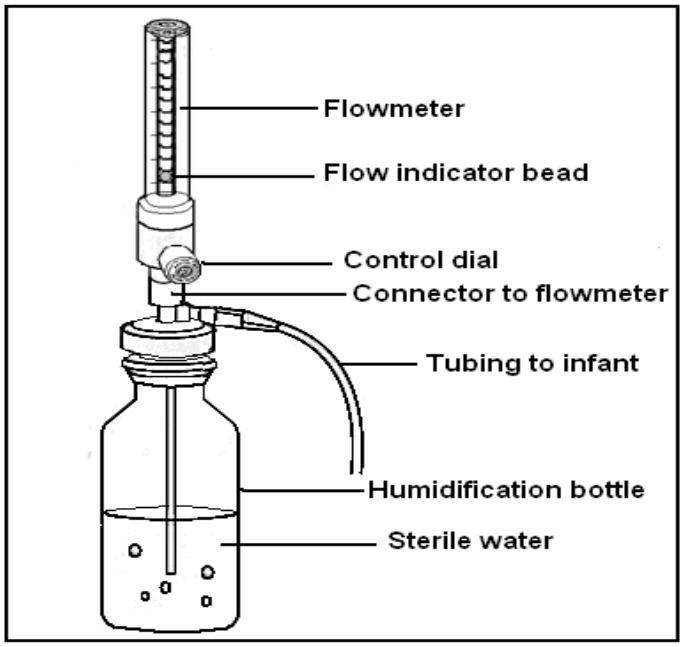


Figure (24-2): An oxygen humidifier attached to a flowmeter

Methods for Oxygen Delivery

Nasal cannula (nasal prongs)

- The nasal cannula provides low-to-moderate O_2 concentrations (22-55%) at flow rates (0.5-2 liter/minute).

- The delivery of inspired oxygen concentration is somewhat unpredictable, depending on how much ambient air is entrained (influenced by inspiratory flow rate and minute ventilation) during inspiration.
- The nasal cannula is the most efficient way to administer oxygen. The delivered oxygen should be warm and humidified.

Head boxes (oxyhood)

- It is useful for infants not tolerating the cannula or the mask.
- It may provide high concentrations of O_2 (more than 60%).
- Oxygen concentrations can be measured by an oxygen analyser.
- The head box should be made of a clear plastic and should be of an appropriate size (enough to cover the infant's head while allowing the infant to move). It should be solid so that the oxygen/air does not leak out or further blend with room air.
- Flow rate must be sufficient to reduce CO_2 accumulation (not less than 4 liter/minute, usually 6-10 liter/minute).
- A thermometer should be available and placed in the head box. The temperature inside the head box should be regulated and maintained within the infant's neutral thermal environment (NTE) range to prevent chilling or overheating.

Incubator

- Oxygen concentration inside usually does not exceed 30-40%. Higher concentrations are difficult to maintain because of intermittent opening of the incubator doors.
- Oxygen concentration can be measured by an oxygen analyser (placed near baby's head and calibrated each shift).
- This method is usually used during oxygen weaning.

Simple face mask

- It delivers an FiO_2 of 35-55% at flow rate 6-10 liter/minute.
- Oxygen concentration cannot be measured, it depends on flow rate.
- It is not commonly used in the NICUs.

Venturi mask

- Venturi mask (also known as air-entrainment mask) is designed to deliver specific oxygen concentrations **(Figure 24-3)**.
- It has several adapters, each with a larger opening that entrains a greater amount of room air. A certain gas flow is required to deliver the desired oxygen concentration.

N.B.: Nasal cannula and head box are the most commonly used methods for oxygen delivery in the NICUs.

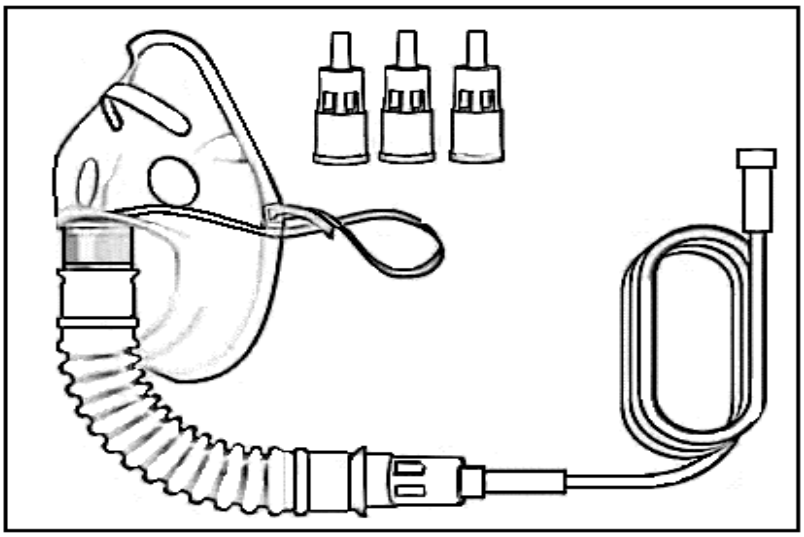


Figure (24-3): Venturi mask

Compressed Air

It is important to have a compressed air source to blend with the 100% oxygen and provide an oxygen concentration to the infant of less than 100%; which can be achieved by using an oxygen blender. If an oxygen blender is not available we may blend compressed air with oxygen by using 2 flowmeters - one for compressed air and the other for oxygen **(Figure 24-1)** and the required O_2 concentration can be calculated according to **(Table 24-1).**

If compressed air is not available, it is necessary to have a mechanism to entrain room air with the 100% oxygen, in order to administer varying oxygen concentrations to the infant. One possible mechanism is the venturi device.

Table (24-1): Oxygen concentrations for air and oxygen mixtures

% O_2 Conc.		Compressed Air (liters/minute)									
		1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Oxygen (liters/minute)	**1**			41%	37%	34%	32%	31%	30%	29%	28%
	2		61%	53%	47%	44%	41%	38%	37%	35%	34%
	3	80%	68%	61%	55%	51%	47%	45%	43%	41%	39%
	4	84%	74%	66%	61%	56%	52%	50%	47%	45%	44%
	5	86%	77%	70%	65%	61%	57%	54%	51%	49%	47%
	6	88%	80%	74%	68%	64%	61%	57%	54%	53%	51%
	7	90%	82%	76%	71%	67%	64%	61%	58%	56%	54%
	8	91%	84%	78%	74%	70%	66%	63%	61%	58%	56%
	9	92%	86%	80%	76%	72%	68%	65%	63%	61%	58%
	10	93%	87%	82%	77%	74%	70%	67%	65%	63%	61%

Monitoring of Oxygen Therapy

Oxygen therapy and infant's oxygenation must be closely monitored. There are many methods to monitor the oxygen therapy; the most common and applicable methods are the pulse oximetry and the blood gas analysis.

Pulse oximetry

- It is a non-invasive method for continuous monitoring of the arterial oxygen saturation (SaO_2).
- The target O_2 saturations should be based on the infant's GA, as demonstrated in **(Table 24-2)**.
- Limitations:
  - Affected by poor perfusion (hypotension, hypovolemia, cold extremities, and acidosis)
  - Motion artifact
  - Light interference (e.g., phototherapy)
  - Failure to detect hyperoxia (PaO_2 >100 mmHg) because of the sigmoid shape of oxyhemoglobin dissociation curve
- Clinical judgment should be used in selecting the target oxygen saturation for an individual patient (e.g., cases with PPHN need higher O_2 saturation)

Arterial blood gas analysis

It measures arterial oxygen pressure (PaO_2)

- Umbilical artery catheter: it is used in preference to peripheral in VLBW infants or infants likely to have prolonged or difficult course.
- In other infants the peripheral artery (e.g., radial artery, posterior tibial artery) may be used.

Capillary blood gas analysis

- This gives an indication of pH and PCO_2 only.
- It is not useful for partial O_2 pressure (PaO_2) assessment.

Table (24-2): The target SaO_2 and PaO_2, based on the infant's gestational age

Infants	PaO_2	Saturation Range*
Preterm infants <32 weeks' gestation	50-70 mmHg	87-92%
Preterm infants ≥32 weeks' gestation	60-75 mmHg	90-93%
Term/post-term infants	60-90 mmHg	90-95%

*For infants who are in air and do not need supplemental oxygen, saturations that are mostly above 90% are regarded as satisfactory.

N.B.: Fraction of inspired oxygen (FiO_2) should be titrated to the lowest concentration required to meet oxygenation goals.

Documentation

Oxygen concentration in percentage or liter flow/minute, the method of oxygen delivery and the water temperature should be documented hourly on the **Daily Neonatal Clinical Record**. All adjustments made based on the neonate's status and/or physician orders must be noted.

Oxygen Therapy Equipment Changes

- Nasal prongs should be changed once a week, or in between if blocked with nasal secretions.
- Oxygen masks/portable oxygen analysers and SaO_2 probes are changed when baby is discharged.

Complications of Oxygen Therapy (Oxygen Toxicity)

(Refer to Chapter 27)

The term "oxygen toxicity" refers to the pathologic tissue changes (whether pulmonary or extrapulmonary) that occur as a result of prolonged and/or high concentrations of supplemental oxygen. Oxygen toxicity is mediated by reactive oxygen species (radicals), which can promote inflammation and induce cell death. There is no well-defined threshold FiO_2 or duration of supplemental oxygen therapy below which oxygen toxicity cannot occur.

Potential adverse clinical consequences of supplemental oxygen therapy include:

Absorptive atelectasis

High concentrations of supplemental oxygen may cause washout of alveolar nitrogen to capillaries and absorptive atelectasis. This could happen when oxygen absorption from the alveoli occurs at a faster rate than its replenishment by inhaled oxygen.

Bronchopulmonary dysplasia-BPD

Bronchopulmonary dysplasia is a chronic lung disease that occurs most often in preterm infants, commonly <32 weeks' gestation. It is characterized by epithelial hyperplasia and squamous metaplasia in the large airways, thickened alveolar walls, and peribronchial and interstitial fibrosis.

Retinopathy of prematurity (ROP)

Retinopathy of prematurity is a vasoproliferative disorder of the retina which occurs principally in preterm infants <32 weeks' gestation. Visual loss may result so screening is mandatory for early intervention.

Chapter 25

Continuous Positive Airway Pressure

Continuous Positive Airway Pressure (CPAP)

Definition

Continuous positive airway pressure (CPAP) is the application of a continuous sustained positive pressure in the airway throughout the respiratory cycle of a spontaneously breathing infant.

Physiologic Effects and Advantages of CPAP

- Increases lung volume and functional residual capacity (FRC) by increasing alveolar size, preventing atelectasis at the end of exhalation, and recruiting collapsed alveoli.
- Achieves better oxygenation by improving ventilation-perfusion matching and decreasing intrapulmonary right-to-left shunting.
- Conserves surfactant, by minimizing surfactant consumption.
- Improves synchrony of respiratory thoraco-abdominal movements; with the application of CPAP, the breathing pattern becomes slower and more regular and grunting generally ceases.
- Splints the airway and increases its diameter.
- Splints the chest wall and the diaphragm.
- Reduces the frequency of obstructive and mixed apneic spells.

N.B.: FRC is the volume of gas contained in the lung after a normal expiration.

Methods of CPAP Application

- CPAP may be delivered via:
  - Nasal prongs (Nasal CPAP)
  - Nasopharyngeal tubes (Nasopharyngeal CPAP)
  - Endotracheal tubes (Endotracheal CPAP)
  - Face mask (Face Mask CPAP)
- Delivery of CPAP by means of nasal prongs or nasopharyngeal tubes is the most commonly used method.

Advantages of Nasal CPAP (NCPAP)

- It is relatively non traumatic, can result in less barotrauma, and prevents the need for endotracheal intubation.
- Nasal prongs allow constant access to the baby and are simple to set up and to maintain.

N.B.: Prolonged endotracheal CPAP should not be used because the high resistance of the endotracheal tube increases the work of breathing, especially in small infants.

Indications of Nasal CPAP

Infants who may benefit from NCPAP are:

- Premature infants with minimal respiratory distress and minimal need for supplemental oxygen (mild to moderate RDS): the key for successful management of RDS is early initiation of CPAP, (i.e., starting CPAP immediately after the onset of respiratory distress or even prophylactically at birth to extremely preterm infants to prevent atelectasis). Use of CPAP appears to reduce the need for subsequent mechanical ventilation.
- Infants with TTN.
- Infants with meconium aspiration syndrome.
- Preterm infants with moderately frequent apneic spells.
- Infants who have been weaned from a mechanical ventilator.
- Infants with airway diseases such as tracheomalacia and bronchiolitis.
- Infant with paralysis of the diaphragm.
- Post operative (e.g., exomphalos, gastroschesis, congenital heart disease, and thoracic surgery).

Criteria for Starting Nasal CPAP

- The inability to maintain a PaO_2 of 60 mmHg with an FiO_2 of 0.6 constitutes an adequate indication for initiating CPAP in infants with RDS.
- NCPAP should be considered if an infant has any of the following:
  - Respiratory rate >60 breaths/minute
  - Moderate to severe grunting
  - Respiratory retraction
  - Oxygen saturation <93% (preductal)
  - Frequent apnea
- Nasal CPAP can be given prophylactically even in the delivery room to extremely preterm babies. Also it can be given after short intubation and surfactant instillation.

Contraindications of NCPAP

- The need for mechanical ventilation because of respiratory failure
- Very unstable respiratory drive with frequent apneas or bradycardias not improved by CPAP
- Upper airway anomalies (e.g., cleft palate, choanal atresia, tracheoesophageal fistula)
- Untreated congenital diaphragmatic hernia
- Severe cardiovascular instability

Characteristics of a Good CPAP System

A good CPAP system should have the following characteristics:

- Flexible and light tubing allowing the infant's position to be changed easily
- Easy to apply and to remove
- Low resistance for the patient to breathe spontaneously
- As non-invasive as possible
- Simple and easily understood by all users
- Safe and cost effective

Components of CPAP System

CPAP system consists of three components:

- A circuit for the flow of inspired gas: the sources of oxygen and compressed air provide the inspired gas. An oxygen blender enables the appropriate FiO_2 to be given. A flowmeter controls the rate of flow of the inspired gas and is usually kept between 5-10 liters/minute. A heated humidifier warms and humidifies the inspired gas.
- A device to connect the circuit to the infant's airway; the nasal catheter (prongs) is the preferred method.
- A means of creating a positive pressure in the circuit.

Methods of Generating Continuous Positive Pressure

The gas mixture delivered via CPAP is derived from either continuous or variable flow.

Continuous-flow CPAP

The generated gas flow is directed against resistance of the expiratory limb of the circuit. Positive pressure in the circuit can be achieved by either: bubble or water-seal CPAP requiring the immersion of the distal expiratory tubing in sterile water to the desired depth (5 cm, in order to provide 5 cmH_2O of CPAP), or by a ventilator-derived CPAP (i.e., a CPAP valve that is adjusted to provide a variable resistance to the gas flow).

Variable-flow CPAP

Continuous pressure is generated at the airway proximal to the infant's nares. Variable-flow devices use dual injector jets directed toward each nasal prong to maintain a constant pressure.

- When the patient makes a spontaneous inspiratory effort, the generator converts the kinetic energy of the flow to pressure, thereby reducing the work of breathing of the patient.
- When the infant starts a spontaneous expiratory effort, there is a decrease in the forward velocity of the gas flow. This creates a "fluidic flip" that causes the flow to flip around and to leave the generator chamber via the expiratory limb. This depends on the phenomenon of the tendency of a fluid or gas to follow the curved surface of a wall. So once the infant starts to exhale, the jet of gas flow easily changes direction from towards the nasal prongs to the expiratory channel **(Figure 25-1)**.
- When expiratory effort stops, the flow instantly flips back to the inspiratory position.

The internal design of the generator allows it to manipulate the gas flow to provide a stable CPAP level at the patient's airway throughout the entire respiratory cycle.

As such, the baby does not have to exhale against high inspiratory flow, and work of breathing is decreased as compared to the continuous-flow CPAP in which the infant is forced to exhale against the incoming gas which increases the work of breathing.

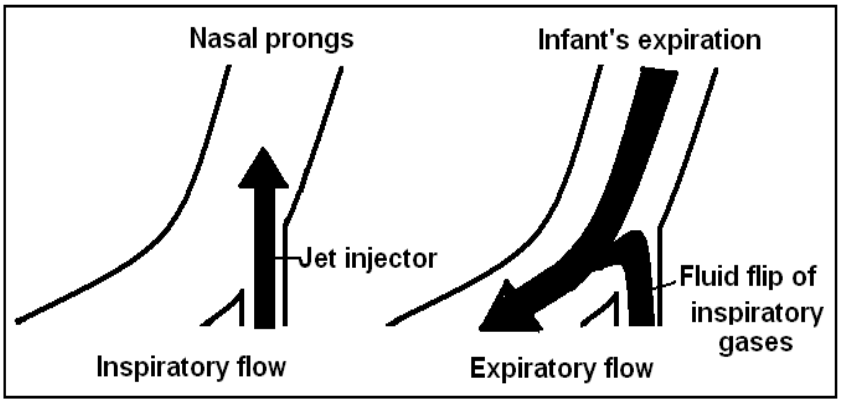


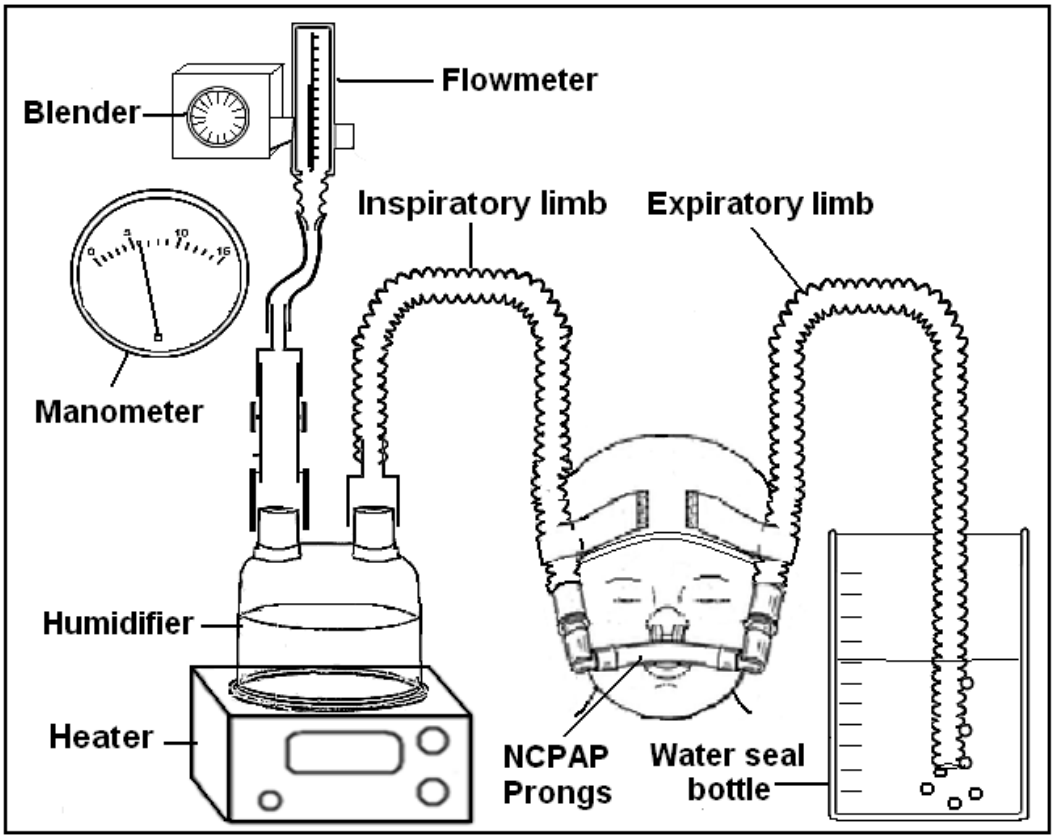
Figure (25-1): Schematic representation of the fluidic flip of the variable-flow CPAP device

Bubble CPAP System

Components

A complete CPAP circuit should be set up and ready for use at **all times.** If an infant requires CPAP, the only delay should be that of opening the correct size nasal catheter (prongs), turning on the humidifier heater and filling the chamber and the outlet bottle with sterile water. The bubble CPAP unit will require the following equipment **(Figure 25-2)**:

- Oxygen and air flow sources
- Oxygen blender with flowmeter
- Tubing to lead from the flowmeter to humidifier
- Humidifier
- Corrugated circuit tubing with humidifier connections
- Nasal catheter set: contains nasal prongs, and hat (bonnet)
  - The correct size prongs should fit the nares without pinching the septum. If the prongs are too small, there will be an unnecessary increased airway resistance and an air leak from around the prongs making it hard to maintain the appropriate pressure. Prongs that are overly large may lead to mucosal damage and septum erosion. General guidelines for the correct size prongs are:
    - Size 2 for weight 1,000-2,000 gm
    - Size 3 for weight 2,000-3,000 gm
    - Size 4 for weight 3,000-4,000 gm
    - Size 5 for weight >4,000 gm



NCPAP: Nasal continuous positive airway pressure

Figure (25-2): Bubble CPAP delivery system

Application of CPAP

Preparing the system

- Adjust the blender to the appropriate FiO_2.
- Turn on the flowmeter to a rate between 5-10 liters/minute depending on the infant's size.
- Fill the humidifier container with sterile water up to the correct mark, turn on the humidifier, and adjust the humidification, thus maintaining the fluidity of the secretions and avoiding insensible water loss. Set the temperature at 36^{o}C to warm the gases delivered to the infant.
- Fill the bottle up to the correct mark with sterile water. Put the distal expiratory end of the corrugated tube in the bottle to the desired level (i.e. 5 cmH_2O).
- Choose the correct size prongs and connect them to the free ends of both of the corrugated tubes.
- Occlude the ends of the nasal prongs to test integrity of the circuit. Observe bubbling in the bottle.

Attaching the system to the infant

- Position the infant with the head of the bed elevated 30°.
- Gently suction the infant's mouth, nose, and pharynx. Use the largest sized catheter that can be passed into the nose without significant resistance. Make sure the infant does not have choanal atresia.

- Place a small roll under the infant's neck/shoulder. Slight neck extension helps maintain an open air way.
- Moisten the prongs with sterile water or saline drops before placing them.
- Ensure a small space between the tip of the septum and the bridge between the prongs.
- Pass an orogastric tube and aspirate the stomach contents. You can leave the tube in place to avoid gastric distension.
- Use an appropriate sized hat (bonnet).
- Start CPAP at a pressure of 5 cmH_2O to be increased by 1-2 cmH_2O increments if necessary (to a maximum of 8 cmH_2O) based on the clinical response and the O_2 requirements.
- Once the system is applied, check that the prongs are positioned appropriately and that the CPAP system is bubbling. This ensures proper application and operation of the NCPAP delivery system.

N.B.: The optimum level of CPAP can be defined as the airway pressure at which SaO_2 and PaO_2 are optimized without adverse effects on cardiac output. If the pressure is increased above this level, cardiac output decreases, O_2 transport is impaired and $PaCO_2$ rises.

Maintaining NCPAP

- Follow the infection control guidelines.
- Every infant on NCPAP should have vital signs checked every 2-4 hours.
- Ensure that infant's nose is in a normal position (i.e., not pushed upwards), his/her eyes are clearly visible and the ears are not folded.
- Suction nasal cavities, mouth, pharynx and stomach, as needed:
  - An increased respiratory effort, an increased need for oxygen and the occurrence of apnea/bradycardia may be indications for suctioning.
  - Use the largest size suction catheter able to pass without significant resistance.
  - Note the amount, consistency, and color of the secretions. To loosen dry thick secretions, use a few drops of sterile 0.9% saline.
- Change the infant's position every 4-6 hrs. This will allow postural drainage of all lung secretions.
- Neuromuscular blocking agents have no place in NICUs adopting gentle ventilation/CPAP strategies. Agitation can be reduced by "nesting" the infant in linen made boundaries, decreasing environmental light and sound stimuli with minimal handling of the infant.
- Change CPAP circuits weekly.

Indicators of Improvement on NCPAP

Clinical

- Decreasing work of breathing – decreased respiratory rate, grunting, flaring, and retracting

- Improving infant's condition

Blood gas analysis

- Decrease or stabilization of oxygen requirements at FiO_2 <0.3 with PaO_2 >50 mmHg (between 60-80 mmHg) or O_2 saturation between 90-93%
- Maintenance of adequate ventilation

  $PaCO_2$ <60 mmHg (permissive hypercapnia with upper limit of CO_2 up to 65 mmHg can be allowed) and pH 7.25-7.45

Radiological

- Improved lung volumes and appearance on chest x-ray films.

Weaning from NCPAP

- After the CPAP is applied, infants should breathe easily and with a noticeable decrease in respiratory rate and retractions. The FiO_2 should be lowered gradually in decrements of 2-5% as guided by the pulse oximeter reading or by the blood gas results. The requirement of FiO_2 usually comes down to room air.
- If the infant is breathing comfortably on CPAP with an FiO_2 of 21%, he/she should be given a trial off of CPAP:
  - The nasal prongs should be separated from the corrugated tubing while the tubing is kept in place; it is a matter of trial and error.
  - A series of trials off CPAP is usually required before the infant can be weaned off completely.
  - During the trial off CPAP, the infant should be assessed for any tachypnea, retractions, oxygen desaturation, or apnea. If any of these signs are observed the trial is considered to be a failure. The infant should be restarted immediately on CPAP for at least a day before another trial is attempted.
- In infants >28 weeks' gestation, CPAP weaning can be successful by either gradual decrement of pressure to 3 cmH_2O or increment of the time off-CPAP (cycling). In infants of <28 weeks' gestation, pressure weaning may prove to be more appropriate.
- If infants are considered ready for a trial off CPAP, ensure that conditions are optimal (e.g., no severe anemia, no symptomatic PDA or early sepsis), if necessary caffeine or aminophylline may be used.
- Fast weaning in an infant who requires a high FiO_2 and is clinically unstable is commonly associated with weaning failure. It is wise to anticipate and prevent lung collapse rather than manage already collapsed lungs.
- While off CPAP, supplemental oxygen can be given, as needed.
- For a period of 12-24 hrs after coming off from the CPAP, infants will usually require nasal and oral suctioning at least as frequently as for the previous 24 hrs.

Feeding with NCPAP

Nasal CPAP is not a contraindication to enteral feedings. It may be necessary to aspirate excess air from the stomach before feeds. If clinically stable, infants receiving NCPAP may

be breastfed, bottle, or tube-fed. An orogastric tube is preferable as this allows enteral feeding to be carried out without obstructing the infant's airways.

Family Centered Care

Infants receiving NCPAP can be cuddled by their parents safely. Kangaroo care can also be practiced. However, it is important for the nurse to assess the overall condition of the infant to decide whether or not such care is appropriate.

CPAP Failure (Indications for Mechanical Ventilation)

Infants on NCPAP of 5 cmH_2O will need mechanical ventilation if any of the following occurs:

- PaO_2 <50 mmHg while breathing 60-80% oxygen
- Respiratory acidosis with pH of less than 7.20-7.25, or $PaCO_2$ >60-65 mmHg
- Persistent hypoxemia and metabolic acidosis with a base deficit of >-8
- Marked retractions observed while on CPAP
- Intractable apnea and bradycardia

Troubleshooting during NCPAP

The bottle is not bubbling

This is due to an air leak somewhere in the circuit. Remove the prongs from the nose and occlude them:

- If the system bubbles, it means that the size of the prongs is not correct (they are probably too small).
- Sometimes, if the infant simply opens his/her mouth, the system will stop bubbling. This can be corrected by ensuring mouth closure using a pacifier or placing a chin strip. However, the use of adhesive strapping of the mouth to keep it closed should be avoided for fear of aspirating gastric contents.
- If the bottle does not bubble, it means the problem is within the circuit. Systematically check each component of the circuit.

The prongs do not stay in place

Check for the following:

- Are the prongs the right size?
- Does the hat fit snugly?
- Are the corrugated tubes fixed correctly to the hat on both sides and at the correct angle to the prongs?

The infant is not settling down

- Check for airway secretions.
- Use a pacifier and swaddle the infant.
- Aspirate excess gas from the stomach, if necessary.

Nasal injury

- Nasal injury ranges from mild (edema or erythema) to severe (nasal snubbing, flaring of nostrils, or septal damage).
- Nasal septum damage is due to continuous pressure and/or friction on the nasal septum.
- Prevention of nasal injury is the key strategy:
  - Use the correct sized prongs.
  - Moisten the prongs with sterile water or saline before placing them. Do not use any gels, creams, or ointment.
  - Ensure appropriate fit of the prongs to infant's nose.
  - Do not allow the bridge of the prongs to touch the nasal septum at any time.
  - If the nose looks red and tender, use Duoderm under the prongs.

Abdominal distension (CPAP belly syndrome)

- This is a benign condition and is not a contraindication to feeding; it is not related to necrotizing enterocolitis.
- This can be minimized by routine use of orogastric tube and suctioning the air accumulated in the stomach by syringe every 3-4 hrs, or leaving the orogastric tube venting.

Pulmonary air leaks

- CPAP is considered to be a safer mode of respiratory support than mechanical ventilation.
- Pulmonary air leaks may occur when oxygen requirements are decreasing and lung compliance is improving.

Chapter 26

Assisted (Mechanical) Ventilation

Assisted (Mechanical) Ventilation

Mechanical ventilation is an invasive life-support procedure with many effects on the cardiopulmonary system. In addition to equipment, requirements for this service include a constant supply of heated humidified oxygen, compressed air, immediate blood gas analysis, chest x-ray accessibility, and 24 hrs availability of staff capable of intubation and pneumothorax decompression. The presence of a ventilator alone, without proper support, is not sufficient for quality care.

The goal is to optimize both gas exchange and clinical status at minimum FiO_2 and ventilator pressure. The ventilator strategy employed to accomplish this goal depends in part on the infant's disease process.

Conventional positive pressure ventilation remains the mainstay of assisted ventilation in neonates despite the development of new ventilatory techniques.

Basic Principles of Ventilation

- A ventilator is an automatic mechanical device designed to move the gas into and out of the lungs. The act of moving the air into and out of the lungs is called breathing, or more formally, ventilation.
- The two goals of ventilation are appropriate oxygenation and appropriate CO_2 elimination.
- Adequate perfusion to alveoli that are well ventilated improves oxygenation.

Gas Exchange during Assisted Ventilation

Oxygen (O_2)

- Oxygen exchange depends largely on the matching of perfusion with ventilation.
- During assisted ventilation, oxygenation is largely determined by the pressure of delivered oxygen which depends on mean airway pressure (MAP) and fraction of inspired oxygen (FiO_2).
- Mean airway pressure (MAP) is a measure of the average pressure to which the lungs are exposed during the respiratory cycle. **(Figure 26-4)**.

Carbon dioxide (CO_2)

- Carbon dioxide elimination depends largely on minute alveolar ventilation.

> **Alveolar minute ventilation = Effective tidal volume × Respiratory rate**

- Tidal volume (Vt) is the volume of gas inspired or expired per breath. It is determined by the pressure gradient between inspiration and expiration [Peak inspiratory pressure (PIP) - Positive end expiratory pressure (PEEP)]. Inspiratory time (Ti) may also partially determine the tidal volume (i.e. tidal volume can be decreased by shortening Ti).
- Effective Vt = Vt - Dead space [anatomic (nose, pharynx, trachea, bronchi) and physiologic (alveoli that are ventilated but not perfused)].

Table (26-1): Principles of adjusting oxygenation and ventilation

Change oxygenation (PaO_2)	• Change fraction of inspired oxygen (FiO_2) • Change mean airway pressure (MAP)
Change ventilation ($PaCO_2$)	• Change tidal volume (Vt) • Change respiratory rate (RR)

Pulmonary Mechanics

The mechanical properties of the respiratory system can be described according to their elastic and resistive forces.

Compliance

- This term is used to describe the elastic properties of a system (the lung and chest wall); it is estimated from simultaneous changes in volume and pressure.

$$\textbf{Compliance (ml/cm}H_2O\textbf{)} = \frac{\textbf{Change in volume (ml)}}{\textbf{Change in pressure (cm}H_2O\textbf{)}}$$

- Therefore, the higher the compliance, the larger the delivered volume per unit changes in pressure. Normal compliance = 0.03-0.06 L/cmH_2O.
- Compliance is decreased with surfactant deficiency (0.005-0.01 L/cmH_2O), excess lung water, and lung fibrosis. In these cases, PIP would have to be increased to maintain Vt. If compliance improves after surfactant therapy, PIP must be lowered; otherwise overinflation and air leak develops.

Resistance

- This term is used to describe the property of the lungs that resists the airflow. The pressure is required to overcome the elasticity of the respiratory system, to force gas through the airways (airway resistance), and to exceed the viscous resistance of the lung tissue (tissue resistance).

$$\textbf{Resistance (cm}H_2O\textbf{/L/sec)} = \frac{\textbf{Change in pressure (cm}H_2O\textbf{)}}{\textbf{Change in flow (L/sec)}}$$

- Resistance in healthy infants = 30 cmH_2O/L/sec. Resistance during inspiration is less than during expiration. Resistance is high in diseases characterized by airway obstruction, such as meconium aspiration and BPD.

Tube resistance

Poisseuille's law (Resistance = Length/radius^4)

- Reduction of radius by ½ results in a 16 fold increase of resistance.
- Resistance can change rapidly if, for example, secretions partially occlude the endotracheal tube.

Tissue resistance

- Tissue resistance is high in neonates due to the low ratio of lung volume to lung weight and relative pulmonary interstitial fluid.

Time constant

- It is the time it takes to equilibrate pressure between proximal airways and alveoli. The time constant (expressed in seconds) can be calculated as follow:

Time constant of the respiratory system = Resistance × Compliance

- The time necessary for the lungs to inflate and deflate depends on the inspiratory and expiratory time constants, respectively. For example, in a healthy infant, one time constant is 0.12 seconds and an inspiratory or expiratory phase of 0.36-0.6 second (3-5 time constant) is necessary for a fairly complete equilibration of pressure (assuming equal inspiratory and expiratory time constants).
- Infants with RDS typically have a decreased compliance and their time constant is shorter. Therefore, their stiff lungs complete inflation and deflation in a shorter time than normal lungs do. In contrast, infants with MAS have longer time constant due to increased resistance to the airways during inspiration and expiration.

Types of Mechanical Ventilators

Ventilators can be classified (according to the way of gas delivery during inspiration is controlled) into:

- Volume ventilators: control the delivered volume (i.e., the ventilator stops inspiratory cycle when set tidal volume is achieved.
- Pressure ventilators: control the inspiratory pressure (i.e., the ventilator stops inspiratory cycle when set PIP is achieved).

Volume ventilators

- Less frequently used to ventilate neonates because of inability to deliver small tidal volume needed by preterm infants.
- Deliver a fixed Vt (generally 6-8 ml/kg in full term and 4-6 ml/kg in preterm infants) which is independent of lung mechanics, so inspiratory pressure is variable.
- The delivered Vt is obtained by adjusting the flow rate to determine the time over which it is delivered, thus determining I/E ratio.

Pressure ventilators

- These are the most frequently used ventilators in the NICUs.
- Traditional pressure ventilators are time cycled, pressure limited, and constant flow devices.
- These ventilators deliver volume of gas until a preset limiting pressure (PIP) is reached (pressure limited) and maintains this pressure throughout the preset inspiratory time (time-cycled). A continuous flow is delivered, allowing the infant to breath between the mechanical breathes.
- Tidal volume delivered with each breath varies according to lung compliance and resistance. The new pressure ventilators allow variable flow capability for infant demand.
- This chapter will discuss this type of ventilators.

Parts of a Ventilator System

- Oxygen and compressed air sources
- Control panel (FiO_2, PIP, PEEP, RR, Ti, I:E ratio and Flow rate)
- Humidifier
  - The gas must be warmed and humidified to prevent hypothermia and inspissation of secretions and necrosis of the airway mucosa.
    - Simple humidifier: it heats the humidified inspired gas to a set temperature. The disadvantage is the excessive condensation in the tubing. These condensations should be discarded periodically.
    - Servo-controlled humidifier has a heated wire in the tubing to prevent condensation while ensuring adequate humidification.
  - Optimal temperature of the gases should be 36-37°C with a relative humidity of 70% at 37°C.
- Breathing circuit: it is preferable to use disposable circuits for every infant. If re-usable circuits are used, they must be changed if visible soiling is seen. Ventilator circuits do not need changing more frequently than every 48 hours.

Parameters of MV

Peak inspiratory pressure (PIP)

- PIP is the maximum pressure reached during inspiration **(Figure 26-1).**
- It is the primary factor used to deliver Vt in pressure ventilators (i.e., increase PIP will increase tidal volume and increase CO_2 elimination).
- PIP should be adjusted initially to achieve adequate Vt as reflected by chest excursion and adequate breath sounds.
- Ventilating an infant with decreased lung compliance: PIP up to 25 cmH_2O in preterm and up to 30 cmH_2O in full term may be required to re-expand the collapsed alveoli. PIP is decreased gradually with improvement of lung mechanics down to 10-12 cmH_2O.
  - If PIP is too low, tidal volume will be low leading to hypoxia.
  - If PIP is too high, tidal volume will be high leading to:
    - Barotraumas and BPD
    - Hyperinflation and air leak
    - Impedance of venous return

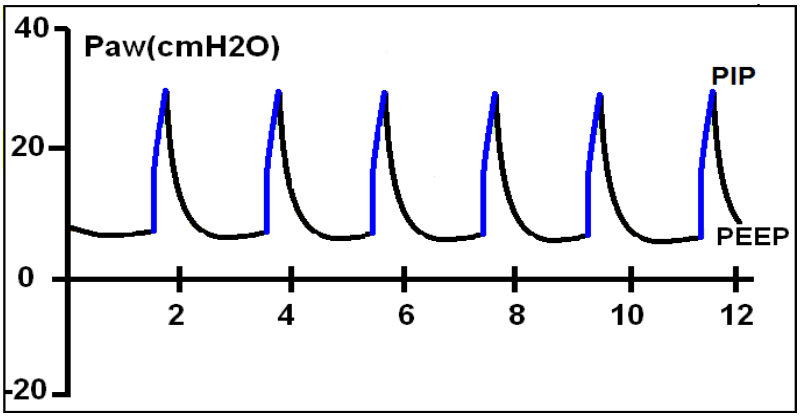


Figure (26-1): Pressure waveform

It has upward inspiration and downward expiration. The uppermost point of the wave represents PIP. The waveform starts and ends at the level of PEEP

Positive end expiratory pressure (PEEP)

- It is the positive pressure applied at the end of expiration to prevent lung collapse and maintain stability of the alveoli **(Figure 26-1).**
- **The optimum PEEP** is the level before which the lung volume is not maintained and above which the lung become overdistended. PEEP can be adjusted as low as 3 cmH_2O and as high as 8 cmH_2O (moderate PEEP is 4-6 cmH_2O).
- **High PEEP >8 cmH_2O**
  - Reduces gradient between PIP and EEP so reduce Vt
  - Impedes venous return
  - Increases pulmonary air leak
  - Produces CO_2 retention secondary to decrease compliance and air trapping
- Ventilated newborn should have a minimum physiologic PEEP of 2-3 cmH_2O.
- **Inadvertent PEEP:** the chosen PEEP may be increased if the expiration time is too short or airway resistance is increased contributing to gas trapping and increase potential of air leak **(Figure 26-2).**

Fraction of inspired oxygen (FiO_2)

- FiO_2 is the simplest and most direct means of improving oxygenation. FiO_2 is adjusted to maintain an adequate oxygenation; it can be as low as 21% (room air) and as high as 100%.

Rate (RR) or frequency/minute

- Respiratory rate determines minute ventilation (RR × Vt) and thus CO_2 elimination.
- Depending on the infant's gestational age, the underlying disease, and the resulting pulmonary mechanics, the use of rapid or slow rates may be needed.
- A respiratory rate of 40-60 breaths/minute is usually sufficient in most of cases. It can be decreased to 20 breaths/minute, allowing for infant's spontaneous breathing during weaning.

- Increasing RR, while keeping the Ti the same, will result in short expiration, and may lead to air trapping **(Figure 26-2)**.

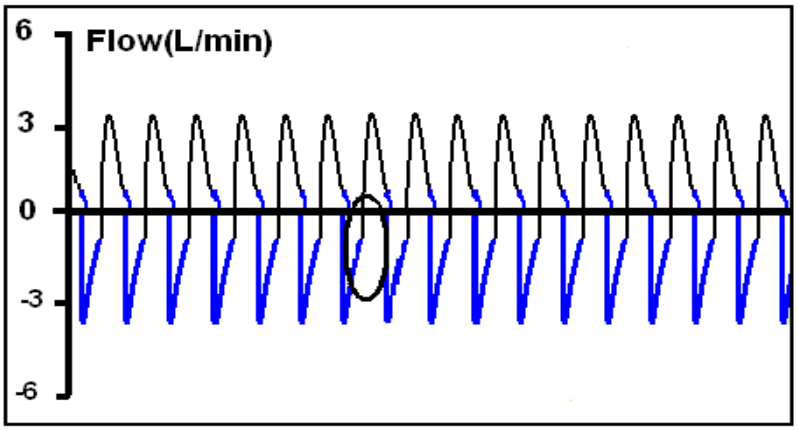


Figure (26-2): Air trapping due to short expiratory time.

Rapid respiratory rate without decreasing the inspiratory time leads to air trapping through short expiratory time

Inspiratory time (Ti)

- It is usually adjusted between 0.35-0.6 second depending on the pulmonary mechanics such as **compliance**, **resistance** and **time constant**.

Inspiratory time (Ti)/expiratory time (Te) ratio (I:E Ratio)

- I:E ratio should not be less than 1:1.2 and should not be reversed in order to maintain an adequate expiratory time necessary for CO_2 elimination.
- Prolonged expiration may be needed to eliminate high CO_2.

Flow Rate [volume of gas passed/time unit (liter/minute)]

- Flow rates of 6-10 liters/minute are sufficient under most circumstances in neonates.
- If low flow rate is used, effective PIP is not reached within appropriate time. However, high flow rates may lead to turbulence in small endotracheal tubes and to barotraumas.
- Recent types of ventilators adjust flow automatically.

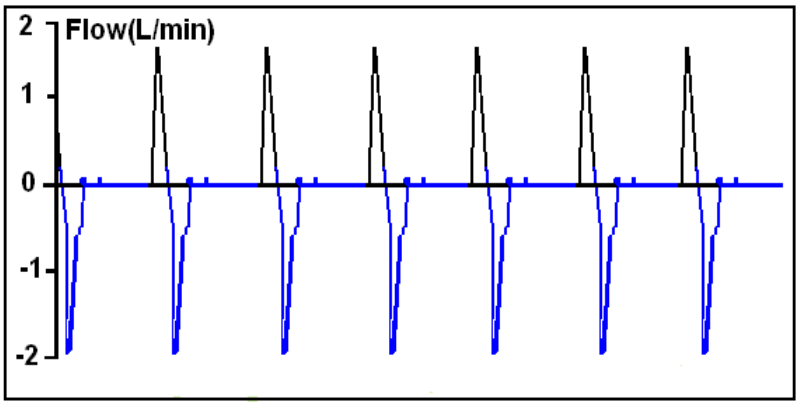


Figure (26-3): Flow waveform

Positive component represents gas flow into the infant (inspiration) and consists of accelerating (ascending flow limb) and decelerating (descending flow limb); negative component: represents gas flow from the infant (expiration)

Mean air way pressure (MAP)

- MAP is a measure of the average pressure to which the lungs are exposed during the respiratory cycle. It is the factor (other than FiO_2) that determines oxygenation.
- MAP is calculated by the ventilator; it can be calculated by using the following equation:

$$MAP = (PIP - PEEP)\left[\frac{Ti}{(Ti + Te)}\right] + PEEP$$

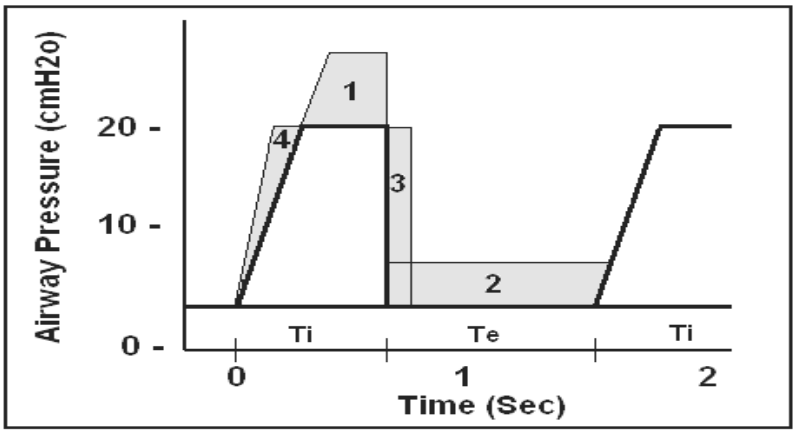


Figure (26-4): Mean airway pressure (MAP)

Is the area under the waveform: 1- PIP, 2- PEEP, 3- Ti, 4- Inspiratory flow

- MAP will be augmented by increasing any of the following:
  - Peak inspiratory pressure (PIP)
  - Positive end expiratory pressure (PEEP)
  - Inspiratory time (Ti)
  - Flow rate
- All these changes lead to higher PaO_2, but each has a different effect on $PaCO_2$.
- MAP is usually adjusted between 10-12 cmH_2O. Higher levels are associated with an increased risk of air leaks.

Modes of Ventilation

Non-triggered modes

This technique involves automatic mechanical ventilation at a rate and pressure determined by the ventilator setting irrespective of the infant's breathing efforts (i.e., a ventilatory cycle occurs periodically at fixed intervals)

- Controlled Mandatory Ventilation or Intermittent Positive Pressure Ventilation (IPPV): the ventilator rate is set faster than the infant's spontaneous respiratory rate (usually 50-80 breaths/minute).
- Intermittent Mandatory Ventilation (IMV): the ventilator rate is lower than the infant's spontaneous respiratory rate (<30 breaths/minute), thus the infant can breathe spontaneously between two controlled ventilator cycles. In this mode breaths above set rate are not assisted.

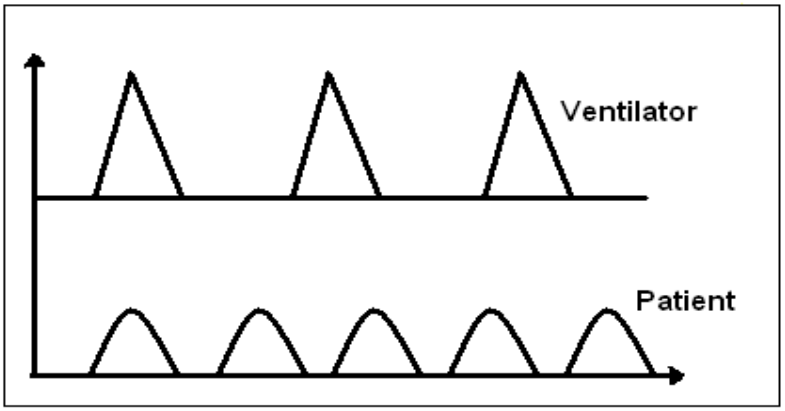


Figure (26-5): Intermittent mandatory ventilation (IMV).
Infant and ventilator function independent from one another

Patient-triggered ventilation (PTV)

The infant's own respiratory drive and rhythm determine the rate of ventilation. The inspiratory effort is detected within milliseconds by means of a pneumatic sensor attached to the abdomen or by sensing the airflow in the endotracheal tube. (Pressure sensor or flow sensor). This signal is sent to activate the ventilator, which is coordinated with the infant's own respiration.

- Assist/Control (A/C) - Synchronized Intermittent Positive Pressure Ventilation (SIPPV)
  - It is synchronized, senses infant's spontaneous breaths, but with a minimum mandatory set rate. All infant-triggered breaths above that rate are also fully assisted (assist).
  - In the event that the infant fails to exhibit spontaneous breathing, the ventilator delivers mechanical breaths at the preset rate (control).
  - Weaning from that mode is done by decreasing the inspiratory pressure.

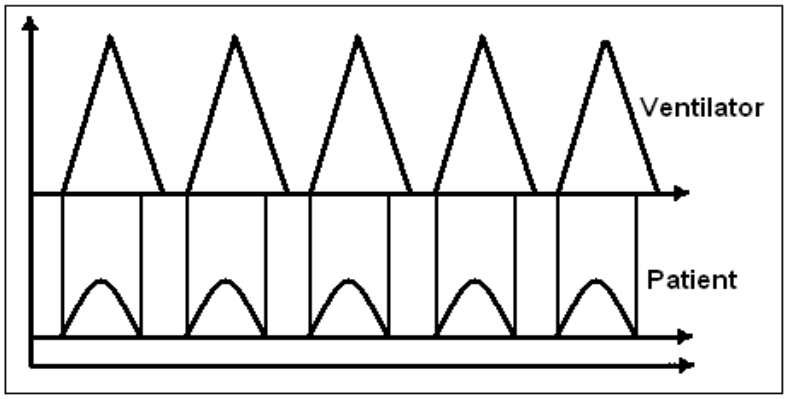


Figure (26-6): Assist/Control Ventilation.

Synchronous start of the infant and mechanical breaths. However inspiratory times of the infant and ventilator are not synchronous

- SIMV (Synchronized Intermittent Mandatory Ventilation)
  - Ventilator synchronizes IMV breaths with infant's effort (senses infant's spontaneous breaths).
  - The infant takes his/her own breaths in between the set rate.

- It will function exactly like IMV if the infant is apneic or the trigger/synchronization fails.
- Weaning from that mode is done by decreasing either the pressure or the rate.

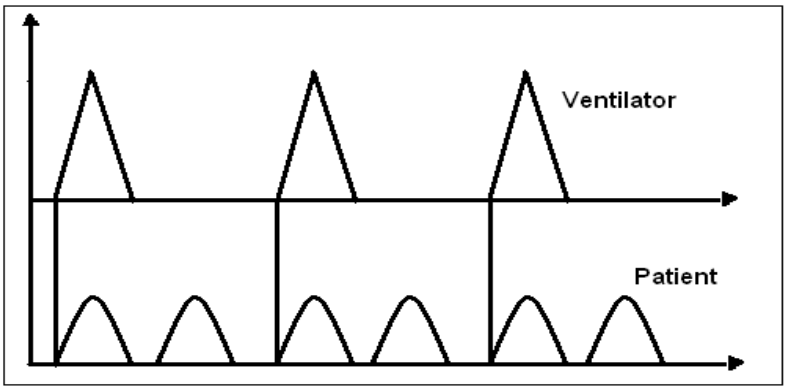


Figure (26-7): Synchronized Intermittent Mandatory Ventilation (SIMV)

The onset of mechanical inspiration is synchronized to the onset of infant inspiration; the infant breathes spontaneously between mechanical breaths

- Pressure Support Ventilation (PSV)
  - This system supplies pressure support (flow) at a preset level but the rate is determined by the infant. Termination of the inspiratory cycle is based on a percentage of the peak flow [usually 5-25% of peak inspiratory flow (flow cycled)], i.e. the infant has full control over how much to breathe (RR) and how long (Ti). This results in complete synchronization of the infant and the ventilator throughout the entire respiratory cycle.
  - PSV depends entirely on the infant's effort, if the infant becomes apneic, the ventilator will not provide any mechanical breath.
  - It is generally used as a weaning mode. It may be used alone if the infant has good respiratory drive or may be used with SIMV to provide a back-up rate in the event of infant apnea or decreased effort.

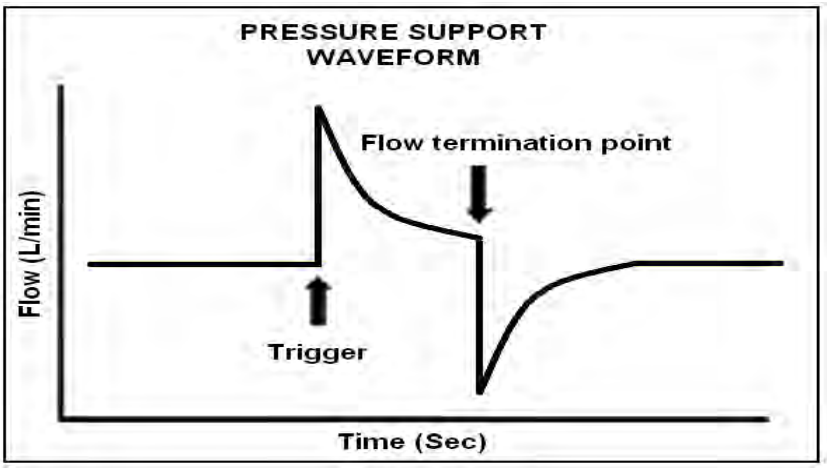


Figure (26-8): Pressure Support Ventilation (PSV)

Synchronizes inspiration by sensing the infant's effort: it also synchronizes expiration by terminating inspiration in response to a decline in airway flow. This results in complete synchronization of the functioning of the infant and the ventilator throughout the entire respiratory cycle.

- Volume Guarantee (VG) ventilation
  - It is a new mode of ventilation.
  - This pressure-controlled ventilation delivers a preset tidal volume (Vt), this volume is continuously monitored by the ventilator and the pressure may increase or decrease to guarantee the targeted volume.
  - The addition of VG (4-6 ml/kg) to A/C or SIMV has the following advantages:
    - Less risk of volutrauma.
    - Allows auto-weaning of PIP which may reduce barotraumas.

Indications for Assisted Ventilation

Absolute indications

- Severe hypoxemia with PaO_2 <50 mmHg despite FiO_2 of 0.6-0.8
- Respiratory acidosis with pH of <7.20-7.25, or $PaCO_2$ >60-65 mmHg
- Intractable apnea and bradycardia

Relative indications

- Frequent intermittent apnea unresponsive to drug therapy or NCPAP
- Early treatment when use of mechanical ventilation is anticipated because of deteriorating gas exchange.
- Relieving work of breathing in an infant with signs of respiratory difficulty.
- Initiation of exogenous surfactant therapy in infants with RDS.

Initiation of ventilation

Endotracheal intubation

Intubate the infant orally with an endotracheal tube according to the guidelines **(Chapter 4)**. The tip of ETT should be located 1-2 cm above the carina and chest x-ray should be done.

Initial settings of mechanical ventilation

Respiratory distress syndrome (RDS)

Because of short time constant, most infants with RDS tolerate high frequencies (rates) and short expiratory times without marked gas trapping and inadvertent PEEP.

- FiO_2: 0.4-0.6
- Low PIP (estimated by good chest excursion): usually 12-20 cmH_2O
- PEEP: 4-5 (up to 6) cmH_2O
- Flow rates: 6-8 liters/minute
- Rapid Rate: >60 breaths/minute
- Ti: 0.2-0.3 second (rarely, longer Ti required to provide adequate oxygenation).
- I:E ratio: not less than 1:1.2, and not to be reversed

Meconium aspiration syndrome (MAS)

Because of long time constant, care must be taken to set the ventilator Ti and rates that permit adequate inspiration to deliver the required tidal volume and adequate expiration to avoid inadvertent PEEP.

- High PIP: 25-30 cmH_2O
- Moderate PEEP: 4-5 cmH_2O
- Moderate rate: 40-60 breaths/minute
- I:E ratio >1:3 (prolonged expiration)
- If gas trapping occurs, decrease PEEP and increase expiratory time.
- Sedation or muscle relaxation may be required to minimize risks of air leak,

Air Leak

The primary goal is to reduce MAP through any of its components (PIP, Ti. PEEP) and to rely on increased FiO_2 to provide oxygenation.

- Low PIP
- Short Ti
- Low PEEP
- Respiratory rate may be increased up to 60 breaths/minute.
- High FiO_2

Apnea

For infants completely dependent on the ventilator, the goal should be to provide physiologic ventilation using:

- FiO_2: 0.21-0.3
- PIP: 10-18 cmH_2O
- PEEP: 3-4 cmH_2O
- Rates: 30-40 breaths/minute
- Ti: 0.35-0.4 seconds
- Flow rate: 7-8 liters/minute

For an infant requiring a ventilator because of intermittent but prolonged apnea, low rates (20 breaths/minute) may be sufficient.

Persistent pulmonary hypertension (PPHN)

(Refer to Chapter 35)

Bronchopulmonary dysplasia (BPD)

(Refer to Chapter 27)

Subsequent Settings of Mechanical Ventilation

Measure arterial blood gases, half an hour after the initial setting and adjust the setting according to guidelines in **(Table 26-2), (Table 26-3).**

Table (26-2): Ventilator manipulations to improve oxygenation

Parameter	Advantages	Disadvantages
↑ **FiO_2**	• Minimizes barotraumas • Easily administrated	• Fails to affect ventilation/perfusion matching • Direct toxicity, especially >0.6
↑ **PIP**	• Increases Vt • Increases CO_2 elimination • Decreases $PaCO_2$	• Barotrauma, air leak and BPD • High PIP, and may also impede venous return and lower cardiac output
↑ **PEEP**	• Prevents alveolar collapse • Maintains lung volume at end expiration • Improves ventilation-perfusion relationships	• Decreases Vt and CO_2 elimination leading to an increase in $PaCO_2$ • Obstructs venous return and decreased cardiac output • Very high levels result in alveolar overdistension and rupture
↑ **Ti**	Increases MAP without increasing PIP	• Long Ti leads to active expiration during the inspiratory cycle • Fighting the ventilator and a higher incidence of pneumothorax
↑ **Flow**	Ensure adequate pressure rise and delivery of the desired PIP (higher inspiratory flows are needed when Ti is short)	High flows can lead to turbulence, an increase in resistance, and gas trapping
↑ **Rate**	Increases MAP while using lower PIP	High ventilator rates result in an insufficient emptying time during expiratory phase, resulting in gas trapping, inadvertent PEEP, and decreased compliance

Table (26-3): Change of ventilator parameters according to desired blood gases

Desired goal	PIP	PEEP	Rate	Ti
Decreased $PaCO_2$	↑	↓	↑	↓
Increased $PaCO_2$	↓	↑	↓	↑
Increased PaO_2	↑	↑	–	↑
Decreased PaO_2	↓	↓	–	↓

Paralysis and sedation

- The use of neuromuscular blockade and/or sedation is not routinely indicated.
- If the infant is fighting the ventilator, sedation using midazolam, phenobarbital and fentanyl or paralysis with pancuronium can sometimes improve the effectiveness of ventilation.
- Paralysis results in considerable third spacing of fluid, requiring added volume expanders to maintain blood pressure and urine output.

Physiotherapy and suctioning

- Tracheal suctioning and chest physiotherapy should be minimized in infants with RDS in the first few days after birth because their secretions are scant.
- Physiotherapy and suctioning should be done for infants on mechanical ventilators to prevent the development of atelectasis, especially in premature infants.
- Continuous monitoring of O_2 saturation by pulse oximetry is recommended.
- During suction, the catheter should not be inserted beyond the lower end of the endotracheal tube to prevent damage to airways.
- During accompanying bagging (periods of manual ventilation), FiO_2 may be increased by 10% over the infant's current requirement.

N.B.: Unless there is evidence of a beneficial effect, the principle of minimum handling of fragile preterm infants should be followed.

Monitoring the Infant on Mechanical Ventilators

- Obtain an initial blood gas within 30 minutes of starting mechanical ventilation.
- Obtain a blood gas within 30 minutes of any change in ventilator settings.
- Obtain a blood gas every 6 hrs unless a sudden change in the infant's condition occurs.
- Continuous monitoring of the O_2 saturation level, as well as heart rate and respiratory rate, is necessary.
- In preterm infants, O_2 saturation should be maintained between 87-93% to avoid O_2 toxicity.

Deterioration during Mechanical Ventilators

Sudden clinical deterioration

- Mechanical or electrical ventilator failure
- Disconnected tube or leaking connection
- Endotracheal tube displacement or blockage
- Pneumothorax

Gradual deterioration

- Inappropriate ventilatory setting
- Intraventricular hemorrhage
- PDA
- Anemia
- Pulmonary interstitial emphysema (PIE)
- Infection/ pneumonia

Weaning From Mechanical Ventilation

It is the process of discontinuing mechanical ventilation

When to wean the infant from the ventilator?

- If the infant is clinically and metabolically stable as evidenced by reduction of the work of breathing, increased chest expansion and aeration by chest auscultation and radiographic evidence of improved lung volume.
- If the infant has an efficient spontaneous respiratory drive.
- If the infant is able to maintain satisfactory blood gas exchange:
  - PaO_2 >50 mmHg
  - Optimal $PaCO_2$ varies according to disease state. For very immature infants or infants with air leaks, a $PaCO_2$ of 50-60 mmHg may be tolerated (permissible hypercarbia), provided that pH is >7.25

Principles of weaning from mechanical ventilation

- Decrease the most potentially harmful parameter first, (FiO_2 and PIP).
- Limit changes to one parameter at a time.
- Avoid changes of large magnitude.
- Follow-up blood gas after each change.

Steps of weaning

- Decrease PIP as tolerated and as chest rise diminishes.
- When PIP is around 20, attention is directed to FiO_2 and then to the respiratory rate alternating with each other, in response to assessment of chest excursion, blood gas results, and oxygen saturation.
- If A/C mode is used, switch to SIMV when FiO_2 is below 0.4 and PIP is less than 12 cmH_2O.
- Decrease the number of ventilator breaths progressively while the infant steadily increases his spontaneous breathing.
- For infants weighing less than 1,750 gm, when PIP is <12 cmH_2O, FiO_2 is <0.3 and the respiratory rate decreased to 20 breaths/minute, wean directly to nasal CPAP if available. Larger infants can be weaned to nasal prongs or to head box.

Extubation

- Provide an FiO_2, as needed.
- Begin with postural drainage and suctioning.
- The ETT is connected to the ambubag and the infant is given a prolonged sigh of 15-20 cmH_2O while the ETT is extracted (this prevents negative pressure from developing in the airway, which may occur upon tube removal and may cause atelectasis).
- The infant should be followed by pulse oximetry.
- Chest x-ray should be done 2 hrs after extubation.
- If the infant is stable, resume feeding 4 hrs after extubation.
- Steroids are not routine before extubation, but if there was prolonged intubation or previous failed attempts of extubation, initiate dexamethasone treatment (0.25 mg/kg/

dose every 12 hrs) beginning 48 hrs before extubation, as well as methylxanthenes (e.g., aminophylline) to increase respiratory drive.

- If stridor caused by laryngeal edema develops after extubation, racemic epinephrine aerosols and steroids may be helpful.
- Tracheostomy must be considered if the baby cannot be extubated for at least 4 times over several weeks

Complications of Mechanical Ventilation

Endotracheal tube complications

- Accidental displacement of the endotracheal tube into main stem bronchus, hypo-pharynx, or esophagus
- Accidental extubation
- Obstruction of endotracheal tube

Airway injury

- Subglottic stenosis
- Edema of the cords after extubation (may result in hoarseness and stridor)
- Prolonged use of orotracheal intubation associated with palatal groove formation
- Necrotizing tracheobronchitis

Infection

- Pneumonia and systemic infections with *Staphylococcus epidermidis*, *Candida* organism, gram-negative organisms, and *Staphylococcus aureus.*

Bronchopulmoary dysplasia/oxygen toxicity

- Bronchopulmonary dysplasia (BPD) is related to increased airway pressure and changes in lung volume.
- Other contributing factors are oxygen toxicity, anatomic and physiologic immaturity, and individual susceptibility.

Air leak syndromes

- Pneumothorax, pulmonary interstitial emphysema (PIE), and pneumomediastinum directly related to increased airway pressure occurring frequently at MAP >14 cmH_2O.

Miscellaneous

- Intraventricular hemorrhage
- Decreased cardiac output
- Feeding intolerance

Chapter 27

Complications of Oxygen Therapy

Complications of Oxygen Therapy

Bronchopulmonary Dysplasia

Bronchopulmonary dysplasia (BPD) is a form of chronic lung disease that develops almost in preterm neonates treated with oxygen and positive-pressure ventilation (PPV). BPD is usually defined as a need for supplemental oxygen at 28 days or 36 weeks' postconceptional age for infants less than 32 weeks' GA.

Incidence

The incidence of BPD is inversely related to the gestational age and birthweight. It occurs most frequently in infants less than 32 weeks' GA. However, full-term infants with meconium aspiration, pneumonia and certain cardiac and GIT anomalies that require chronic ventilator support may also develop BPD.

Pathogenesis and Risk Factors

The pathogenesis of BPD is multifactorial. BPD results from a variety of toxic factors that can injure small airways and interfere with alveolarization and vascularization. These factors include:

- Oxygen toxicity.
- Barotrauma, and volutrauma, resulting from mechanical ventilation.
- Inflammation: cellular and interstitial injury resulting in the release of pro-inflammatory mediators causing ongoing inflammatory cell recruitment and decrease epithelial cell integrity**,** leading to leakage of water and protein.
- Infection (e.g., *Ureaplasma urealyticum*).
- Nutritional deficiency and vitamin A deficiency.
- Excessive fluid administration and PDA.
- Family history of atopic disease.

Pathological Changes

The following pathological changes are seen: necrotizing bronchiolitis, obstruction of the small airway lumens by debris and edema, areas of peribronchial, interstitial fibrosis, and areas of atelectasis alternating with areas of emphysema.

Clinical Manifestations

- Infants with severe BPD are often extremely immature and have very low birth weights. Their requirements for oxygen and ventilatory support often increase in the first 2 weeks of life. At 2-4 weeks' postnatal age, oxygen supplementation, ventilator support, or both are often increased to maintain adequate ventilation and oxygenation.
- Physical examination reveals tachypnea, tachycardia, increased work of breathing (with retractions, nasal flaring, and grunting), frequent desaturations, wheezing or prolongation of expiration.
- In severe cases, right-sided heart failure may occur.

Investigations

- Blood gas analysis may show hypoxemia and hypercarbia.
- Chest x-ray: radiographic findings may be quite variable **(Refer to Appendix 9)**
  - Early - BPD appears as diffuse haziness and lung hypoinflation with small round radiolucencies dispersed throughout the lungs.
  - Later - it shows streaky interstitial densities, patchy atelectasis, and cyst formation with concomitant hyperinflation.

Management

- Prevention of BPD is the cornerstone of management by avoiding, as much as possible, factors that predispose to injury.
- Goals of treatment:
  - Minimize further lung injury (baro-volutrauma, O_2 toxicity, inflammation)
  - Maximize nutrition
  - Diminish O_2 consumption

Respiratory support

Mechanical ventilation

- Early CPAP application in extremely preterm infants and early weaning from PPV to CPAP are management strategies that may be associated with decreased risk of BPD.
- Ventilator adjustments are made to minimize airway pressures and tidal volumes while providing adequate gas exchange:
  - Apply the lowest PIP with the least tidal volume (no more than 6 ml/kg) necessary to obtain adequate ventilation, using inspiratory times between 0.3-0.5 seconds.
  - Allow permissive hypercarbia by keeping $PaCO_2$ between 50-65 mmHg and an arterial pH of >7.25.
- Weaning these infants from the ventilator is difficult and has to be accomplished gradually. When the infant can maintain an acceptable PaO_2 and $PaCO_2$ with low PIP (lower than 12-15 cmH_2O), and FiO_2 lower than 0.30-0.40, the ventilator rate is gradually reduced.
- Meticulous primary nursing care is essential to ensure airway patency and facilitate extubation.
- In small infants, aminophylline or caffeine can be used as a respiratory stimulant during the weaning phase.
- When the infant is able to maintain acceptable blood gas levels for several hours on low ventilator rates (15-20 breaths/minute), extubation should be attempted.
- During the days after the extubation, it is important to provide chest physiotherapy.
- In smaller infants, the use of NCPAP after extubation can stabilize respiratory function and reduce the need to reinstitute mechanical ventilation.

Supplemental oxygen

- The least required oxygen should be delivered to minimize oxygen toxicity.
- Maintain a PaO_2 between 55-80 mmHg.
- Arterial oxygen saturation (SaO_2) should be monitored, correlated with PaO_2 and maintained between 90-95%.

PDA management

- Aggressive early management of a hemodynamically significant PDA is essential.

Fluid management

- Restrict fluid to 130 mL/kg/day or less (adequate to maintain urine output at least 1 ml/kg/hr and a serum sodium concentration of 140-145 mEq/L).
- Later, when respiratory status is stable, fluid restriction is gradually released.

Diuretics

- Furosemide (0.5-1 mg/kg/dose IV one to two times daily)
- Chlorothiazide (20-40 mg/kg/day orally, divided every 12 hrs)
- Combination of chlorothiazide (20 mg/kg/day), and spironolactone (2 mg/kg/day): ideal for chronic management

Bronchodilators

- Albuterol (specific β_2-agonist), 0.02-0.04 ml/kg (up to 0.1 mL total) in 2 ml normal saline solution, nebulized as needed every 6-8 hrs, to treat bronchospasm in acute exacerbations of BPD.
- Ipratropium bromide (muscarinic antagonist) with more potent bronchodilator effects (75-175 μg, diluted in 3 ml normal saline via nebulizer every 6-8 hrs).
- Combination of albuterol and ipratropium bromide may be more effective.
- Theophylline improves lung function in BPD; its beneficial actions include smooth airway muscle dilation, improved diaphragmatic contractility, central respiratory stimulation, and mild diuretic effects.

Corticosteroids

- The use of dexamethasone for prevention of BPD is not recommended.
- The routine use of dexamethasone in infants with established BPD is not currently recommended unless severe pulmonary disease exists.
- If dexamethazone is used, start at 0.2-0.3 mg/kg/day divided every 12 hrs for 48 hrs, then halve the dose every 48 hrs and try to limit the entire course to <7-10 days.
- Inhaled beclomethasone (100-200 μg 4 times/day) decreases the need for systemic steroids, but seems to be much less efficient.

Nutritional support

- Protein and fat supplementation is progressively increased to provide approximately 3-3.5 gm/kg/day.

- Vitamin A supplementation (5,000 units three times weekly for the first 28 days of age) may improve lung repair.
- Supplementation of trace minerals (e.g., copper, zinc, manganese) is needed.
- Early enteral feeding of small amounts followed by slow, steady increases in volume appears to optimize tolerance of feeds and nutritional support.
- Enteral feedings of breast milk provides the best nutrition while preventing feeding complications.
- Infants with BPD frequently have high caloric needs (120-150 kcal/kg/day or more).

Blood transfusions

- Maintain hematocrit level at approximately 30-35% as long as supplemental oxygen is needed (furosemide should be given immediately following the transfusion).

Prognosis

- It is good for infants who have been weaned from oxygen before discharge from the NICU.
- The first 2 years are the dangerous periods for airways disease.
- Mortality in infants with BPD ranges from 10-25%. Cardiorespiratory failure and acquired infection (respiratory syncytial virus) are common causes of death.
- Survivors with BPD often go home on a regimen of oxygen, diuretics, and broncho-dilator therapy.
- Noncardiorespiratory complications include growth failure, psychomotor retardation, parental stress, and sequelae of therapy (e.g., electrolyte imbalance).
- Immunization: in addition to standard immunization, infants with BPD should receive pneumococcal and influenza vaccines and palivizumab (monoclonal antibodies against respiratory syncytial virus).

Retinopathy of Prematurity

Retinopathy of prematurity (ROP) is a multifactorial vasoproliferative retinal disorder that increases in incidence with decreasing gestational age. ROP is a disease of premature infants. All infants <1,500 gm birth weight or <32 weeks' GA at birth are at risk of developing ROP.

Pathogenesis

- Exposure of the immature retina to an initial insult or insults, such as hyperoxia, hypoxia or hypotension can result in retinal vasoconstriction and irreversible capillary endothelial cell destruction.
- As the area becomes ischemic, angiogenic factors, such as vascular endothelial growth factor (VEGF), is made by the ischemic retina to provide new vascular channels (neovascularization).
- These new vessels grow through the retina into the vitreous. These immature vascular channels are permeable, so hemorrhage and edema can occur.
- Extensive severe extraretinal fibrovascular proliferation can lead to retinal detachment and abnormal retinal function.

Diagnosis and Screening

- Because affected newborns have no symptoms, diagnosis depends on a careful eye examination by an ophthalmologist expert in ROP screening.
- Infants with a birth weight of <1,500 gm or gestational age of <32 weeks and selected infants with a birth weight between 1,500-2,000 gm or gestational age of >32 weeks, with an unstable clinical course, including those requiring cardiorespiratory support should have retinal screening examinations performed after pupillary dilation using indirect ophthalmoscopy to detect ROP.

Table (27-1): Suggested schedule for the timing of the initial eye examinations based on postmenstrual age and chronologic (postnatal) age to detect ROP

Gestational age at birth (weeks)	Age at initial examination (weeks)	
	Postmenstrual	Chronologic
25	31	6
26	31	5
27	31	4
28	32	4
29	33	4
30	34	4
31*	35	4
32*	36	4

*If necessary

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- Follow-up examinations should be recommended by the examining ophthalmologist on the basis of retinal findings.
  - Examination should continue every 2 weeks until retina becomes mature and fully vascularized.
  - Infants with ROP should be examined every 1-2 weeks to monitor progression of the disease. The frequency of examination depends on the severity and rapidity of progression of the disease.

Management (Prevention and Treatment)

- In premature infants who need oxygen, oxygen levels are monitored carefully so that the lowest amount of oxygen necessary can be used (in general, keep SaO_2 between 87-93%).
- In many affected infants, the disease process is mild and regresses spontaneously.
- For very severe ROP, laser treatment is done on the outermost portions of the retina. This treatment stops the abnormal growth of blood vessels and decreases the risk of retinal detachment and loss of vision.

Chapter 28

Neonatal Sepsis

Neonatal Sepsis

Neonatal sepsis (sepsis neonatorum) is the term used to describe any systemic bacterial infection documented by a positive blood culture in the first month of life.

Bacterial sepsis and meningitis continue to be major causes of morbidity and mortality in the newborn particularly in LBW infants.

Sepsis neonatorum is devastating and surviving infants can have significant neurologic sequelae because of CNS involvement, septic shock**,** or hypoxemia secondary to severe parenchymal lung disease and persistent pulmonary hypertension.

Types of Neonatal Sepsis

Based on the postnatal age at onset, neonatal sepsis can be classified into:

Early onset (first 7 days of life)

- Usually it is a fulminant, multisystem infection, acquired by vertical transmission from the mother and with a higher case fatality rate than late-onset sepsis.

Late onset (between >7 days to 3 months of life)

- It is usually more insidious but may have an acute onset and either nosocomial or community acquired.

Very late (>3 months of life)

- It affects premature VLBW infants who are in the NICU and often is caused by Candida species or by commensal organisms**,** such as coagulase-negative staphylococci (CONS).
- Usually it is associated with prolonged instrumentation, such as indwelling intravascular lines and endotracheal intubation.

Table (28-1): Characteristics of neonatal sepsis

	Early onset (<7 days)	**Late onset (≥7 days to 3 months)**	**Very late onset (>3months)**
Intrapartum complications	Often present	Usually absent	Varies
Transmission	Vertical; organism often acquired from mother's genital tract	Vertical or through postnatal environment	Usually postnatal environment
Clinical manifestations	Fulminant course, multisystem involvement, pneumonia common	Insidious or acute, focal infection, meningitis common	Insidious
Case-fatality rate	5-20%	5%	Low

Etiology

Causative organisms

The pathogens associated with neonatal sepsis vary in different countries and tend to change over time. In Egypt, gram-negative bacilli [*Klebsiella pneumoniae* and *Escherichia coli (E. coli)*] are the most common pathogens. In the USA and Western Europe, group B streptococci (GBS) are predominant. Recently, with the massive use of antimicrobial prophylaxis, *E. coli* has become most prevalent in early onset sepsis (EOS) and coagulase negative staphylococci in late onset sepsis (LOS).

Bacterial infections

Common bacterial pathogens responsible for neonatal sepsis are listed in **(Table 28-2).**

Table (28-2): Most common bacterial pathogens responsible for sepsis

Early onset sepsis	Late onset sepsis
• Gram-negative enteric bacilli (e.g., *E.coli, Klebsiella* species*)* • *Enterococci* • Coagulase-negative *Staphylococci* • Group B streptococci (GBS)	• Coagulase-negative staphylococci • *Staphylococcus aureus* (methicillin resistant *Staphylococcus aureus* - MRSA) • Gram-negative enteric bacilli • Group B streptococci (GBS)

Others

Fungal infections

- Candida species: *C. albicans, C. parapsilosis*
- Other fungi (e.g. *Curvularia* species, *Aspergillus* species, *Trichosporon*)

Viral infections

- Meningoencephalitis and neonatal sepsis can be also caused by infection with adenovirus, enterovirus, or coxsackievirus.
- Neonatal herpes simplex virus (HSV) infections are transmitted from an infected mother, usually vertically, during delivery.

Transmission

- Early onset infection is most often transmitted vertically by ascending amniotic fluid infection and by delivery through an infected or colonized birth canal. The pathogens that cause late onset disease may be acquired vertically in the peripartum period or horizontally from fomites in the environment or from colonized caregivers after delivery.
- Inadequate hand washing by the NICU staff can promote the spread of microorganisms from an infected to an uninfected infant or from the hands of colonized caregivers to the newborn. It is probably the single most important factor for sepsis in neonatal care units.

Risk Factors

Maternal risk factors

- Maternal urinary tract infection.

- Intrapartum fever of more than 37.5°C
- Preterm labor
- Prolonged rupture of membranes (ROM) ≥18 hrs.
- Chorioamnionitis
- Maternal GBS colonization
- Pregnancy on intrauterine device or with cervical circulage increases the incidence of *Candida* infection.

Neonatal risk factors

- Prematurity
- Low birth weight (<2,500 gm)
- Perinatal asphyxia
- Multiple gestations
- Neonates with endotracheal tubes, central lines, IV catheters…etc.
- Formula-fed neonates
- Congenital immune defects or asplenia
- Galactosemia (serious *E.coli* infections are more common in untreated newborns with galactosemia)
- Malformations leading to high inoculation of bacteria (obstructive uropathy)
- **Prolonged antibiotic** use increasing the incidence of *Candida* infection

Risk factors for late onset sepsis in VLBW infants

- Birth weight <750 gm
- Central venous catheters
- Delayed enteral feeding
- Prolonged hyperalimentation
- Mechanical ventilation
- Complications of prematurity:
  - Patent ductus arteriosus
  - Bronchopulmonary dysplasia
  - Necrotizing enterocolitis

Other risk factors

A high infant-to-nurse ratio in the NICU

Clinical Manifestations

- Physical findings may be nonspecific and subtle.

- Clinical manifestations may include the following:
  - Respiratory distress is the most common presenting symptom, particularly in EOS. Respiratory symptoms range from tachypnea and grunting, to respiratory failure.
  - PPHN may accompany sepsis.
  - Lethargy, poor reflexes and irritability may be presenting symptoms.
  - Temperature instability is present with hypothermia (more common) or hyperthermia.
  - Poor perfusion, hypotension and shock may accompany sepsis.
  - Gastrointestinal symptoms may be present: poor feeding, vomiting, diarrhea, abdominal distension and ileus.
  - Disseminated intravascular coagulopathy (DIC) with purpura and petechiae may be presenting symptoms.
  - Hepatomegaly and jaundice may present.
  - Meningitis may present without neurologic symptoms or with bulging or full fontanelle, seizures, apnea, and depressed sensorium.

N.B.: A high index of suspicion is required to identify and evaluate at-risk infants.

Differential Diagnosis

- Sepsis with respiratory distress: TTN and meconium aspiration.
- CNS symptoms: intracranial hemorrhage and inborn errors of metabolism.
- GIT symptoms: intestinal obstruction, gastric perforation, and NEC.
- Some nonbacterial infections such as disseminated HSV infection are indistinguishable from bacterial sepsis.

Investigations

Laboratory studies

Complete blood count (CBC) with differential

Total WBC count

- Depressed total WBC (leucopenia): WBC count <5,000/μL

N.B. Elevated WBC count (leucocytosis) is nonpredictive in newborn infants.

Neutropenia

- Absolute neutrophil count (ANC) <1,500/μL

Immature: Total neutrophil ratio (I:T ratio)

- I:T ratio ≥0.2
- I:T rises not specific only to infections: seizures, hypoglycemia, meconium aspiration and pneumothorax also associated with a rise in I:T ratio

- The sensitivity of I/T ratio ranges from 60-90%, and elevations may be observed with other causes, limiting the positive predictive value of these ratios; therefore, when diagnosing sepsis, the elevated I/T ratio should be used in combination with other signs.

Thrombocytopenia

- Can be found in severely ill infants

N.B: The usefulness of these tests is improved if a second CBC is obtained in 12-24 hrs.

C-reactive protein (CRP)

- CRP is a non specific marker for inflammation or tissue necrosis.
- Normal value is <0.5 mg/dl. Some laboratories may have different values depending on the methodology**.**
- An increasing CRP value is usually detectable within 6-18 hrs, and the peak CRP is seen at 8-60 hrs after onset of the inflammatory process.
- Serial determination of CRP at 12 hrs intervals after the onset of signs of sepsis increases the sensitivity of CRP in detecting sepsis.
- Infants with onset of infection in the first 12 hrs of life and infants with GBS infection may not have an elevated CRP value.
- Noninfectious processes (e.g., meconium aspiration) can have an elevated CRP.

N.B: CRP has a low positive predictive value and should not be used alone to diagnose sepsis. It is particularly more important for follow-up.

Cultures

- All cultures should be obtained prior to starting antibiotic therapy.
- If a culture is positive, repeat the cultures 48 hrs after starting antibiotic therapy to confirm the clearance of the organism.

Blood Culture

- Use two culture bottles; one aerobic and other anaerobic.
- The sensitivity of a single blood culture in identifying septicemia is only 80%. Obtaining more than one blood culture may improve the results and can be helpful in distinguishing blood culture contaminants from true pathogens.

N.B.: A definitive diagnosis of sepsis can only be made with a positive blood culture

Urine Culture

- A specimen should be obtained in all neonates with suspected sepsis.
- A sterile specimen is obtained either by catheterization or by a suprapubic bladder aspiration.
- If bagged urine is used for culture, results may be less reliable. In that case, a colony count is mandatory. A colony count of less than 10,000/ml indicates contamination,

10,000-100,000/ml is suspicious, and more than 100,000/ml of a single organism is reliable.

Cerebrospinal Fluid (CSF) Culture

- The routine lumbar puncture (LP) to evaluate asymptomatic neonates at risk of EOS remains controversial. LP should be incorporated in the evaluation of any infant with clinical evidence of probable sepsis that is confirmed by the rapid screening tests for sepsis (CBC, CRP).
- Meningitis accompanies sepsis in approximately 10% of infants with EOS and more often with LOS and it cannot be diagnosed or excluded solely on the basis of the symptomatology.
- Blood cultures can be sterile in 10-15% of infants with EOS and in one third of infants of VLBW with LOS.
- A lumbar puncture for CSF cell count, protein and glucose concentrations, Gram stain and culture should be performed before the administration of antibiotics if the infant is clinically stable.

Table (28-3): Normal CSF finding in newborn infants

	Normal Values
Cell count (WBCs/mm³)	
Preterm (mean)	9.0 (0 - 25.4)-57% PMN
Term (mean)	8.2 (0 - 22.4)-61% PMN
Glucose (mg/dl)	
Preterm	24-63 (mean, 50)
Term	34-119 (mean, 52)
CSF glucose/blood glucose (%)	
Preterm	55-105
Term	44-128
Protein (mg/dl)	
Preterm	65-150 (mean, 115)
Term	20-170 (mean, 90)

PMN: polymorphonuclear leukocytes

Local Site Culture

- Tracheal aspirate culture should be obtained in intubated infants with a clinical picture suggestive of pneumonia, or when the quality and volume of the secretions change substantially.
- Skin wound culture may be needed.

- Stool culture assists in the diagnosis of neonatal septicemia caused by enteric pathogens such as *Shigella*, *Salmonella*, and *Campylobacter*.

Serum glucose level

- Hypoglycemia or hyperglycemia may be present.

Arterial blood gas analysis

- Metabolic acidosis may be present.
- Arterial blood gas analysis should be done for infants with respiratory symptoms.

Evidence of disseminated intravascular coagulopathy (DIC)

- The diagnosis of DIC is based on compatible clinical features in conjugation with specific laboratory findings **(Refer to Chapter 34).**
- Laboratory findings in severe DIC are characterized by prolonged PT, APTT, and INR, and increased fibrin degradation products.

Imaging studies

- Chest radiography may reveal segmental or lobar infiltrate but more commonly reveals a diffuse, fine, reticulogranular pattern. Pleural effusions may be observed.
- Echocardiography may be of benefit in severely ill, cyanotic infants to determine if significant pulmonary hypertension or cardiac failure is present.
- Cranial ultrasonography in infants with meningitis may reveal evidence of ventriculitis, and abnormal parenchymal echogenicities. Serial cranial ultrasonography may be needed to detect the progression of complications such as obstructive hydrocephalus.
- CT scanning or MRI may be needed late in the course of meningitis to document obstructive hydrocephalus, ventricular dilation, and multicystic encephalomalacia.

Prevention

The most important step in management is prevention of neonatal sepsis by following strict infection control policies in the NICU.

Intrapartum antimicrobial prophylaxis (IAP)

The 2002 revised guidelines from the Centers for Disease Control and Prevention (CDC) recommend vaginal and rectal GBS screening at 35-37 weeks' gestation for all pregnant women (unless the patient had GBS bacteriuria during the current pregnancy or had a previous infant with invasive GBS disease).

Intrapartum antimicrobial prophylaxis (IAP) is given to the pregnant women at the time of labor or ROM

Indications of IAP

- Previous infant with invasive GBS disease
- GBS bacteriuria during the current pregnancy
- Positive GBS screening culture during current pregnancy (unless a planned cesarean section, in the absence of labor or ROM, is performed)

- Unknown GBS status and any of the following:
  - Delivery at <37 weeks' gestation
  - Rupture of membranes ≥18 hrs.
  - Intrapartum maternal fever (≥38°C)

Neonates born to mothers who received IAP

Depending on the infant's status at birth, the duration of prophylaxis, and the gestational age of the infant:

- If an infant has signs of sepsis → obtain cultures and start antibiotics.
- If an infant has no signs of sepsis, but is <35 weeks' gestation or the mother received only one dose of antibiotics (<4 hrs) → obtain a CBC and blood culture and observe. No antibiotics are required.
- If an infant has no signs of sepsis, is ≥35 weeks' gestation and the mother received at least 2 doses of antibiotics (>4 hrs) → observe the infant closely for ≥48 hrs. No cultures or antibiotics are needed.

Prophylactic antimicrobial therapy

- Prophylactic use of antibiotics can be justified if directed against single pathogens, for example, antimicrobial prophylaxis given to the mother at birth reduces the colonization rate and the incidence of an early onset of GBS infection.
- Antibiotics, however, should not be used as broad-spectrum coverage against many potential pathogens. This may encourage the emergence of resistance strains and alter the normal flora of gastrointestinal and respiratory tracts with overgrowth of potentially virulent organisms. Furthermore, broad coverage prophylaxis can mask the development of clinical disease and delay the administration of more effective therapy.
- Prophylactic administration of fluconazole during the first 6 weeks of life is effective in preventing fungal colonization and invasive fungal infection in VLBW and ELBW infants. Fluconazole, 3 mg/kg/dose is administered, once daily 3 times weekly for the first 2 weeks, then every other day for total of 4-6 weeks (longer duration for infants <1,000 gm).

Treatment

Antimicrobial therapy

- Initial (empiric) therapy: treatment is most often begun before a definite causative agent is identified.
- Continuing therapy is based on culture and sensitivity results, clinical course, and other serial laboratory studies (e.g., CRP).
- Cultures of blood and CSF should be repeated 48 hrs after initiation of therapy. If cultures are still positive and the clinical course is not improved, alteration of therapy may be necessary.
- For drug dosing, monitoring, and side effects **(Refer to Chapter 45).**

Selection of the appropriate antimicrobial therapy

Early onset neonatal sepsis

- Cultures should be obtained first.
- Organisms targeted with therapy are gram-negative bacilli (*E.coli, Klebsiella and Pseudomonas*), GBS, and *Listeria monocytogenes*.
- The recommended first line antibiotics are ampicillin and gentamicin.
- Third generation cephalosporins (cefotaxime or ceftazidime) may be added to gentamicin if meningitis is clinically suspected or if gram-negative rods are dominant in the unit.

Late onset neonatal sepsis

- Staphylococcus species (CONS) is the predominant cause of late onset nosocomial infection followed by gram negative organisms (e.g., *E coli, Klebsiella and, Pseudomonas aerogenosa*), then followed by fungal species (e.g., *Candida albicans*).
- Generally, staphylococcal coverage with vancomycin plus either an aminoglycoside or a third-generation cephalosporin is started.

Anaerobic infection

- Clindamycin

Fungal infection

- Fluconazole can be successfully used for systemic infections, meningitis and severe superficial mycoses caused by *Candida* species.
- Amphotericin B: the medication should be given slowly over 2-6 hrs to minimize the risk of seizures and arrhythmias during infusion. Liposomal preparation of amphotericin B is less toxic and causes less irritation at the site of infusion.
- CNS fungal infection is treated with an additional second agent commonly 5-fluorocytosine (flucytosine 5-FC) (100-150 mg/kg/day).
- Remove central catheters to eradicate infection.

Duration of therapy

- In neonatal sepsis therapy should continue for 10-14 days. In neonatal sepsis complicated with meningitis**,** therapy should continue for 14-21 days.
- In cases of osteomyelitis and septic arthritis, therapy should continue for 3-4 weeks after systemic and local signs have been resolved.
- In cases of urinary tract infections, therapy should continue for 10-14 days. Screening for renal anomalies should be carried out.

Monitoring of therapy

- All infants receiving aminoglycosides must have serum concentrations monitored.
- All infants receiving vancomycin must have serum concentrations monitored.
- Toxic levels of commonly used drugs are outlined in **(Table 28-4).**

Table (28-4): Toxic serum levels for various antimicrobial agents

Antimicrobial	Peak (µg/mL)	Trough (µg/mL)
Gentamicin	>10	>2
Amikacin	>30	>10
Vancomycin	>40	>10

N.B.: Infants with shock or renal compromise should have serum levels monitored after the first dose to determine further dosing.

Supportive therapy

- Provide inotropes and volume support for hypotension and poor perfusion.
- Maintain fluid and electrolyte therapy.
- Provide enteral or parenteral nutrition according to the needs of the infant.
- Maintain mechanical ventilation and/or exogenous surfactant for pneumonia and RDS.
- Give sodium bicarbonate for metabolic acidosis.
- Give anticonvulsants for seizures.

Adjunctive immunotherapies

Intravenous immunoglobulin (IVIG)

- A single dose of IVIG (500-750 mg/kg/dose over 2-6 hrs) for infants with overwhelming sepsis is a reasonable adjunctive therapy in seriously ill infants.
- Further studies are warranted before IVIG use in infections can be recommended as routine therapy.

Focal Bacterial Infections

Cellulitis

Cellulitis indicates an acute spreading infection of the dermis and subcutaneous tissues resulting in pain, erythema, edema, and warmth. It occurs when micro-organisms invade traumatized skin sites (e.g., lacerations, fissures, or venipuncture sites).

Etiology

- Colonization of the newborn skin begins at birth with organisms acquired from the mother's birth canal. Subsequently, infants may acquire organisms from the environment or from the hands of the NCU personnel.
- Staphylococcus aureus is most frequently associated with neonatal skin infections.

Management

- Localized erythema and/or discharge in a term infant can be treated with careful washing and local antisepsis with antibiotic ointment and close monitoring.
- Cellulitis at sites of intravenous access or venipuncture in preterm infants must be promptly discovered and carefully treated, due to the risk of local and systemic spread, especially in VLBW infants.
  - Obtain a CBC and blood culture and administer intravenous antibiotics (oxacillin or nafcillin and gentamicin). Vancomycin should substitute nafcillin for methicillin-resistant strains (i.e., MRSA).
  - If blood culture is negative, continue treatment for a total of 5-7 days with resolution of the cellulitis.
  - If blood culture is positive, obtain a lumbar puncture to rule out meningitis and carefully examine the infant to rule out accompanying osteomyelitis or septic arthritis. Therapy should be adjusted according to the identified organism.

Omphalitis

Omphalitis is an infection of the umbilical stump. It is characterized by erythema and/or induration of the periumbilical area with purulent discharge from the stump. Low birth-weight, prolonged labor, prolonged rupture of membranes or maternal infection, non-sterile delivery, umbilical catheterization, home birth and improper cord care are the major risk factors.

Etiology

- *Staphylococcus aureus* and *E. coli* are frequent pathogens.
- Group A *streptococci,* anaerobic bacteria, and polymicrobial infections may occur.

Clinical manifestations

- Purulent, foul smelling discharge from the umbilical stump may be noted.
- Periumbilical erythema and induration may be noted.
- If extensive periumbilical edema or involvement of the abdominal wall is noted, necrotizing fasciitis should be considered.

Complications

- Necrotizing fasciitis; a life-threatening condition resulting from rapidly spreading destruction of the fascia and subcutaneous tissue around the umbilicus and can be associated with bacteremia, coagulopathy, and shock and frequently progresses to death.
- Septic embolization with metastasis to the lungs and kidneys can occur.
- Pyelophlebitis (suppurative thrombophlebitis of portal or umbilical veins), liver abscess, septic umbilical arteritis, peritonitis have been also described.

Management

- Gram-stain and culture (for aerobic and anaerobic bacteria) of the purulent umbilical discharge and a full sepsis work-up (CBC, CRP, and blood culture) should be done.
- Combination therapy should be administered to provide broad-spectrum coverage. Vancomycin or nafcillin should be provided for gram-positive coverage. An aminoglycoside, or a third-generation cephalosporin, can be given for gram-negative coverage.
- Metronidazole should be added in the presence of crepitus or black discoloration of the periumbilical tissues suggesting an anaerobic or mixed infection.
- Necrotizing fasciitis requires extensive supportive care and early surgical consultation for aggressive debridement.

N.B.: Neonatal tetanus may follow contamination of the umbilical stump by the anaerobic bacterium *Clostridium tetani* under poor sanitary conditions in the babies of unimmunized mothers. Treatment consists of the administration of tetanus toxoid (500 U IM) and penicillin G (100,000-300,000 U/kg/day for 10-14 days) as well as supportive care with mechanical ventilation, sedatives, and muscle relaxants. Infants require standard tetanus immunizations after recovery.

Conjunctivitis (Ophthalmia Neonatorum)

Neonatal conjunctivitis (ophthalmia neonatorum) refers to inflammation of the conjunctiva within the first 28 days of life. It is most commonly infective in origin (bacteria and herpes simplex virus) but may also occur as a reaction to topical medications as silver nitrate (chemical conjunctivitis). Chemical conjunctivitis is a self limiting condition, and usually resolves within 48 hours.

Etiology

- *Chlamydia trachomatis* and *Neisseria gonorrhoeae* are the most important causes of conjunctivitis in the newborn period.
- Other bacteria (e.g., *Staphylococcus aureus*, GBS, *Pseudomonas* species, *Streptococcus pneumoniae*, and *Haemophilus* species) can also be causative.

Clinical manifestations

Gonorrheal conjunctivitis

- Onset: 1-4 days after birth but may occur later
- Manifestations: acute conjunctival injection and chemosis, lid edema and profuse, purulent ocular discharge. Corneal ulceration and perforation may occur.

Chlamydial conjunctivitis

- Onset: 5-14 days after birth
- Manifestations: watery discharge which becomes copious and purulent later on. Conjunctival scarring can occur, although the cornea is usually not involved.

Other bacterial conjunctivitis

- Onset: often longer incubation period than for the other infective causes.
- Manifestations: depending on the causative agent, there may be variable degrees of inflammation, lid swelling and discharge.
- Pseudomonas conjunctivitis occurs most often in hospitalized preterm infants and can cause a rare and devastating form of conjunctivitis that is often associated with systemic complications.

Diagnosis

- History of previous or concurrent sexually transmitted disease can be obtained.
- Gram-stain and culture of the purulent ocular discharge should be done.
- When evaluating for chlamydial infection, conjunctival scrapings (obtained by gentle but firm scraping of the lower portion of palpebral conjunctiva with a blunt spatula) should be examined because the organism resides in the epithelial conjunctival cells. Care must be taken not to injure the conjunctiva during the process.

Prevention

- At delivery the newborn's eyes should be cleaned with sterile cotton to remove secretions and debris.
- Prophylactic eye drops are given to all neonates on the first day of life. Newborns should receive topical antimicrobial prophylaxis against *Neisseria gonorrhoeae.*
- Care should be taken to prevent contamination of the eyes with drips from suction catheters after suctioning the nasopharynx or endotracheal tube.

Treatment

Gonococcal conjunctivitis

- Frequent irrigation of the conjunctival sac with sterile isotonic saline until the discharge has resolved.
- Ceftriaxone (25-50 mg/kg, IV or IM, not to exceed 125 mg) as a single dose should be administered. An alternative therapy is cefotaxime in a single dose (100 mg/kg, given IV or IM).
- Infants should be hospitalized and evaluated for disseminated disease (i.e., sepsis, meningitis, arthritis). For disseminated neonatal gonococcal infection, the recommended therapy is ceftriaxone (25-50 mg/kg) given once daily or cefotaxime (50-100 mg/kg daily) given in two doses for 7-14 days (10-14 days for meningitis).
- The infant and mother should be screened for coincident chlamydial infection.

Chlamydial conjunctivitis

- Oral erythromycin, 50 mg/kg daily in four doses for 14 days. The efficacy of treatment is approximately 80%, and infants must be evaluated for the need for a second course of treatment.
- Topical treatment is ineffective and is not indicated.
- Infants should also be evaluated for the concomitant presence of chlamydial pneumonia that may require additional supportive respiratory care.

Bacterial infection

- Conjunctivitis caused by *Pseudomonas* species requires parenteral treatment with an aminoglycoside and an antipseudomonal penicillin in addition to topical treatment.
- Local saline irrigation can be done.
- Topical antibiotics (ointments or solutions) containing a combination of bacitracin, neomycin, and polymyxin can be applied every 6 hrs for 7-10 days for other forms of bacterial conjunctivitis.

Pneumonia

(Refer to Chapter 22)

Osteomyelitis and Septic Arthritis

These infections are rare in newborns, and may result from hematogenous spread in the setting of bacteremia, or direct extension from a skin source of infection.

Etiology

- The most frequent causative agents are *Staphylococcus aureus*, *E. coli*, and *GBS*.
- Uncommon etiologic agents include *Neisseria gonorrhoeae*, *Haemophilus influenzae*, and group A *streptococci*.

Clinical manifestations

- The hip, knee, and wrist are commonly involved in septic arthritis, and the femur, humerus, tibia, radius, and maxilla are the most common bone sites of infection.
- Positional preferences, lack of use of the involved extremity ("pseudoparalysis"), and evidence of discomfort when handled or having the diaper changed.
- Localized erythema and swelling.

Diagnosis

- When the physical examination suggests the possibility of osteomyelitis, radiographs should be obtained. Neonates demonstrate radiographic changes 7-10 days after onset of infection. The earliest finding is deep soft tissue swelling. Later in the course of infection, periosteal thickening, cortical destruction, irregularities of the epiphysis and periosteal new bone formation are seen.
- The evaluation should be as for sepsis, including blood, urine, and CSF culture, and culture of any purulent skin lesions.
- Synovial fluid obtained from infants with joint involvement should be Gram stained and cultured.

- Ultrasonography should be performed in infants with suspected bacterial arthritis of the hip; it can be used to guide diagnostic aspiration

Treatment

- Empiric parenteral treatment should be initiated with an antistaphylococcal agent, such as nafcillin or vancomycin, and either an aminoglycoside or an extended-spectrum cephalosporin for gram-negative coverage. Vancomycin should be used empirically when MRSA are prevalent in the community.
- When the specific organism has been identified, treatment should be continued with the most appropriate antibiotic. The dosages used should be those used for treatment of septicemia or meningitis. Therapy should be continued for 3-4 weeks or longer until clinical and radiographic findings indicate healing.
- Infant is considered to be responsive to treatment only if:
  - Has been afebrile for 48-72 hrs
  - Local signs and symptoms of infection are reduced considerably
  - WBC has normalized
  - CRP and/or ESR has decreased
- Adjunctive therapies may include pain control and physical therapy.
- Surgical decompression may be required if pus is aspirated from the site of involvement. When the hip or shoulder joints are involved, prompt surgical decompression and drainage are crucial.

Prognosis

- Significant disability can result from joint or epiphyseal growth plate damage.

Chapter 29

Perinatal Asphyxia and Hypoxic Ischemic Encephalopathy

Perinatal Asphyxia and Hypoxic Ischemic Encephalopathy

Definitions

Hypoxia or anoxia

It is defined as partial (hypoxia) or complete (anoxia) lack of oxygen in the tissues or blood.

Ischemia

It is defined as a reduction or cessation of blood flow to the tissues which compromises both oxygen and substrate delivery to the tissue.

Asphyxia

It is the state of impaired gas exchange in the placenta or lungs leading to progressive hypoxemia, hypercarbia, and acidosis.

Essential characteristics of perinatal asphyxia are defined jointly by the American Academy of Pediatrics (AAP) and the American College of Obstetricians and Gynecologists (ACOG):

- Profound metabolic or mixed acidosis (pH <7.0) in umbilical cord arterial blood sample, if obtained.
- Persistence of an Apgar score of 0-3 for >5 minutes.
- Neurologic manifestations in the immediate neonatal period to include seizures, hypotonia, coma, or hypoxic-ischemic encephalopathy (HIE).
- Evidence of multiorgan system dysfunction in the immediate neonatal period.

Hypoxic-ischemic encephalopathy (HIE)

A clinically defined syndrome of disturbed neurological function with an abnormal neurobehavioral state in the earliest days of life, manifested by difficulty with initiating and maintaining respiration, depression of tone and reflexes, subnormal level of consciousness, and often seizures as a result of a hypoxic-ischemic event.

Etiology

In term infants, 90% of asphyxial events occur in the antepartum or intrapartum periods as a result of impaired gas exchange across the placenta. The remainder of these events occurs in the postpartum period, and is usually secondary to pulmonary, cardiovascular, or neurologic abnormalities.

Maternal factors

- Inadequate oxygenation of maternal blood:
  - Hypoventilation during anesthesia
  - Cyanotic heart disease
  - Respiratory failure
  - Carbon monoxide poisoning
  - Status epilepticus

- Low maternal blood pressure:
  - Acute blood loss
  - Severe anaphylactoid reaction
  - Compression of the vena cava and aorta by the gravid uterus

Uteroplacental factors

- Uterine tetany and inadequate relaxation of the uterus as a result of administration of excessive oxytocin.
- Uterine rupture.
- Placental abruption.
- Placental insufficiency from toxemia or postmaturity.
- IUGR possibly developing in chronically hypoxic fetuses without the traditional signs of fetal distress. Uterine contractions may further reduce umbilical oxygenation and result in low Apgar scores and postnatal hypoxia in the delivery room.
- Umbilical cord accidents: prolapse, compression, or true knot.

Fetal/neonatal factors

- Failure of oxygenation
  - Severe forms of cyanotic congenital heart disease
  - Severe pulmonary disease (e.g. RDS, MAS, or pneumonia)
- Anemia, severe enough to lower the oxygen content of the blood
  - Severe hemorrhage (e.g., twin-to-twin transfusion syndrome, or fetomaternal hemorrhage)
  - Severe isoimmune hemolytic disease
- Shock, severe enough to interfere with the transport of oxygen to vital organs
  - Overwhelming sepsis
  - Massive blood loss
  - Intracranial or adrenal hemorrhage
  - Cardiac arrhythmia

Pathophysiology

- The initial circulatory response to perinatal asphyxia involves the redistribution of cardiac output with increased perfusion of vital organs (e.g., brain, heart, adrenals), and with concomitant decreased blood flow to other organs (e.g., the lungs, kidneys, liver), the so-called “diving reflex”.
- Prolonged hypoxic-ischemic insult results in systemic hypotension and impairment of cerebrovascular autoregulation → impaired cerebral blood flow → anaerobic metabolism and eventual intracellular energy failure.
- Acute hypoxic-ischemic insult leads to events that can be categorized as:
  - Early (primary) neuronal death: predominantly due to necrosis.

- Delayed (secondary) neuronal death: starting at about 6-24 hrs after the initial injury, and is predominantly apoptotic.

- After an episode of hypoxia and ischemia, anaerobic metabolism occurs, this generates increased amounts of lactate and inorganic phosphates. Excitatory and toxic amino acids, particularly glutamate, accumulate in the damaged tissue. Increased amounts of intracellular sodium and calcium may result in tissue swelling and cerebral edema (cytotoxic edema). There is also increased production of free radicals and nitric oxide in these tissues.

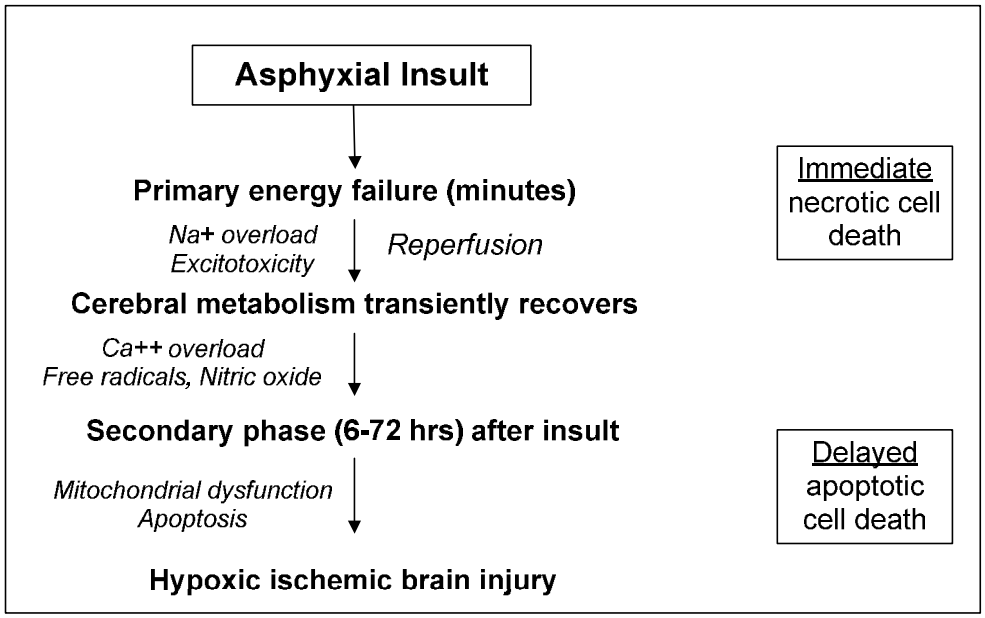


Figure (29-1): Pathophysiology of hypoxic-ischemic brain injury in the developing brain

Clinical Manifestations

The incidence of perinatal asphyxia is inversely related to the gestational age and birthweight. A higher incidence is noted in term infants of diabetic or toxemic mothers, infants with IURG, breech presentation, and postdates infants.

During labor

(Refer to Chapter 2)

- Slow fetal heart rate, and loss of beat-to-beat variability
- Variable or late deceleration pattern
- Fetal scalp blood analysis may show a pH <7.20
- Yellow, meconium-stained amniotic fluid

After birth

- At birth, these infants are frequently depressed and fail to breathe spontaneously.
- Diagnosis of perinatal HIE requires an abnormal neurologic examination on the first day after birth.
- According to Sarnat and Sarnat, HIE can be classified into 3 stages **(Table 29-1).** Infants can progress from mild to moderate and/or severe encephalopathy over the 72 hrs following the insult.

- In infants on musculoskeletal blockade for mechanical ventilation, seizures may be manifested by abrupt changes in BP, HR, and oxygenation.

Table (29-1): Clinical staging of hypoxic ischemic encephalopathy in term infants

Signs	Stage 1 (mild)	Stage 2 (moderate)	Stage 3 (severe)
Level of consciousness	Hyperalert	Lethargic	Stuporous, coma
Muscle tone	Normal	Hypotonic	Flaccid
Posture	Normal	Flexion	Decerebrate
Tendon reflexes/clonus	Hyperactive	Hyperactive	Absent
Myoclonus	Present	Present	Absent
Moro reflex	Strong	Weak	Absent
Pupils	Mydriasis	Miosis	Unequal, poor light reflex
Seizures	None	Common	Decerebration
Electroencephalographic	Normal	Low voltage changing to seizure activity	Burst suppression to isoelectric
Duration	<24hr	2-14 days	Hours to weeks
Outcome	Good (about 100% normal)	Variable 80% normal; abnormal if symptoms >5-7 days	Death (50%), remainder with severe deficits

Modified from Sarnat HB, Sarnat MS: Neonatal encephalopathy following fetal distress: A clinical and electroencephalographic study. Arch Neurol 1976; 33: 696–705.

- Other multi-organ system dysfunctions secondary to inadequate perfusion, include:
  - Renal: the kidney is the most common organ to be affected in perinatal asphyxia:
    - Acute tubular or cortical necrosis
    - Hematuria
  - Hematological
    - Anemia
    - Thrombocytopenia
    - Disseminated intravascular coagulopathy (DIC)
  - Cardiovascular
    - Cardiomyopathy
    - Hypotension/shock

- Pulmonary
  - Persistent pulmonary hypertension of newborn (PPHN)
  - Meconium aspiration syndrome (MAS)
  - Respiratory distress syndrome (RDS)
  - Pulmonary hemorrhage
- Hepatic necrosis
  - Cholestasis
  - Hypoglycemia
  - Coagulopathy
  - Elevated serum transaminases and ammonia levels
- Gastrointestinal
  - Necrotizing enterocolitis (NEC)
  - Distension
  - Bloody stools
- Adrenal insufficiency
  - Hypoglycemia
  - Hyponatremia/hyperkalemia
  - Hypotension
- Syndrome of inappropriate secretion of ADH (SIADH): manifested by hyponatremia and hypo-osmolarity in combination with inappropriately concentrated urine with elevated urine specific gravity, osmolarity, and sodium **(Refer to Chapter 16)**

Differential Diagnosis

- Sedation and/or analgesia
- Sepsis and/or meningitis
- Viral encephalitis
- Congenital malformations
- Neuromuscular disease
- Birth trauma

Investigations

- Complete blood count with differential
- Serum glucose level
- Arterial blood gas analysis
- Serum electrolytes, calcium, phosphorus and magnesium levels

- Renal evaluation:
  - BUN, creatinine, fractional sodium excretion (FE-Na)
  - Urine analysis (β_2 microglobulin)
  - Renal ultrasound
- Cardiac evaluation: serum cardiac troponin and creatine kinase (CK-MB) levels
- Hepatic evaluation:
  - Serum liver enzymes [aspartate transaminase (AST) and alanine transaminase (ALT)]
  - Serum albumin, bilirubin and ammonia levels
  - PT and APTT
- Neurologic evaluation: serum CK-BB, may be increased within 12 hrs of the insult
- Brain imaging:
  - Cranial sonar: it has a limited utility in evaluation of hypoxic injury in term infants; however, it is the preferred modality in evaluation of preterm infants.
  - CT scans: It is helpful in the identification of focal hemorrhagic lesions, diffuse cortical injury, and damage to the basal ganglia. CT has limited ability to identify cortical injury within the first few days of life.
  - Diffusion-weighed MRI: it is the preferred imaging modality.
- EEG: to evaluate for seizure activity and also to define abnormal background activity.
- Brain stem function responses (Somato-sensory Evoked Potential, Visual Evoked Potential and Auditory Evoked Potential) have a prognostic significance.

Management of Perinatal Asphyxia

Time is crucial in managing HIE and even a few minutes of delay can lead to long-term disability or death.

Prevention

Prevention is the best management

- Proper antenatal care for pregnant mothers and identification of high risk pregnancies.
- Proper antenatal fetal assessment (nonstress test, contraction stress test, and biophysical profile).
- Proper intrapartum fetal assessment (fetal heart rate and rhythm abnormalities).
- Proper resuscitation measures.

Supportive measures

Adequate ventilation and oxygenation

- Maintain adequate ventilation: CO_2 should be maintained in the normal range. Hypercapnia can cause cerebral acidosis and impair cerebral autoregulation Hypocapnia (CO_2 <25 mmHg) may lead to severe hypoperfusion of the brain.

- Maintain adequate oxygenation (PaO_2 >40 mmHg in premature infants and PaO_2 >50 mmHg in term infants). Hypoxia should be treated by supplemental oxygen and/or mechanical ventilation. Avoid hyperoxia, as it may lead to additional brain injury from possible reduction in cerebral blood flow and exacerbation of free radical damage.

Thermoregulation

- Maintain temperature in the normal range.
- Avoid hyperthermia.

Correction of metabolic acidosis

- Maintain the blood gases and acid-base status in the physiological ranges.
- Use volume expanders **cautiously**.
- Use bicarbonate only when cardiopulmonary resuscitation is prolonged and the infant remains unresponsive. $NaHCO_3$ administration may lead to hypercarbia and intracellular acidosis and increase lactate.

Cardiovascular support

- Perfusion
  - Maintain arterial blood pressure in the normal range for gestational age and weight. Volume expanders and inotropic support are often required
  - Avoid systemic hypotension and hypertension with continuous monitoring of mean arterial BP.
  - Avoid fluid overload.
  - Monitoring of central venous pressure (CVP)
    - It is helpful in assessment of circulatory status and adequacy of cardiac preload in order to make a correct adjustment in intravascular volume.
    - A level between 5-8 mmHg is a reasonable target in term infant.
- Cardiac dysfunction
  - The resulting circulatory failure is differentiated from that caused by hypovolemic shock by an elevated CVP.
  - Infants with cardiac compromise may need inotropic agents (e.g., dopamine or dobutamine) which can be used to maintain an adequate cardiac output and blood pressure.

Maintenance of an optimum metabolic status

- Maintain blood glucose level of 75-100 mg/dl, avoid hypoglycemia (neuronal injury), and hyperglycemia (increases brain lactate, brain edema and further disturbance of vascular autoregulation).
- Maintain calcium within normal range because hypocalcemia can compromise cardiac contractility and may cause seizures.

Feeding

- Feeding should be withheld until good bowel sounds are heard and stools are negative for blood and/or reducing substances.

Renal support

- Monitor continuously by measuring urine output.
- Carefully assess the infant's volume status.
- Oliguria is managed by careful maintenance of fluid balance (insensible loss + urine output) with daily measurements renal function tests, serum electrolytes**,** as well as daily assessment of the infant's weight **(Refer to Chapter 16).**
- Consider low dose dopamine infusion (<5 µg/kg/minute).

Liver support

- Monitor liver function.
- Monitor levels of drugs that are eliminated through the liver.

Hematological support

- Monitor coagulation profile.
- Correct abnormalities with FFP and/or platelet transfusion.

Control of brain edema

- In the first 2 days of life, restrict IV fluids to two thirds of the daily requirement in light of the high frequency of acute tubular necrosis and the SIADH.
- No other therapeutic interventions, including corticosteroids, mannitol, have yet proven helpful in the clinical setting.

Control of seizures

- Phenobarbital 20 mg/kg/dose: add 5 mg/kg until seizures are controlled or the maximum dose of 40 mg/kg is reached. Maintain on 3-5 mg/kg/day.
- If seizures are not controlled by the maximum allowable dose of phenobarbital: add phenytoin at 20 mg/kg/dose. Maintain on 4-8 mg/kg/day, given every 8 hrs in divided doses.
- Benzodiazepines are considered third line drugs and include lorazepam 0.05-0.1 mg/kg/dose IV.
- Correct the metabolic cause if present (e.g., hypoglycemia, hypocalcemia**,** and hypo-magnesemia).

Emerging Neuroprotective Strategies

- Magnesium sulfate
  - Glutamate plays a critical role in the hypoxic, ischemic, neuronal death.
  - Mechanisms of glutamate induced neuronal death:
    - Rapid cell death: occurs in minutes.
    - Delayed cell death: it is initiated principally by the activation of the N-methyl D-aspactate (NMDA) receptor. Magnesium is an NMDA receptor blocker.
  - Magnesium sulfate infusion (at 250 mg/kg/dose for 3 doses, 24 hrs apart) is effective in improving outcomes for term infants with severe perinatal asphyxia

when it is given early (within 6 hrs). However, more studies are needed to confirm the results.

- ► Beware of hypotension, respiratory depression, depressed cardiac function, and hypermagnesemia. Use with caution in patients with renal insufficiency.

- Selective head cooling coupled with mild systemic hypothermia may be a potentially useful treatment for asphyxiated term infants.

Prognosis

- The outcome of HIE correlates to the timing and severity of the insult and ranges from complete recovery to death.
- The prognosis varies depending on whether the metabolic and cardiopulmonary complications (hypoxia, hypoglycemia, shock) are treated, the infant's GA (outcome is poorest if the infant is preterm), and the severity of the encephalopathy.
- The overall mortality rate is 10-30%. The frequency of neurodevelopmental sequelae is 15-45%.
- A low Apgar score at 20 minutes, absence of spontaneous respirations at 20 minutes of age, and the persistence of abnormal neurologic signs at 2 weeks of age also predict death or severe cognitive and motor deficits.
- Infants with stage 2 and 3 encephalopathy are at the highest risk for adverse outcome.
- The combined use of an early EEG and MRI is useful in predicting outcome in term infants with HIE. Normal MRI and EEG findings are associated with a good recovery, whereas severe MRI and EEG abnormalities predict a poor outcome.
- The presence of seizures increases an infant risk of cerebral palsy 50-70 times.

Chapter 30

Neonatal Seizures

Neonatal Seizures

Seizures are paroxysmal alteration of neurologic function, including behavioral, motor, and/or autonomic changes.

- According to their pathophysiology and neuronal origin, seizures can be either epileptic or non-epileptic.
  - Epileptic seizures originate from the cortical neurons and are associated with EEG changes.
  - Non-epileptic seizures are initiated in the subcortical area and are not usually associated with any EEG changes. They are due to loss of cortical inhibition on the brain stem reflexes.
- The overall incidence is 0.5% of all term and preterm neonates. The incidence is higher in preterm neonates.

Etiology

Common causes

Hypoxic ischemic encephalopathy (HIE)

Cerebral hypoxia-ischemia i.e., asphyxia possibly occurring in the antenatal, intrapartum, or neonatal periods, is the most common causal factor associated with neonatal seizures. Perinatal asphyxia accounts for 25-40 % of neonatal seizures.

Seizures due to HIE in the newborn usually occur within 12 -24 hrs after the insult. The timing is usually related to the severity of the asphyxia insult. The diagnosis of intrapartum asphyxia is highly suspected if the umbilical artery pH is <7.0 with a base deficit >-12 mEq/L. An Apgar score of <5 at 5 minutes is an accurate practical criterion to reflect asphyxia.

Seizures after asphyxia may be associated with trauma, intracranial hemorrhage, or other brain damage based on neurologic diagnoses besides asphyxia.

Focal ischemic injury

Neonatal arterial stroke is the second most common cause of neonatal seizures. In most cases the cause is unknown. The left middle cerebral artery is most commonly involved. Infants usually appear normal before and after seizures.

Cerebral infarction in the venous distribution of the brain may also lead to neonatal seizures. Lateral or sagittal sinus thromboses can occur secondary to systemic infection, polycythemia, or dehydration. Venous infarction in the deep white matter of the preterm brain also occurs in association with intraventricular hemorrhage. Infants usually have a depressed mental status between seizures.

Intracranial hemorrhage

(Refer to Chapter 31)

It is implicated in about 10% of neonatal seizures.

Infections

(e.g., congenital infections, meningitis, septicemia)

Transient metabolic disturbances

- Hypoglycemia
- Hypocalcemia
- Hypomagnesemia
- Hyponatremia (may result from inappropriate secretion of ADH after severe brain trauma, infection, or asphyxia): an uncommon isolated cause of neonatal seizures
- Hypernatremia (e.g., after repeated doses of $NaHCO_3$)

Less common causes

Inborn errors of metabolism

Examples:

- Pyridoxine (vitamin B6) dependency
- Glycine encephalopathy (nonketotic hyperglycinemia), a deficiency in the glycine cleavage resulting in high levels of glycine in the brain and CSF
- Maple syrup urine disease
- Folinic acid responsive seizures

Congenital brain anomalies

(e.g., holoprosencephaly and lissencephaly)

Epileptic syndromes

(e.g., benign familial neonatal seizures, benign idiopathic neonatal seizures, and neonatal myoclonic encephalopathy)

- Benign familial neonatal seizures: autosomal dominant, typically occurring in the first 48-72 hrs of life; and disappearing by age 2-6 months.
- Benign idiopathic neonatal seizures (fifth-day fits): occur on day 5 of life (4-6 days) in normal-appearing neonates; multifocal seizures present for less than 24 hrs.

Maternal drug withdrawal

(e.g., Heroin, barbiturates, methadone, and cocaine)

Kernicterus

(Refer to Chapter 21)

N.B.: A newborn with convulsions may have more than one underlying cause (e.g., HIE associated with hypocalcemia or sepsis associated with hypoglycemia).

Clinical Manifestations

Most seizures in the neonate are focal, although generalized seizures have been described in rare instances. This is probably because, in neonates, generalization of the electrical activity is impeded by lack of myelination and incomplete formation of dendrites and synapses in the brain. Four types of seizures are frequently encountered in neonates:

Subtle seizures

- The most common subtype comprising about 50% of all seizures in term and premature infants (more common in full-term infants). They usually occur in association with other types of seizures. They are usually not associated with EEG seizures and have poor response to conventional anticonvulsants. They may manifest in any of these ways:
  - Stereotypic movements of the extremities**,** such as bicycling or swimming movements.
  - Deviation or jerking of the eyes with repetitive blinking of the eyelids.
  - Drooling, sucking or chewing movements.
  - Apnea or sudden changes in the respiratory pattern, unlike apnea due to respiratory center depression, and associated with tachycardia rather than bradycardia.
  - Rhythmic fluctuations in vital signs.
- Despite the "subtle" expression of this seizure category, these infants may have suffered significant brain injury.

Tonic seizures

Tonic seizures involve stiffening of parts of the body and can be either focal or generalized.

Generalized tonic seizures

- They mainly manifest in preterm infants with diffuse neurologic dysfunction or major IVH as a result of extensive neocortical damage or dysfunction permitting the emergence of uninhibited subcortical expressions of extensor movements.
- They closely mimic decerebrate or decorticate posturing and typically present as tonic flexion or extension of the upper extremities, neck or trunk, and associated with tonic extension of the lower extremities.
- The majority of cases are not associated with electrographic seizures.

Focal tonic seizures

- They present with asymmetric truncal posturing, tonic movements of a limb, or sustained head or eye turning. They are often associated with electrographic seizures.

Clonic seizures

- Clonic seizures consist of stereotypic and repetitive biphasic movements composed of a fast contraction phase and a slower relaxation phase. The rhythm of clonic movements is usually slow, 1-3 movements/second.
- Clonic movements should be distinguished from the symmetric "to-and-fro" movements of jitteriness. Gentle flexion of the affected body part easily suppresses the tremor, whereas clonic seizures persist.
- They can involve any body part, such as the face, arm, leg, and even diaphragmatic or pharyngeal muscles; most often involve one extremity or one side of the body.
- They may be unifocal, multifocal or generalized:
  - Clonic seizures that remain unifocal are usually not associated with loss of consciousness. The most common cause of unifocal clonic seizures is neonatal

stroke. Other causes include focal traumatic contusion, subarachnoid hemorrhage, or metabolic disturbances.

- Multifocal or migratory clonic activities spread over body parts, either in a random or anatomically appropriate fashion. They may alternate from side to side and appear asynchronously between the two halves of the infant's body. They may also resemble myoclonic seizures. Neonates with this seizure description suffer death or significant neurologic morbidity.

Myoclonic seizures

- Myoclonic movements are brief jerks of the extremities or body that tend to involve distal muscle groups. Myoclonus lacks the slow return phase of the clonic movement complex described previously.
- They can be focal, multifocal, or generalized.
  - Focal myoclonic seizures typically involve the flexor muscles of an extremity.
  - Multifocal myoclonic seizures present as asynchronous twitching of several parts of the body.
  - Generalized myoclonic seizures present as massive flexion of the head and trunk with extension or flexion of the extremities. They are associated with severe brain dysfunction or damage and poor long term prognosis.

Diagnosis

The diagnosis of seizures and their underlying causes is based on:

- Obtaining good maternal and obstetric histories
- Careful physical examination
- Laboratory investigations

Maternal and obstetric history

- Maternal infections
- Drug exposure
- Previous abortions or infants with seizures (in case of inborn errors of metabolism)
- Medical conditions (e.g., diabetes, hypertension…etc.)
- Family history of neonatal seizures
- Chorioamnionitis, fever, antepartum hemorrhage, difficult labor or fetal distress, and low Apgar scores

Laboratory investigations

Primary tests

- Blood glucose
- Serum calcium and magnesium
- Complete blood count, differential leukocytic count and platelet count
- Serum electrolytes

- Arterial blood gas
- CSF analysis
- Blood and CSF cultures

Other tests

- Search for specific suspected causes (TORCH titers, ammonia level, amino acids in urine, head sonogram…etc).
- EEG is normal in about one third of cases.
- Video EEG monitoring and interpretation by an experienced person is the most reliable test.
- Cranial ultrasound is done to diagnose hemorrhage and scarring.
- Brain CT scan or MRI is done to diagnose cerebral malformations and hemorrhage.

Benign Movements Simulating Seizures

Jitteriness

- Clinically it differs from clonic seizures in these aspects:
  - The flexion and extension phases are equal in amplitude.
  - Infants are generally alert, with no abnormal gaze or eye movements.
  - Passive flexion or repositioning of the limb diminishes the tremors.
  - Tremors are provoked by tactile stimulation, though they may be spontaneous.
  - No EEG abnormalities are present.
- Jitteriness is often seen in infants with hypoglycemia, drug withdrawal, hypocalcemia, hypothermia, and in SGA infants. These tremors spontaneously resolve within a few weeks.

Benign neonatal sleep myoclonus

- Benign neonatal sleep myoclonus occurs in healthy preterm and term infants during active sleep and is rapidly abolished by arousal.
- Unlike other nonepileptic behaviors, these movements may be precipitated by gentle rhythmic rocking or tactile stimuli, and gentle restraint may increase them. These events never occur during wakefulness.
- They resolve spontaneously within a few months and do not require medication.

Sleep apnea

- Sleep apnea is not associated with abnormal movements, but is usually associated with bradycardia.
- On the other hand, when seizures present with apnea, they are usually associated with abnormal movements, and the predominant autonomic changes are tachycardia with an increased blood pressure.

Management of Seizures

- Achieve systemic homeostasis: patent airway, adequate breathing and circulation.

- Correct the underlying cause, if possible
  - Hypoglycemia should be treated immediately by IV glucose 10% solution (2 ml/kg) infusion over 1 minute, followed by a continuous infusion **(Refer to Chapter 17).** The target blood glucose level is 50-125 mg/dl.
  - Hypocalcemia-induced seizures should be treated with an IV infusion of 200 mg/kg (2 ml/kg) of calcium gluconate. Hypocalcemia is suspected in IDMs, infants with asphyxia or infants with previously documented hypocalcemia. Infuse slowly with close observation of heart rate and rhythm. This dosage should be repeated every 6 hrs over the first 24 hrs.
  - Serum magnesium concentrations should also be measured in infants treated for hypocalcemia, because hypomagnesemia may accompany hypocalcemia; 0.2 mg/kg of magnesium sulfate 50% should be given by IM injection.
  - Start antibiotics for infants with suspected sepsis after obtaining the appropriate culture.
- Specific anticonvulsant agents: **(Table 30-1)**
- Treat with pyridoxine when seizures are refractory to the preceding regimen. Pyridoxine dependency must be excluded. Diagnosis is made by pyridoxine 50-100 mg IV with EEG monitor as a therapeutic trial. Seizures will stop within minutes if pyridoxine dependency is the cause. If diagnosis is made, oral pyridoxine is given as maintenance 10-100 mg/day according to response.
- Treat with folinic acid in infants failing to respond to anticonvulsants and pyridoxine. Give a trial of folinic acid for 24-48 hrs. The starting dose is 2.5 mg enteral folinic acid twice/day, but may have to be increased to 8 mg/kg/day.
- Other oral antiepileptic drugs (AEDs)
  - Clonazepam: 0.1 mg/kg in 2-3 doses
  - Carbamazepine: 10 mg/kg, then 15-20 mg/kg per day in 2 doses
  - Valproic acid: 10 to 25 mg/kg, then 20 mg/kg per day in 3 doses
  - Lamotrigine: 12.5 mg in 2 doses

Table (30-1): Neonatal anticonvulsants guidance, dosages and side effects

Drug	Guidance	Dose	Side Effect
Phenobarbital	• The drug of choice • Therapeutic level: 20 µg/ml	• Loading dose: 10-20 mg/kg over 10-15 minute Add extra 5 mg/kg until a maximum of 40 mg/kg IV or control of seizures • Maintenance dose: 3-5 mg/kg/day	• Hypotension • Apnea • Long-term effects on brain growth • Monitor respiratory status during administration and assess the IV site

Table (30-1): Neonatal anticonvulsants guidance, dosages and side effects (continued)

Drug	Guidance	Dose	Side Effect
Phenytoin	• If seizures are not controlled with phenobarbital alone	• Loading dose: 20 mg/kg IV. Infusion rate not more than (1 mg/kg/minute) • Maintenance dose: 3-5 mg/kg/day • Phenytoin is dissolved in normal saline solution as it precipitates in glucose solutions	• Arrhythmias • Hypotension • Cerebellar damage • Toxicity is a problem with this drug
Benzodiazepines	• Use in status epilepticus • Repeat every 15 minutes for 2 - 3 doses, if needed	• Lorazepam: 0.05-0.1 mg/kg/ dose • Diazepam: 0.1-0.3 mg/kg/ dose • Midazolam: 0.02-0.1 mg/kg IV bolus followed by 0.01-0.06 mg/kg/hr	• Respiratory depression • Interferes with bilirubin binding to albumin

When to Stop Anti-Epileptic Drugs (AEDs)

- There are no specific practice guidelines for the timing of stopping these medications.
- Stopping AEDs, two weeks after the last seizure episode, is acceptable as prolonged medications for months or years can adversely affect the developing brain.
- Discontinuation of AEDs before discharge from the neonatal unit is generally recommended unless the infant demonstrates a significant brain lesion on cranial sonography or CT or has abnormal neurological signs at the time of discharge. In these cases, slower tapering of AEDs is required with close follow-up.
- The duration of treatment following neonatal seizures is determined by the underlying cause. If, at the time of discharge from NICU, the infant's neurologic examination and EEG are normal, an early withdrawal of phenobarbital may be considered. Otherwise, the need for continued phenobarbital therapy should be re-evaluated at 6-12 weeks intervals.

Prognosis

- The major predictors of long-term outcome are:
  - Underlying etiology
  - EEG findings
  - Gestational age
  - Neurologic examination findings
  - Neuroimaging findings

- The best prognosis exists when the seizures are caused by:
  - Hypocalcemia
  - Pyridoxine dependency
  - Subarachnoid hemorrhage
- The worst prognosis exists when the seizures are caused by:
  - Brain malformation
  - Severe IVH
  - Prolonged or persistent hypoglycemia
  - Hypoxia
- Sequelae can include:
  - Chronic seizures (15-20%)
  - Mental retardation
  - Cerebral palsy

Chapter 31

Intracranial Hemorrhage

Intracranial Hemorrhage

Bleeding in the skull can occur

- External to the brain into epidural, subdural**,** or subarachnoid space
- Into the parenchyma of cerebrum/cerebellum
- Into the ventricles from the subependymal germinal matrix or choroid plexus

Subdural (SDH) and Epidural (EH) Hemorrhages

Subdural hemorrhage (SDH) accounts for <5-10% of intracranial hemorrhage in the newborn.

Etiology

- Subdural hemorrhage (SDH) is most often related to birth trauma and is more common in term infants.
- Risk factors for SDH include:
  - Cephalo-pelvic disproportion: large head size in proportion to the maternal pelvic outlet
  - Vaginal breech delivery
  - Shoulder dystocia
  - Very rapid or prolonged labor
  - Difficult instrumental delivery

Pathogenesis

- SDH results from laceration of the major veins and sinuses that occupy the subdural space.
- Excessive molding of the head may play a role in the genesis of subdural hemorrhage.

Clinical manifestations

- SDH should be suspected in cases with a history of trauma or a difficult delivery with the development of focal neurologic signs (e.g., unequal pupils, eye deviation, or hemiparesis).
- Symptoms may present over a period of a few hours to days, depending on severity and degree of hemorrhage.
- The newborn often presents with non-specific signs as irritability, lethargy, and poor Moro reflex.
- With increased intracranial pressure, there may be a bulging anterior fontanelle and/or widely split sutures.
- Systemic signs as hypovolemia and anemia may be present with massive hemorrhage.
- Posterior fossa hemorrhage (infratentorial SDH) may manifest with opisthotonus, apnea, bradycardia, altered mental state, and seizures.

Diagnosis

- History and clinical examination

- CT scan or MRI

N.B.: - Ultrasound is inadequate for demonstrating SDH.
- If a large SDH is suspected, lumbar puncture is contraindicated until after CT scan (risk of herniation).

Management

- Most infants do not require surgical intervention and are managed with supportive care. However, if SDH is associated with displacement of the midline, the patient should be referred for a neurosurgical opinion for evacuation by subdural tap or craniotomy, especially if there is clinical deterioration with signs of transtentorial herniation.
- Massive subdural hemorrhage located in the posterior fossa may require surgical evacuation.
- Monitor closely for detection of signs of deterioration in neurologic state.
- Monitoring the head circumference is important at follow-up visits as hydrocephalus or less frequently**,** chronic subdural effusion may occur.

Prognosis

- The outcome for nonsurgical SDH is usually good provided there is no other significant neurologic injury.
- The prognosis for infants with major lacerations of the tentorium or falx is poor.
- Concomitant hypoxic-ischemic cerebral injury is the critical factor in determining outcome.

N.B.: Epidural hemorrhage is reported in only few cases. EH appears to be correlated with trauma.

Subarachnoid Hemorrhage (SAH)

Primary subarachnoid hemorrhage refers to hemorrhage within the subarachnoid space that is not secondary to extension of subdural hemorrhage, IVH, or cerebellar hemorrhage.

Etiology

- Subarachnoid hemorrhage in the newborn is usually self-limiting and of venous origin, originating from small vessels in the leptomeningeal plexus or in bridging veins within the subarachnoid space.
- Trauma or hypoxic events may be important antecedents of major degrees of primary subarachnoid hemorrhage, although the pathogenesis is usually uncertain.

Clinical manifestations

- The majority of cases have minimal or no clinical signs.
- Less frequently, seizures may occur on the second day of life, and the infant is usually well between seizures.
- Rarely, when associated with massive subarachnoid hemorrhage, there is rapid neurologic deterioration. The infant usually has also sustained severe hypoxic-ischemic

cerebral injury, with or without trauma, or has a major vascular abnormality, (e.g., arteriovenous malformation or aneurysm).

Diagnosis

The diagnosis is based on the finding of uniformly blood-stained CSF with lumbar puncture in an infant in whom other forms of intracranial hemorrhage have been excluded by CT scan or MRI.

Management

Usually symptomatic

- Seizures are treated with anticonvulsant medication.
- Rarely, with a very large SAH, blood transfusion and cardiovascular support should be provided as needed, and neurosurgical intervention may be required.

Prognosis

- In the absence of preceding severe trauma, hypoxic-ischemic, cerebral injury or ruptured vascular lesion, the outcome is favorable.
- In massive subarachnoid hemorrhage with catastrophic deterioration, death and hydrocephalus are common.

Intraparenchymal Hemorrhage (IPH)

Etiology

Intracerebral hemorrhage

It is uncommon in all newborns. It may occur rarely as a primary event related to rupture of an arteriovenous malformation or from a coagulation defect. More commonly, it occurs as a secondary event (e.g., as hemorrhage into a region of hypoxic ischemic brain injury).

Intracerebellar hemorrhage

It is more common in preterm infants. It may be a primary hemorrhage or may result from extension of IVH.

Clinical manifestations

Clinical presentation varies according to extent and site of hemorrhage. In term infants, intracerebral hemorrhage may manifest with focal neurological signs as seizures or hemiparesis.

Diagnosis

- CT scan or MRI.
- Cranial ultrasound may be used as a rapid bedside imaging study.

Management

Small hemorrhages require supportive care. However, a large hemorrhage with severe neurologic compromise should prompt neurosurgical intervention.

Prognosis

The prognosis is largely related to location and size of IPH and gestational age of the infant.

Germinal Matrix Hemorrhage (GMH)/Intraventricular Hemorrhage (IVH)

IVH is an intracranial hemorrhage that originates in the periventricular, subependymal germinal matrix with subsequent entrance of blood into the ventricular system.

Etiology

- IVH is found principally in preterm newborns; incidence is 15-20% in infants born at < 32 weeks' gestation.
- Risk factors include:
  - Ischemia/reperfusion (e.g., rapid volume expansion after hypotension, and administration of hypertonic sodium bicarbonate)
  - Fluctuation in cerebral blood flow (e.g., breathing out of synchrony with the mechanical ventilator, large PDA)
  - Increase in cerebral blood flow (e.g., hypertension, anemia, hypercarbia and seizures)
  - Increase in cerebral venous pressure (e.g., pneumothorax, high CPAP or PEEP, and aggressive tracheal suctioning)
  - Platelet dysfunction and coagulopathy
- IVH occurs in a small percentage of term newborns, often in association with hypoxic-ischemic or traumatic insults.

Pathogenesis

- The germinal matrix (GM), a weakly supported and highly vascularized area, is located between the caudate nucleus and the thalamus. This periventricular area is the site of origin for embryonal neurons and fetal glial cells, which migrate outwardly to the cortex. The blood vessels in these areas are irregular, with large luminal areas, and are prone to rupture. GM begins to involute after 34 weeks' postconceptional age.
- In preterm infants, IVH results from the fragile involuting vessels of the subependymal germinal matrix. In term infants, primary IVH typically originates in the choroid plexus or in association with venous thrombosis and thalamic infarction. It may also occur in the small remnants of the subependymal germinal matrix.

Clinical manifestations

- Preterm infants:
  - IVH is usually silent and recognized only when a routine cranial ultrasound is performed (25-50% of cases have no obvious clinical signs).
  - Some infants present with gradual clinical deterioration with decreased levels of consciousness and spontaneous movements, hypotonia or abnormal extremity or eye movements.
  - Less often, the infant presents with catastrophic deterioration, noted by a sudden deterioration in the infant's clinical state, with an increase in oxygen or ventilatory requirement, a fall in blood pressure or acidosis, and severe neurologic signs such as coma, severe hypotonia, decerebrate posturing and apnea. More often, however, a drop in hematocrit is seen without a clear change in the infant's condition.

- Term infant: typically presents with signs as seizures, apnea, irritability or lethargy, vomiting or a full fontanelle. Catastrophic presentation is rare, unless there is another intracranial hemorrhage such as large SDH or IPH.

Complications

There are 2 major complications of GMH/IVH**:**

- Periventricular hemorrhagic infarction (PVHI): risk factors for its development are low birth GA, low Apgar score, early life acidosis, PDA and pneumothorax.
- Post-hemorrhagic ventricular dilatation (PVD): it may occur after days or weeks. Clinically, it may be asymptomatic or may present with increasing head growth, bulging fontanelle, disturbed consciousness, worsening respiratory status.

Diagnosis

- Cranial ultrasound is the procedure of choice for screening and diagnosis. Cranial ultrasound must be done in all preterm infants <32 weeks' GA [on /or around days 3, 7, 30, 60 (or just before discharge)] and in those >32 weeks' GA with risk factors (e.g., perinatal asphyxia or pneumothorax) or who present with abnormal neurologic signs.
- CT scan and MRI can be done, but are more expensive and require transport from the unit.
- Grading is important for management and prognosis **(Figure 31-1)**.
  - By cranial ultrasound:
    - Grade I: GMH with no or minimal IVH (<10% of ventricular volume)
    - Grade II: IVH occupying 10-50 % of ventricular volume
    - Grade III: IVH occupying >50% of ventricular volume with dilated ventricles.
    - Separate notation: periventricular echodensity (location and extent).
  - By CT scan:
    - Grade I: Isolated GMH
    - Grade II: IVH without ventricular dilatation.
    - Grade III: IVH with ventricular dilatation
    - Grade IV: IVH with parenchymal hemorrhage

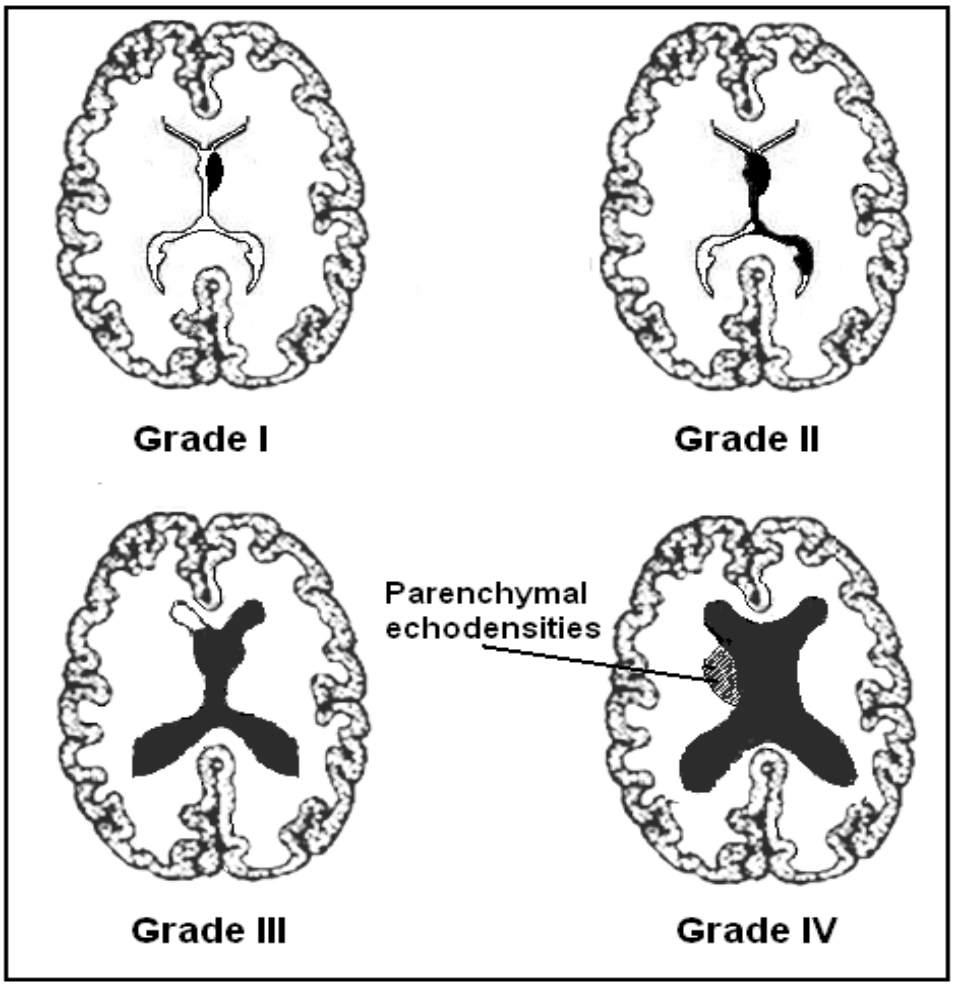


Figure (31-1): Grades of intraventricular hemorrhage

Management

- Prevention is the primary goal:
  - Antenatal glucocorticoids reduce the risk.
  - Infusion of colloids and hyperosmolar solutions should be given slowly.
  - Avoid hypotension and avoid fluctuations in arterial blood pressure.
- Supportive care:
  - Maintain normal blood pressure and circulating volume.
  - Maintain normal acid base balance and electrolyte homeostasis.
  - Transfuse with packed RBC's in large IVH to restore blood volume.
  - Correct thrombocytopenia and coagulation disorders.
  - Treat seizures; if present.
- Management of post-hemorrhagic ventricular dilatation (PVD):
  - Take serial cranial ultrasonography for careful monitoring of ventricle size.
  - Perform serial lumbar punctures.
  - Initiate surgical interventions to divert CSF flow.

- Rarely, give medications to reduce CSF production (acetazolamide and furosemide).

Prognosis

Markers for fair or good prognosis:

- A less severe grade of IVH
- A normal cranial sonography at discharge from the NICU
- Absence of ventricular dilation
- Absence of periventricular white matter injury
- Shorter neonatal hospitalization.

Chapter 32

Birth Injuries

Birth Injuries

Birth injury is an impairment of the infant's body function or structure due to adverse influences that occurred at birth. Injury may occur antenatally, intrapartum**,** or during resuscitation**.** The injury may be avoidable or unavoidable and occur despite skilled and competent obstetric care.

Risk Factors

- Primiparity
- Cephalopelvic disproportion
- Dystocia
- Prolonged or unusually rapid labor
- Oligohydramnios
- Abnormal presentation of the fetus
- Very low birth weight or extreme prematurity
- Macrosomia
- Fetal anomalies
- Use of forceps or vacuum extraction

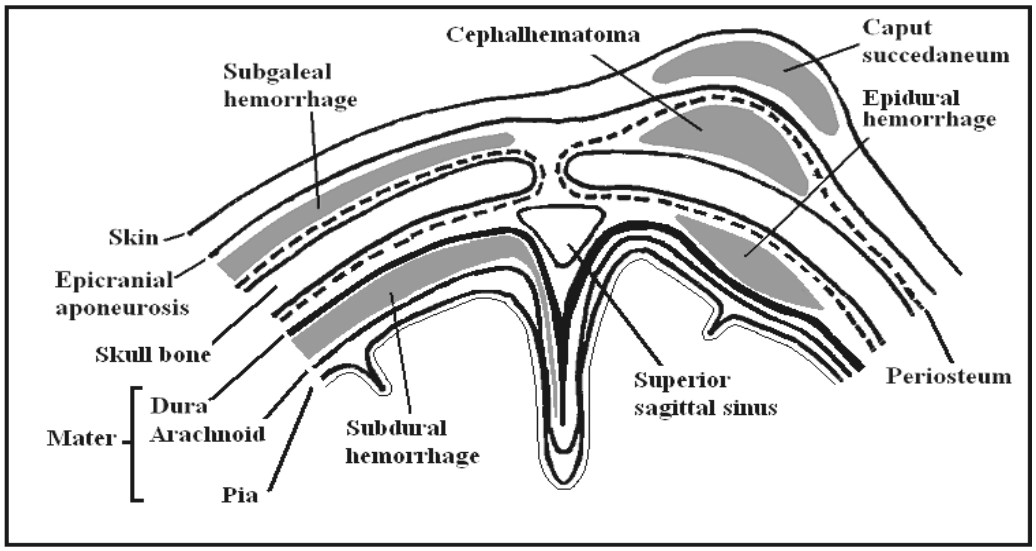


Figure (32-1): Sites of extracranial (and extradural) hemorrhages in the newborn infant

Injuries to the Head

Caput succedaneum

A soft swelling is usually a few millimeters thick and may be associated with overlying petechiae, purpura, or ecchymoses. It has poorly defined margins and may extend across the midline of the skull and across suture lines (external to periosteum). Its size is maximum just after birth.

Management

Often treatment is not required and the condition usually resolves spontaneously within several days.

Cephalhematoma

Cephalhematoma is a subperiosteal collection of blood overlying a cranial bone. It is caused during labor by rupture of blood vessels that traverse from skull to periosteum.

The bleeding is sharply limited by periosteal attachments to the suture lines, and hence there is no extension across suture lines. The bleeding usually occurs over one or both parietal bones. Less often it involves the occipital bones and, very rarely, the frontal bones.

- The overlying scalp is not discolored.
- The swelling may not be apparent for few hours after birth.
- The cephalhematoma may feel fluctuant and a few days later, it is often bordered by a slightly elevated ridge of organizing tissue that gives the false sensation of a central bony depression.
- It may be associated with skull fractures - usually linear - in about 10% of cases.
- It usually resolves within 6-12 weeks, occasionally with a residual calcification.

Management

- Treatment is not needed for an uncomplicated cephalhematoma**.**
- Incision or aspiration is **contraindicated** due to risk of infection.
- A blood transfusion is required with massive cephalhematoma resulting in marked blood loss.
- Significant hyperbilirubinemia may result, necessitating phototherapy or even an exchange transfusion depending on the level of bilirubin.
- Associated linear fractures do not require specific therapy, but follow-up radiographs at 4-6 weeks should be obtained. Depressed fractures require immediate neurosurgical consultation.

Subgaleal hemorrhage (SGH)

Subgaleal hemorrhage (SGH) is a collection of blood in the soft tissue space between the galea aponeurotica and the periosteum of the skull.

The most common predisposing factor is difficult instrumental delivery, particularly midforceps delivery and vacuum extraction.

Clinical manifestations

- Early manifestations may be limited to pallor, hypotonia, and diffuse swelling of the scalp. The development of a fluctuating mass straddling cranial sutures, fontanelles, or both is highly suggestive of the diagnosis. The hemorrhage can spread across the entire calvarium.
- The hematoma may grow slowly or increase rapidly and result in hypovolemic shock (up to 100 ml of blood may accumulate in the subgalial space).
- Ecchymotic discoloration of the scalp is a later finding (as the blood accumulates beneath the aponeurotic layer). This often is associated with pitting edema and progressive posterior spread toward the neck and lateral spread around the ears, frequently displacing the ears anteriorly. Periorbital swelling and ecchymosis are also common.

- The clinician should be aware of occasional "silent presentation," in which a fluctuant mass is not apparent initially despite serial clinical examinations.

N.B.: SGH should be considered in infants who show signs of hypoperfusion and falling hematocrit after attempted or successful vacuum delivery, even in the absence of a detectable fluctuant mass.

Management

- Close observation is essential for detection of signs of hypovolemia and progression.
- Prompt restoration of blood volume with fresh frozen plasma or blood is essential.
- Phototherapy should be provided, if hyperbilirubinemia develops.
- Investigation for coagulopathy should be considered, in case there is no evidence of trauma or instrumental delivery.
- In the presence of continued deterioration, surgical drainage may be considered.

Intracranial hemorrhage (Refer to Chapter 31)

Injuries to the Neck and Shoulder

Fractured clavicle

This is the most frequent fracture during labor and delivery. Most clavicular fractures are of the greenstick type, but occasionally the fracture is complete.

The major causes are difficult delivery of the shoulders in vertex presentations and extended arms in breech deliveries. Vigorous, forceful manipulation of the arm and shoulder usually has occurred.

Clinical manifestations

- Movement of the ipsilateral arm is decreased.
- Pain on passive movement is observed.
- Tenderness, crepitus is present over the clavicle
- Absent Moro reflex presents on the involved side
- About one third of the cases are not diagnosed before discharge from the hospital and present with a palpable mass (callus) at 7-14 days of life.
- An x-ray confirms the diagnosis.

Management

Immobilize the affected arm and shoulder for 7-10 days.

Brachial palsy

- Brachial palsy is a paralysis involving the muscles of the upper extremity that follows mechanical trauma (excessive traction of the head, neck, and arm during birth as in cases of shoulder dystocia and breech presentation) to the spinal roots of the 5^{th} cervical through the 1^{st} thoracic nerves (the brachial plexus) during birth.

- In most patients the nerve sheath is torn and the nerve fibers are compressed by the resultant hemorrhage and edema.
- Less often the nerves are completely ruptured and the ends severed, or the roots are avulsed from the spinal cord with injury to the spinal gray matter.

Erb's paralysis

Clinical manifestations

- The affected infant is frequently large and asphyxiated. The affected arm is held in adduction, internal rotation, with extension at the elbow, and pronation of the forearm and flexion of the wrist.
- Moro, biceps, and radial reflexes are absent on the affected side. The grasp reflex is intact.
- Any signs of respiratory distress may indicate an accompanying ipsilateral phrenic nerve root injury.

Management

- Maintain a partial immobilization of the affected extremity for 1-2 weeks in a position opposite to that held by the infant.
- Start gentle massage and passive exercises after 1-2 weeks, and continue for up to 3 months to prevent contractures.
- If there is no improvement, refer the infant to a neurosurgeon for possible intervention.

Klumpke's paralysis

- Involves the intrinsic muscles of the hand and the long flexors of the wrist and fingers. The hand is paralyzed, and voluntary movements of the wrist cannot be made. The grasp reflex is absent; the deep tendon reflexes are intact.
- Frequently, dependent edema and cyanosis of the hand and trophic changes in the fingernails develop. After some time there may be flattening and atrophy of the intrinsic hand muscles.
- Usually an ipsilateral Horner's syndrome (ptosis, miosis, and enophthalmos) also is present because of injury involving the cervical sympathetic fibers of the first thoracic root.

Total brachial plexus injury

- The entire arm is paralyzed: it is usually completely motionless, flaccid, and powerless, hanging limply to the side. All reflexes are absent. The sensory deficit may extend almost to the shoulder.

Prognosis

The prognosis for full recovery varies with the extent of injury. If the nerve roots are intact and not avulsed, the prognosis for full recovery is excellent (>90%).

Physiotherapy and passive range of movements should be started at 7-10 days. Notable clinical improvement in the first 2 weeks after birth indicates that normal or near-normal function will return.

Most infants recover fully by 3 months of age. If there is no notable improvement by 2 weeks, electromyography (EMG) and nerve conduction velocity should be performed.

Phrenic nerve paralysis (C3-4-5)

Phrenic nerve paralysis results in diaphragmatic paralysis and rarely occurs as an isolated injury in the neonate. Most injuries are unilateral and are associated with ipsilateral upper brachial plexus palsy.

Etiology

The most common cause is a difficult breech delivery. Lateral hyperextension of the neck results in overstretching or avulsion of the third, fourth, and fifth cervical roots, which supply the phrenic nerve.

Clinical manifestations

The first sign may be recurrent episodes of cyanosis, usually accompanied by irregular and labored respirations.

- The breathing is almost completely thoracic, so that is no bulging of the abdomen with inspiration on the affected side.
- There are diminished breath sounds over the affected side.
- In a severe injury, tachypnea, weak cry, and apneic spells may occur.
- Radiologic evidence of elevated corresponding copula of the diaphragm is present.
- The diagnosis is established by ultrasonography or fluoroscopy of the chest, which reveals the elevated hemidiaphragm with paradoxic movement of the affected side with breathing.

Treatment

Most infants require only nonspecific medical treatment.

- The infant should be positioned on the involved side, and oxygen should be administered for cyanosis or hypoxemia.
- Intravenous fluids may be necessary for the first few days. If the infant begins to show improvement, progressive oral or gavage feedings may be started.
- Antibiotics are indicated if pneumonia occurs.
- Infants with more severe respiratory distress, particularly those with bilateral phrenic nerve palsy, may require assisted ventilation shortly after delivery.
- The absence of definite improvement after 1 month is considered evidence of disruption of the phrenic nerve, thereby minimizing chances of complete spontaneous recovery. These infants should be considered candidates for plication of the diaphragm early in the second month of life.

Prognosis

- Many infants recover spontaneously.
- If avulsion of the cervical nerves has occurred, spontaneous recovery is not possible, and in the absence of surgery the infant is susceptible to pneumonia in the atelectatic lung.

Sternocleidomastoid muscle (SCM) injury (muscular or congenital torticollis)

A well circumscribed, immobile, palpable mass, in the mid-portion of the SCM that may be present at birth (more often it is noted at 1-4 weeks of age).

Etiology

Uncertain

- The most likely cause is a muscle compartment syndrome as a result of abnormal intrauterine positioning of the head resulting from forward flexion with lateral bending and rotation resulting in ipsilateral SCM kinking on itself, which if prolonged can result in ischemic injury followed by edema, and the development of a compartment syndrome.
- It may also arise during delivery as the muscle is hyperextended and ruptured, with the development a hematoma and subsequent fibrosis.

Clinical manifestations

- A mass in the midportion of the SCM may be evident at birth, although usually it is first noted 10-14 days after birth. It is 1-2 cm in diameter, hard, immobile, fusiform, and well circumscribed; there is no inflammation or overlying discoloration. The mass enlarges during the following 2-4 weeks and then gradually regresses and usually disappears within 3-4 months in the great majority of cases.
- This results in a transient torticollis after birth. The head tilts toward the involved side, and the chin is elevated and rotated. The head cannot be moved passively into normal position.

Management

- Treatment should be instituted as early as possible. The involved muscle should be stretched to an overcorrected position by gentle, even, and persistent motion with the infant supine. The head is flexed forward and away from the affected side, and the chin is rotated toward the affected side. The mother can be instructed to repeat this maneuver several times a day.
- Conservative therapy should be continued for 6 months. If the deformity has not been fully corrected, surgery should be considered.

Prognosis

Most infants treated conservatively show complete recovery within 2-3 months.

Intra-Abdominal Injuries

- Although birth trauma involving intra-abdominal organs is uncommon, it must be considered by the physician because deterioration can be fulminant in an undetected lesion and therapy can be very effective when a lesion is diagnosed early.
- Intra-abdominal injuries can involve rupture or subcapsular hemorrhage in the liver, spleen or adrenal gland.
  - Rupture of the liver
    - The liver is the most frequently injured abdominal organ during the birth process.

- It usually occurs in large infants, infants with hepatomegaly, and infants delivered in breech position.
- Trauma to the liver more often results in subcapsular hematoma than actual laceration of the liver.

- Rupture of the spleen
  - Rupture of the spleen in the newborn occurs much less often than rupture of the liver. However, recognition of this condition is equally important because of its similar potential for fulminant shock and death if the diagnosis is delayed.
  - The condition is most common in large infants, infants delivered in breech position, and infants with erythroblastosis fetalis (enlarged and friable spleen).

Clinical manifestations

- History of a difficult delivery may be reported.
- Intra-abdominal trauma should be suspected in any newborn with shock and abdominal distention or pallor, anemia, and irritability without evidence of external blood loss.
- Subcapsular hematomas are generally not symptomatic at birth. Nonspecific signs of blood loss as pallor, poor feeding, tachypnea, tachycardia**,** and jaundice developing during the first 1-3 days after birth. Rupture of hematoma results in circulatory collapse.
- In splenic injury, a mass is sometimes palpable in the left upper quadrant and the stomach bubble may be displaced medially on an abdominal radiograph.
- In case of adrenal hemorrhage, findings suggesting adrenal insufficiency may be present including poor feeding, vomiting, diarrhea, dehydration, irritability, hypoglycemia, listlessness, and shock.

Investigations

- Abdominal ultrasound
- Adrenal function

Management

- A laparotomy may be required in cases of hepatic or splenic injury.
- Immediate management consists of prompt transfusion with packed red blood cells, as well as recognition and correction of any coagulation disorder. This should be followed by laparotomy with evacuation of the hematoma and repair of any laceration with sutures placed over a hemostatic agent.
- Adrenal insufficiency may require steroid therapy **(Refer to Chapter 38).**

Chapter 33

Common GIT Problems

Common GIT Problems

Gastroesophageal Reflux

Gastroesophageal reflux (GER) is spontaneous and effortless regurgitation of the gastric contents into the esophagus. It is the most common esophageal disorder occurring during the neonatal period.

Pathophysiology

Gastric contents normally are retained within the stomach through:

- The lower esophageal sphincter (LES), which is a zone of high pressure in the distal esophagus, that remains tonically contracted except during deglutition. Incompetent LES will result in excessive and passive reflux of gastric contents.
- The anatomy of the stomach and esophagus, and their relationship to the diaphragm and related structures. It is encountered more frequently in infants with neurological abnormalities.

Types of GER

Physiologic GER

It occurs in most premature infants, and decreases in frequency as the pressure of the LES rises over the first several months of infancy.

Pathologic GER (Gastroesophageal reflux disease, GERD)

It is frequently associated with delayed gastric emptying and esophageal motility disorders.

Etiology

GER may exist as a primary disorder as a result of LES incompetence or intermittent relaxation, or it may be a secondary manifestation of another disorder (e.g., pyloric stenosis). Finally, it may be due to drugs that lower the LES pressure (e.g., xanthines).

Clinical Manifestations

- GER is more frequent in preterm infants.
- GER typically presents with continual regurgitation and spitting up or nonbilious vomiting of small quantities of formula after feeding. Forceful vomiting may be due to pylorospasm in cases of delayed gastric emptying.
- Other manifestations, such as signs of aspiration (e.g., increased pulmonary secretions, episodes of pulmonary deterioration, apnea, airway obstruction, bradycardiac episodes), and signs of esophagitis (e.g., refusal to feed, irritability, arching of the back during feeding) may be present.
- Repeated episodes of significant vomiting may lead to inadequate caloric intake and failure to thrive.

Diagnosis

- In mild cases: careful clinical assessment may be sufficient for diagnosis and can be confirmed by assessment of response to therapy.

- In severe complex cases:
  - Upper GIT contrast series: this test primarily aims to exclude gastric outlet obstruction or proximal small intestine partial obstruction.
  - Twenty-four-hour pH monitoring: this test is much less reliable during the neonatal period due to the inconsistency of acid secretion.
  - Radio-nucleotide studies (99Tc scintiscan): may be useful for measuring gastric emptying delay, which may coexist with GER.
  - Endoscopic biopsy: this test is less useful during the neonatal period because pathologic reflux has not had sufficient time to cause esophageal mucosal injury.

Differential Diagnosis

Vomiting in neonates

- Annular pancreas and pyloric stenosis
- Cow milk protein enterocolitis and infectious enteritis
- Inborn errors of metabolisms
- Infections
- Renal diseases
- Increased intracranial pressure

Treatment

Treatment of GER is based on the severity of symptoms.

Non-pharmacological

- Positioning:
  - Prone position with head elevation (about 30°) may be used during awake periods when the infant is observed.
  - Placing the infant in an upright position for 20-30 minutes after feeding is recommended. However, the use of infant seat is discouraged as it increases intra-abdominal pressure.
- Frequent feeding with small volumes can decrease gastric distension. Continuous gastric or transpyloric feeding can also be given.
- Thickening formula or expressed breast milk with cereal, by adding 1 tablespoon of rice cereal per 2 ounce (oz) of milk, may help to reduce the frequency of reflux. For formula-fed infants, premixed "anti-reflux" formulas are available, which contain rice starch to thicken the formula.

N.B.: The AAP recommends non-prone positioning during sleep to reduce the risk of sudden infant death syndrome (SIDS).

Pharmacological

- Promotion of gastric emptying and GI motility:
  - Metoclopramide: PO 0.1-0.2 mg/kg/dose every 6 hrs 30 minutes before feeds, or IV infusion over >30 minutes.

- Erythromycin: PO 12 mg/kg/dose every 6 hrs.

- Inhibition of gastric acid secretion and relieving esophagitis:
  - H_2 receptor antagonists:
    - Cimetidine: PO or IV infusion over 15-30 minutes (2.5-5 mg/kg/dose every 6-12 hrs), although recommended limited use due to the potential of significant drug interactions.
    - Ranitidine: PO 2 mg/kg/dose every 8 hrs, or IV 0.5 mg/kg/dose every 6 hrs infused over 30 minutes, or IV infusion 0.0625 mg/kg/hr.
  - Proton pump inhibitors: omeprazole; 0.5-1.5 mg/kg/dose PO, once daily.
- Sodium alginate could be used.

N.B.: Suppression of gastric acidity may actually be harmful, as it increases gastric colonization, which could lead to increased risk of sepsis and pneumonia.

Surgical

Persistent, clinically compromising GER (recurrent aspiration pneumonia, failure to thrive, or apparent life-threatening apnea) may require fundoplication.

Gastric Aspirate (Residuals)

Definition

It is a procedure by which the stomach is aspirated with an oral or nasogastric tube. The procedure is usually performed before each feeding to determine whether the feedings are being tolerated and digested or not.

Etiology

Characteristic of the aspirate is bilious, non bilious**,** or bloody in color.

Bilious in color

Usually indicates an obstructive lesion distal to ampulla of Vater:

- Bowel obstruction
- Necrotizing enterocolitis (NEC)
- Meconium plug
- Meconium ileus
- Hirschsprung's disease
- Malrotation of the intestine
- Volvulus
- Ileus
- Factitious: passage of feeding tube into the duodenum or jejunum instead of stomach

Non bilious in color

- Problems with the feeding regimen:
  - Aspirate containing undigested formula may be seen if feeding interval is too short.
  - Aspirate containing digested formula may be seen if there is delayed gastric emptying, overfeeding, or increased osmolarity of formula by the added vitamins.
- Others:
  - NEC
  - Pyloric stenosis
  - Post-NEC stricture
  - Infections
  - Inborn errors of metabolism
  - Constipation; especially if the abdomen is full but soft and no stool has passed in 48-72 hrs
  - Congenital adrenal hyperplasia (CAH) or adrenal hypoplasia
  - Formula intolerance: if stool pH is acidic (<5.0), lactose intolerance may be present (with usually a strong family history of milk intolerance). In that situation, it is more common to see diarrhea than gastric aspirates

Bloody in color

(Refer to GIT bleeding section in this chapter)

Clinical Manifestations

Depend on:

- The volume of the aspirate: considered to be excessive, if >30% of the total formula given at the last feeding.
- The character of the aspirate: bilious, bloody, digested or undigested.
- The vital signs of the infant: abnormal vital signs may indicate a possible intra-abdominal pathologic process.
- Abdominal examination: absence of bowel sounds may indicate ileus. Also, absence of bowel sounds, distension, tenderness and erythema may indicate peritonitis.
- Frequency of stools: knowing when the last stool was passed, as constipation may lead to abdominal distension, possibly causing feeding intolerance and increased gastric aspirates.

Investigations

Laboratory studies

- CBC with differential to evaluate sepsis, hematocrit and platelet count if bleeding occurs.
- Blood culture, if sepsis is suspected.
- Serum potassium level, if ileus is present.
- Stool pH, if there is family history of milk intolerance.
- Coagulation profile and Apt test, if swallowed maternal blood is expected.

Radiological studies

- Upright plain x-ray film of the abdomen (if there is bilious aspirate, abnormality on physical examination or aspirates continue) and if the infant's general conditions are stable: look for unusual gas pattern, pneumatosis intestinalis, ileus or bowel obstruction (multiple fluid levels) **(Refer to Appendix 9)**.
- Abdominal ultrasonography and Doppler studies could be diagnostic in severe cases as pyloric stenosis, NEC, and volvulus.

Endoscopy

To be considered for ulcer evaluation.

Management

Bilious aspirate

- Surgical problem (bowel obstruction, malrotation, and volvulus): place nasogastric tube for decompression of the stomach with continuous nasogastric suction; request pediatric surgeon consultation.
- NEC: keep NPO **(Refer to NEC section in this chapter).**

- Ileus: keep NPO, decompression of the stomach through nasogastric tube placement, and treatment of the underlying causes (sepsis, NEC, hypokalemia, pneumonia, hypothyroidism).
- Factitious: an x-ray film will confirm the position of the nasogastric tube distally in the duodenum. Replace or reposition the tube in the stomach.

Non bilious aspirate

Aspirate containing undigested formula

- Use breast milk wherever available as it favors more rapid gastric emptying than formula.
- If the volume of undigested formula in the aspirate <30% of the previous feed and the physical examination and vital signs are normal, the volume can be replaced.
- Feeding interval may be increased to 3 hrs instead of 2 hrs.
- If aspirate continues, re-evaluation should be done, an abdominal x-ray film should be obtained, continuous gavage feedings may be tried, and oral feedings may be discontinued for a time to rest the gut.

Aspirate containing digested formula

- The aspirate is usually discarded, especially if it contains a large amount of mucus. If vital signs and physical examination are normal, continue feeding and stomach aspiration.
- Be sure that overfeeding is not occurring.
- If aspirate continues, infant must be reassessed; take an abdominal x-ray film, and discontinue oral feedings for a time to rest the gut.

Treat the underlying cause

Bloody aspirate

(Refer to GIT bleeding section in this chapter)

Bleeding from Upper GI Tract

Definition

Bleeding from the upper GI tract is defined as vomiting bright red blood or active bleeding as seen from nasogastric tube.

Etiology

- Idiopathic: more than 50% have no clear diagnosis, usually resolving within several days
- Swallowing of maternal blood: about 10% of cases, typically occurring during cesarean section deliveries
- Liver diseases
- Swallowed blood from nasal bleeding on oropharyngeal trauma, such as repeated intubation trials
- Stress ulcer
- Nasogastric trauma
- Necrotizing enterocolitis
- Coagulopathy (e.g., hemorrhagic diseases of newborn "HDN", DIC, hemophilia A and B).
- Drug induced bleeding: such as, tolazoline, indomethacin, corticosteroids, dexamethasone (either during antenatal or postnatal periods), and theophylline "a rare cause"
- Gastric volvulus, Hirschsprung's disease, and gastric duplication " rare causes"
- Pyloric stenosis: non-bilious projectile vomiting (occasionally bloody) at 3rd to 4th week of life
- Severe fetal asphyxia

Clinical Manifestations

- They may vary from a clinically stable newborn with normal vital signs to a newborn with severe signs of shock, infection, and fetal asphyxia.
- Vomiting of bright red blood or the presence of bright red blood in the NG tube during the first day of life in a clinically stable infant is frequently secondary to swallowing of maternal blood during delivery.
- Bleeding from other sites suggests DIC or another coagulopathy.
- Abdominal distension, erythema, and/or edema of the abdominal wall suggest volvulus or NEC.
- Jaundice, easy bruising, change in color of stools may signal liver disease.
- Examine the nose and oral cavity for the presence of blood.

Investigations

Laboratory studies

- Apt test:
  - It should be performed if swallowing of maternal blood is the possible cause. It is used to differentiate between hemoglobin A of the maternal blood and hemoglobin F of the fetus.
  - Blood is placed in a test tube; sterile water is added to hemolyze the RBCs yielding free hemoglobin. This solution then is mixed with 1% NaOH.
    - If the solution turns to yellow brown, the blood is maternal.
    - If it remains red, the newborn is the source of bleeding.
- Hematocrit should be checked as soon as possible for a base line value and checked serially to assess the extent of blood loss and the need for a transfusion.

N.B.: With an acute episode of bleeding, the hematocrit may not reflect the blood loss for several hours.

- Check platelet count estimation.
- Conduct coagulation studies (PT, PTT, and fibrinogen) to rule out DIC and other coagulopathies.

Radiologic studies

- Take abdominal x-ray film to assess the bowel gas pattern and to rule out NEC.
- Conduct abdominal ultrasound if pyloric stenosis is suspected.

Endoscopy

- To be considered for ulcer evaluation.

Management

General measures

- If acute bleeding is suspected and there is hemodynamic instability, access with 2 large bore IV catheters (23 gauge) must be obtained.
- To stop bleeding:
  - Give gastric lavage with ½ normal saline or normal saline (avoid cold solutions for the risk of hypothermia).
  - Proceed with epinephrine lavage (1:10,000 solution), 0.1 ml diluted in 10 ml of sterile water, if tepid water lavage failed.
  - Give crystalloid replacement, if blood pressure is dropping (usually normal saline).
  - Transfuse with blood replacement (depending on hematocrit).

Specific measures

- Idiopathic cases: bleeding usually subsides and no other treatment is necessary.
- Swallowing of maternal blood: no specific treatment is indicated.

- Stress ulcer: give ranitidine or cimetidine.
- Nasogastric trauma: use the smallest nasogastric tube possible with gentle insertion.
- Necrotizing enterocolitis: **Refer to NEC section in this chapter.**
- Coagulopathy:
  - HDN: vitamin K_1 IV or SC (IM injection can result in severe hematoma). Consider fresh frozen plasma administration **(Refer to Chapter 34)**.
  - DIC: treat the underlying cause; support of blood pressure with multiple transfusions of colloid and platelets may be needed.
  - Congenital coagulopathies: request pediatric hematologist consultation.
  - Drug induced bleeding: stop the causative drug.
- Gastric volvulus and gastric duplication: request urgent surgical intervention.
- Pyloric stenosis: initiate hydration and surgical pyloromyotomy.

Necrotizing Enterocolitis (NEC)

Definition

Necrotizing enterocolitis is an acute intestinal necrosis syndrome which occurs as an end result of a serious intestinal injury after a combination of vascular, mucosal, and metabolic insults to a relatively immature gut.

Incidence

- It is the most common serious surgical disorder among infants in NICU.
- Although the incidence of NEC varies between 1-2/1000 live births, NEC represents 1-5% of all NICU admissions.
- NEC incidence is inversely proportional to birth weight. 70 to 90% of babies with NEC are preterm infants (predominantly VLBW infants), whereas 10-25% are full term newborns.
- The mortality rates vary from 10-50%.

Etiology

The etiology of NEC is unknown; however its pathogenesis is probably complex and multifactorial. Immaturity of the GIT is the greatest risk factor.

Pathophysiology

- The most acceptable theory is an initial ischemic or toxic mucosal damage resulting in loss of mucosal integrity. Subsequently, with enteral feeding there is a suitable substrate for gas producing bacteria to proliferate and start invading the damaged intestinal mucosa. The sequence of events may progress to transmural necrosis or gangrene of the bowel and finally perforation and peritonitis.
- NEC has been observed to occur in epidemics in NICUs, supporting the role of microbial agents in pathogenesis.
- The most commonly affected areas of bowel are where the microcirculation is the poorest, the terminal ileum and cecum.
- Endotoxin and cytokines release by colonizing bacteria and bacterial fermentation with gaseous distension may play a role. Evidence supports a critical role for platelet activating factor (PAF).

Risk factors

Prematurity

It is the single greatest risk factor because of immaturity of circulatory and immune systems. The mean gestational age of infants with NEC is 30-32 weeks.

Asphyxia and acute cardiopulmonary diseases (including PDA)

Asphyxia and acute cardiopulmonary disease may occur due to redistribution of cardiac output away from mesenteric circulation leading to episodes of intestinal ischemia.

Enteral feeding

The explanation of the risk related to enteral feeding includes:

- Enteral feeding provides necessary substrate for proliferation of enteric pathogens.
- Hyperosmolar formula or medications cause altered mucosal permeability and direct mucosal damage.
- Formula feeding lacks immunoprotective factors available in breast milk. Preterm formula-fed infants are 6-10 times more likely to develop NEC than breastfed infants.
- Rapid advancement in enteral feedings causes changes in enteric blood flow and oxygen requirements.

Polycythemia and hyperviscosity syndromes

Probably because of diminished perfusion and intestinal ischemia

Exchange transfusion

Mainly due to intestinal ischemia, due to wide variation of venous or arterial perfusion pressure

Enteric pathogenic microorganisms

Including *E.coli*, *Klebsiella*, *Enterobacter*, *Pseudomonas,* and *Salmonella* have been implicated

Others

Maternal cocaine usage and umbilical artery catheterization

Clinical Manifestations

- Early diagnosis of NEC is the most important factor in determining outcome. This is accomplished by careful clinical observation for nonspecific signs in infants who are at risk to develop NEC.
- The age of onset is inversely proportional to birth weight and gestational age (smaller babies present later); smaller and more immature infants (<28 weeks' gestation) tend to have NEC at an older age than larger and more mature (>31 weeks' gestation) infants. For VLBW infants, the onset is usually between 14-20 days following initial enteral feeding. For full term infants, the onset is usually within the first week.
- The clinical features of NEC can be divided into systemic and abdominal signs. Most infants have a combination of findings.

Systemic signs

- Respiratory distress
- Apnea and/or bradycardia
- Lethargy
- Temperature instability
- Irritability
- Poor feeding/glucose instability
- Hypotension

- Decrease peripheral perfusion/shock
- Acidosis (metabolic/respiratory)
- Oliguria
- Bleeding diathesis/DIC

Abdominal (enteric) signs

- Delayed gastric emptying (feeding residual)
- Abdominal distention (usually one of the earliest and most consistent clinical signs)
- Abdominal tenderness
- Vomiting (bilious or hematemesis or both)
- Ileus (decreased or absent bowel sounds)
- Abdominal wall erythema or induration
- Persistent localized abdominal mass
- Ascites
- Occult/gross blood in stool

Investigations

Laboratory studies

- CBC with differential: WBC frequently normal but more frequently elevated with shift to the left and thrombocytopenia; a sign of deterioration with the presence of neutropenia.
- Blood culture: for aerobes or anaerobes and fungi.
- Stool analysis**:** for blood and carbohydrate (positive stool Clinitest).
- Arterial blood gas measurements: metabolic or combined acidosis expected.
- Serum BUN, creatinine and electrolytes.
- Serial C-reactive protein.

N.B.: Thrombocytopenia, persistent metabolic acidosis, and severe refractory hyponatremia are the most common triad of signs of advanced cases.

Radiologic studies

- Abdominal x-ray studies (both anteroposterior and left lateral decubitus views) are done every 6-8 hrs during the first 2-3 days.
- Films may reveal **(Refer to Appendix 9)**:
  - Bowel wall edema and a fixed-position loop on serial studies
  - Pneumatosis intestinalis; the radiologic hallmark used to confirm diagnosis
  - Portal or hepatic venous air

- Pneumoperitoneum: air under diaphragm (small amounts of free gas may give rise to lucency below the diaphragm), and football sign (on the supine view, larger amounts of gas may give rise to this sign, where the gas outlines the whole of the peritoneal cavity).

Staging Criteria of NEC

Allow for uniformity of diagnosis and treatment based on severity of illness

Table (33-1): Modified Bell Staging Criteria for diagnosis according to severity of illness

Stage	Systemic Signs	Intestinal Signs	Radiological Signs
IA Suspected NEC	Nonspecific (apnea, bradycardia, lethargy and temperature instability)	Elevated pre-gavage residuals, Mild abdominal distension, Emesis, and Heme-positive stools	Normal or nonspecific (intestinal dilatation, mild ileus)
IB Suspected NEC	Same as stage IA	Bright red blood from rectum	Same as stage IA
IIA Definite NEC (Mildly ill)	Same as stage IA	Same as stage IA + absent bowel sounds, +/- abdominal tenderness	Intestinal dilatation, Ileus, and Pneumatosis intestinalis
IIB Definite NEC (Moderately ill)	Same as stage IIA + Mild acidosis, and thrombocytopenia	Same as stage IIA + absent bowel sounds, + definite abdominal tenderness +/- abdominal cellulitis or right lower quadrant mass	Same as stage IIA + Portal venous gas +/- Ascites
IIIA Advanced NEC (Severely ill, bowel intact)	Same as stage IIB + Respiratory and metabolic acidosis, severe apnea, hypotension, decreased urine output, neutropenia and DIC	Same as stage IIB + Signs of generalized peritonitis, marked tenderness and distention of the abdomen, discoloration and induration of abdominal wall,	Same as stage IIB + Definite ascites
IIIB Advanced NEC (Severely ill, bowel perforated)	Same as stage IIIA	Same as stage IIIA	Same as stage IIIA + Pneumoperitoneum

(Walsh and Kleigman, 1986)

Management

Basic NEC protocol

General rules

Management should be started promptly when signs suggestive of NEC are present, based on the severity of the condition.

- Stop enteral feedings immediately. Support IV fluids and TPN to maintain basal nutritional needs (90-110 kcal/kg/day).
- Manage gastric drainage: appropriate-sized nasogastric tube should be placed for either free drainage or intermittent suction to keep bowel decompressed.
- Monitor closely:
  - Vital signs and abdominal circumference
  - Fluid intake and output. Maintain urine output of 1-3 ml/kg/hr
  - GIT bleeding.
- Obtain bacterial cultures including cultures for anaerobic organisms from the stool, blood, nasogastric aspirate, and cerebrospinal fluid. Lumbar puncture is optional depending on the degree of illness and suspicion of meningitis.
- Antibiotics: **(Refer to Chapter 45)**
  - Start ampicillin IV (100 mg/kg/day every 8-12 hrs) and gentamicin IV (4-5 mg/kg/dose every 24-48 hrs) or cefotaxime IV (100-150 mg/kg/day every 8-12 hrs).
  - Add metronidazole (15-30 mg/kg/day every12 hrs) for anaerobic coverage.
  - Therapy can be adjusted based on culture results.
  - Treatment is maintained for 7-14 days depending on the severity at the initial presentation.
  - If no organism is found and the diagnosis of NEC is questionable, antibiotics may be stopped after three days.
  - There is no evidence suggesting that enteral antibiotics play a role in the treatment of NEC, except for clostridium species, where oral vancomycin is recommended.
  - If staph epidermidis is suspected, a combination of vancomycin and gentamicin may be chosen instead of ampicillin and gentamicin.

Evaluate frequently (every 6-8 hrs initially)

- Physical examination including abdominal girth
- Abdominal x-ray studies with lateral decubitus
- Serum electrolytes
- Arterial blood gases
- Complete blood count

Consider other interventions

- Clotting studies if bleeding develops.

- Supplemental oxygen and mechanical ventilation, as required (in cases of persistent respiratory and/or metabolic acidosis).
- Cardiovascular support with volume expansion (10 ml/kg - normal saline or fresh frozen plasma). Impending circulatory collapse will often be reflected by poor perfusion and oxygenation, although arterial blood pressure may be maintained. In such cases repeated boluses administration to maintain urine output is mandatory.
- Low dose dopamine (3-5 μg/kg/minute) to optimize the effect on splanchnic and renal blood flow.
- Removal of the umbilical catheter and placement of peripheral line.
- Paracentesis, if deterioration or abdominal erythema develops.
- Metabolic acidosis will respond to volume expansion, treatment with sodium bicarbonate (2 mEq/kg).
- Severe thrombocytopenia is corrected by platelet transfusions.
- Packed RBCs to maintain hematocrit above 35%.
- Fresh-frozen plasma to treat DIC.

Surgical treatment

Indications for surgery:

- Highly specific indications:
  - Pneumoperitoneum
  - Positive paracentesis
  - Erythema on the abdominal wall
  - Abdominal mass
  - Portal venous gas
- Nonspecific supportive findings
  - Abdominal tenderness
  - Persistent thrombocytopenia
  - Progressive neutropenia
  - Clinical deterioration
  - Severe GI bleeding
- The main stay of surgical treatment is resection with enterostomy although resection with primary anastomosis is useful in selected cases.
- If there is extensive involvement, a “second look” operation may be done within 24-48 hours.
- Peritoneal drainage under local anesthesia: recommended under carefully selected instances with severe NEC to allow stabilization and later surgical intervention. Progressive sepsis after local drainage mandates laparotomy.

Guidelines for refeeding

- Feedings may be started when:
  - Antibiotic therapy is completed.
  - Abdominal x-ray is normal.
  - Clinical signs and symptoms of NEC are absent.
- Generally NG decompression is stopped after 2 weeks of treatment. Feedings can be started very slowly with TPN gradually tapered off.
- Breast milk is better tolerated and preferred.
- Volume and strength should not be increased simultaneously. Advance feeds over 10-14 days.

Prognosis

- NEC is the most common cause of death in neonates undergoing surgery. The average mortality is 30-40%.
- Late complications of NEC:
  - Stricture and adhesions
  - Fistula formation
  - Recurrent NEC
  - Short-gut syndrome and malabsorption

Chapter 34

Common Neonatal Hematological Problems

Common Neonatal Hematological Problems

Bleeding

Hemostasis (arrest of bleeding after injury) involves the vascular wall, blood platelets, the coagulation system and the fibrinolytic system. A defect of any part of the hemostatic system results in bleeding. While healthy newborns have low levels of some coagulation factors, this is normally balanced by the parallel decrease in fibrinolytic activity.

Etiology

Deficient clotting factors

- Transient deficiency of vitamin K dependent factors II, VII, IX, X is characteristic of neonatal period.
- Disturbance of clotting mechanism related to DIC, shock, NEC, and renal vein thrombosis.
- Inherited abnormalities of clotting factors:
  - X-linked recessive inheritance: factor VIII deficiency (hemophilia A) and factor IX deficiency (hemophilia B) are expressed in males.
  - Autosomal inheritance in Von Willebrand disease (VWD), inheritance can be autosomal dominant or recessive; the incidence of bleeding in newborns is very low.

N.B.: Von Willebrand factor (VWF) serves as a carrier for factor VIII and functions in platelet adhesion and aggregation.

Platelet disorders

Transient disorders

Maternal drug use: interfering with vitamin K effect on synthesis of clotting factors or platelet function as phenytoin, phenobarbital, or salicylate

Qualitative disorders (thrombasthenia)

Hereditary conditions: Glanzmann thrombasthenia and Bernard-Soulier syndrome

Quantitative disorders (thrombocytopenia)

Maternal disorders causing neonatal thrombocytopenia

- Drug use (e.g., heparin, quinine, hydralazine, tolbutamide, and thiazide diuretics)
- Infections (e.g., TORCH, bacterial or viral infections)
- Maternal pre-eclampsia or HELLP syndrome (**h**emolytic anemia, **e**levated **l**iver enzymes and **l**ow **p**latelet count)
- Immune thrombocytopenia:
  - Neonatal alloimmune (isoimmune) thrombocytopenia: results from placental transfer of maternal allo-antibodies directed against paternally inherited antigens present on the fetal platelets but absent from maternal platelets (mostly anti-

HPA1a allo-antibodies). The infant appears healthy with low platelet count <20,000/μL. The mother has a normal platelet count.

- Neonatal autoimmune thrombocytopenia: can occur in newborns of mothers with immune thrombocytopenia due to ITP, lupus erythematosus, or other autoimmune disorders. Antibody is directed against an antigen on the mother's platelets shared in common with the baby's platelet. The mother usually has thrombocytopenia or history of ITP. Thrombocytopenia is usually moderate (platelet count 20,000-50,000/μL) and the baby is healthy.
- Immune thrombocytopenia can accompany some cases of hemolytic disease of the newborn (e.g., ABO incompatibility can result in both hemolysis and thrombocytopenia).

Neonatal disorders causing thrombocytopenia

- Disorders causing decreased platelet production or congenital absence of megakaryocytes include:
  - Wiskott-Aldrich Syndrome
  - Amegakaryotic thrombocytopenia
  - Thrombocytopenia with absent radii (TAR) syndrome
  - Fanconi anemia
  - Bone marrow replacement: congenital leukemia, or congenital neuroblastoma
  - Others:
    - Toxic injury to megakaryocytes due to infections (bacterial or viral) or drug induced
    - Congenital CMV and rubella (due to both underproduction and increased destruction)
    - Trisomies 13, 18, and 21
- Causes of increased platelet destruction include:
  - Increased platelet consumption occurs in many sick infants not associated with any specific pathologic state (about 20% of newborns admitted to NICU), present by 2 days of life, reaches a nadir by 4 days and usually recovers to normal by 10 days of life
  - Pathologic states associated with increased platelet destruction:
    - Direct toxic injury to platelets: sepsis (bacterial or viral)
    - TORCH infections
    - DIC
    - Neonatal cold injury
    - Birth asphyxia
    - NEC
  - Platelet destruction associated with giant hemangioma (Kasabach-Merritt syndrome)
  - Neonatal thrombosis (e.g., catheter associated, renal vein thrombosis)

- Thrombocytopenia after exchange or other transfusion; blood more than 24 hrs old has few viable platelets
- Thrombocytopenia associated with polycythemia, hyperviscosity

Vascular causes

(e.g., arteriovenous malformations, hemangiomas)

Miscellaneous problems

- Trauma (e.g., rupture of spleen, subcapsular hematoma of the liver, large cephal-hematoma, subdural hematoma)
- Liver dysfunction

Types of Bleeding Disorders

Hemorrhagic disease of the newborn (HDN)

- It occurs in 1 out of every 200-400 neonates not given vitamin K prophylaxis.
- The cause of this bleeding disorder is a deficiency of vitamin K-dependent coagulation factors II, VII, IX and X. These factors are synthesized in the liver and activated by vitamin K.
- Vitamin K is a fat soluble vitamin that is normally obtained from the diet and from intestinal flora synthesis. It can be absorbed from the GI tract in the presence of bile salts.
- The GI tract is sterile at birth, and its population with vitamin K-producing flora occurs after feedings are instituted. Because lactation requires several days to become established, infants who are exclusively breastfed or those who are not fed orally are at risk for vitamin K deficiency. Furthermore, vitamin K-dependent coagulation factors become deficient during the first days of life as the maternally derived vitamin K stores are depleted and vitamin K deficiency becomes worse.
- Broad-spectrum antibiotic therapy can be associated with vitamin K deficiency if the intestinal flora is eliminated.

Clinical manifestations

- Early disease (first day of life): occurs in the first 24 hrs of life and generally is seen in infants born to mothers taking oral anticoagulant or anticonvulsant drugs (e.g., phenytoin, or phenobarbital). These infants often have serious bleeding; including intracranial hemorrhage. The mother should be given 10 mg vitamin K_1 IM 24 hrs before delivery.
- Classic disease (day 2-7 of life): in the healthy baby, HDN may occur when the baby is not given vitamin K prophylaxis at birth. It is usually characterized by cutaneous, GI, or circumcision bleeding. General bruising may be seen around the nose or the umbilical cord.
- Late onset disease occurs in infants beyond one week of age (between 2^{nd} week and 6^{th} month) and sometimes is associated with breastfed infants who are not receiving supplementation. It is more commonly associated with chronic diseases that impair absorption of the fat-soluble vitamins or that obliterate intestinal flora, such as biliary

atresia, hepatitis, cystic fibrosis, chronic diarrhea, and antibiotic therapy. Affected infants may develop cutaneous, GI, or intracranial hemorrhages (30-60%).

Laboratory findings

- Platelet count is normal.
- Prothrombin time (PT) and activated partial thromboplastin time (APTT) are prolonged.

Management

- Prophylaxis**:**
  - Vitamin K_1 0.5-1 mg IM should be given at the time of delivery.
  - Infants receiving TPN or antibiotics for more than 2 weeks should be given 0.5-1 mg vitamin K_1 IM or slowly IV weekly.
  - Infants with chronic malabsorption or biliary disorders should be routinely given vitamin K_1.
- Treatment:
  - Give one dose vitamin K_1 (1-2 mg slow IV). Intramuscular injection should be avoided due to bleeding risk.
  - For serious bleeding:
    - Give fresh frozen plasma: 10 ml/kg IV.
    - Give fresh blood transfusion.

N.B.: Identification of early warning signs and prompt treatment will decrease the incidence of serious bleeding, particularly intracranial hemorrhage.

Disseminated intravascular coagulation (DIC)

- DIC is a pathologic process in which small blood clots develop throughout the bloodstream resulting in depletion of plasma clotting factors and platelets. DIC occurs as a result of activation and dysregulation of the hemostatic system.
- Depending on the patient's compensatory capacity to inactivate and clear the products of hemostasis and fibrinolysis and to regenerate components of the hemostatic system, the patient could experience bleeding or thrombosis or both, or might only show laboratory evidence of DIC. The prognosis is poor.

Risk factors

DIC is associated with:

- Infection: (e.g., gram negative septicemia, systemic candidiasis, and neonatal herpes viral infections)
- Acidosis
- Hypoxia
- Hypotension
- Respiratory distress syndrome (RDS)
- Massive hemolysis

Clinical manifestations

The baby usually appears sick; he/she may show:

- Petechiae
- Gastrointestinal hemorrhage
- Oozing from venipunctures
- Infection
- Asphyxia
- Generalized bleeding from body orifices

Laboratory findings

- Decreased platelet count
- Prolonged PT and APTT
- Fragmented RBCs in blood smear
- Decreased fibrinogen
- Increased fibrinogen degradation products (FDP's) and D-dimer

Management

- Treatment of underlying cause is the most important therapeutic intervention.
- Give vitamin K_1 (1 mg slowly IV).
- Give platelets transfusion to keep platelets above 50,000/μL.
- Administer fresh frozen plasma.
- If bleeding persists, one of the following is done:
  - Exchange transfusion with fresh citrated whole blood to remove fibrin and fibrinogen split products.
  - Continue transfusion of platelets, packed red cells**,** or fresh frozen plasma, as needed.
  - Give cryoprecipitate (10 ml/kg)
  - If DIC is associated with thrombosis and not with concurrent bleeding give heparin (10-15 units/kg/hr as a continuous IV infusion). Heparinization is generally contraindicated in presence of intracranial hemorrhage.

Neonatal thrombocytopenia

Neonatal thrombocytopenia is characterized by a low platelet count in the neonate.

- Platelet count <150,000/μL in a full term infant
- Platelet count <100,000/μL in a preterm infant

Causes

(See causes of thrombocytopenia pages 389-391)

Clinical manifestations

- Generalized superficial petechiae and bruising are present.
- Mucosal bleeding and spontaneous hemorrhage may occur, if the platelet count is <20,000/μL.
- Intracranial hemorrhage may also occur with severe thrombocytopenia.

Diagnosis

(Table 34-1) shows the diagnostic approach to neonatal thrombocytopenia.

Table (34-1): Diagnostic approach to neonatal thrombocytopenia

Sick infant		Healthy infant	
Normal PT, APTT	↑ PT, APTT	Normal mother's platelet count	↓ Mother's platelets
• Infection (Without DIC) • Hypersplenism • Bone marrow infiltration • NEC	• DIC • Sepsis • Hypoxia • Acidosis • Cold stress • Severe liver disease	• Neonatal alloimmune thrombocytopenia • Neonatal drug • Hemangioma • Congenital thrombocytopenia • Maternal ITP in remission	• Maternal ITP • Maternal drugs • Familial

Management

- Treat underlying cause.
- Give a platelet transfusion, through a peripheral vein, when there is bleeding or platelet count is <20,000/μL (a single unit of platelets can raise the platelets count by 40,000-50,000/μL-100,000/μL, unless there is peripheral destruction of platelets). Dose: one unit of platelets/3 kg.
- Management of alloimmune thrombocytopenia:
  - Platelet transfusion: if the infant has bleeding or has a platelet count <20,000/μL, mother's platelets (HPA-1a-negative), which were collected 24 hrs before delivery, are transfused into the infant. Using washed maternal platelets re-suspended in plasma is better in order to avoid possible reaction that may occur as a result of the presence of HPA-1a-positive antibodies in the mother's serum. If not previously collected**,** mother's whole blood or platelets from HPA-1a-negative platelet donor can be used.
  - High-dose IV gamma globulin (IVIG), 1 g/kg per day for 2 days or 0.5 gm/kg per day for 4 days, is effective in raising the platelet count in most cases, although its effect may be delayed for 1-2 days.
  - In cases with continued low platelet counts or continued bleeding, prednisone (2 mg/kg/day) may be given.
  - Perform cranial ultrasonography after delivery to document any intracranial hemorrhage.

  - The recurrence rate in a subsequent pregnancies is high (>75%). Antenatal therapy includes intrauterine platelet transfusion, maternal IVIG and corticosteroids. These infants are usually delivered by cesarean section.
- When Kasabach-Merritt syndrome is diagnosed:
  - Manage heart failure, if present.
  - Give platelet transfusion, fresh frozen plasma (FFP), cryoprecipitate/fibrinogen concentrates and prednisone.
  - Embolization and surgery may be necessary.
  - Recently propranolol use has been reported to be remarkably successful in shrinking proliferative hemangioma.

Diagnostic Work-Up of a Bleeding Newborn

One must first determine whether the bleeding is localized or generalized. For example, subperiosteal, intraventricular, or intrapulmonary hemorrhage always has a local cause. Disseminated intravascular coagulation and hemorrhagic disease are systemic disorders.

Laboratory evaluation of bleeding in a newborn is demonstrated in **(Table 34-2)**.

Apt test

To rule out maternal blood swallowed during labor or from a bleeding breast

PT (for extrinsic pathway), APTT (for intrinsic pathway)

Both tests evaluate the common pathway (factors V, II and fibrinogen)

Table (34-2): Laboratory evaluation of bleeding in a newborn

Condition	Platelet Count	PT	APTT
Well neonate			
• Vitamin K deficiency	Normal	↑	↑
• Thrombocytopenia	↓	Normal	Normal
• Hemophilia	Normal	Normal	↑
• Localized cause	Normal	Normal	Normal
Sick neonate			
• DIC	↓	↑	↑
• Liver disease	Normal - ↓	↑	↑
• Infection	Normal - ↓	Normal	Normal - ↑

PT: prothrombin time, APTT: activated partial thromboplastin time

Peripheral blood smear

To determine the number, size and kind of platelets and the presence of fragmented RBCs

Fibrinogen assay

May be decreased in liver disease and in DIC states

D-dimer assay

Measures fibrin degradation products in patients with DIC and liver diseases

Specific factor assays and Von-Willebrand panels

Particularly for infants with positive family history

Platelet function tests

May be required in suspected cases with platelet dysfunction and VWD

Bleeding times

It is less reliable to use

Neonatal Anemia

Anemia is defined by a central venous hemoglobin level of <13 gm/dl or a capillary hemoglobin level of <14.5 gm/dl during the neonatal period (0-28 days of life) in infants of >34 weeks' GA.

Anemia is usually defined by hemoglobin or hematocrit value that is more than two standard deviations below the mean for age **(Refer to Appendix 5).**

Normal Physiology

- After birth, erythropoiesis decreases as a result of increased tissue oxygenation (caused by the onset of breathing and closure of the ductus arteriosus)**,** and an associated decrease in production of erythropoietin (lack of relative renal hypoxia present in fetal life).
- Term infants develop physiologic anemia caused by the combined effects of decreased erythropoiesis and a shortened red blood cell life span. The hemoglobin level in these infants typically reaches a nadir 11 gm/dl at approximately 8-12 weeks after birth. This is known as the physiologic anemia of infancy; it is not a functional anemia as oxygen delivery to tissues is adequate.
- Premature infants develop the anemia of prematurity (AOP), associated with the earlier onset of a more pronounced anemia that is inversely proportional to the gestational age at birth and reaching a nadir of 7-9 gm/dl at 4-8 weeks because of the following:
  - Decreased RBC survival in preterm infants in comparison with term infants
  - More rapid rate of growth
  - Frequent blood sampling for laboratory tests
  - Vitamin E deficiency is common in preterm infants

Etiology

Hemorrhagic anemia

If blood loss is recent, hematocrit (Hct) and reticulocyte count may be normal with normal bilirubin level, while the infant may be in shock. Hct will fall later because of hemodilution.

Obstetric causes

- Abruptio placenta and placenta previa
- Incision of placenta during caesarian section
- Rupture of the cord
- Fetoplacental transfusion, holding the neonate above the level of the placenta at birth

Occult blood loss

- Fetomaternal bleeding or transplacental hemorrhage: bleeding moves from fetal circulation into the maternal circulation.
- Twin-twin transfusion syndrome: occurs in monozygotic, monochorionic twin pregnancies when one twin (the donor) bleeds into the other (the recipient) due to vascular placental anomalies. After birth, this syndrome is to be considered if the

twins are monozygotic, and significant differences in size or appearance of the twins are noted **(Table 34-3)**. Hydrops fetalis may develop in either twin.

Table (34-3): Twin to twin transfusion

Donor twin	Recipient twin
SGA >20% smaller than recipient twin	LGA >20% larger than donor twin
Pale – anemic	Plethoric - polycythemic
Poor peripheral perfusion	Jaundice

SGA: small for gestational age, LGA: large for gestational age

Bleeding in the neonatal period

- Non-exteriorized bleeding
  - Intracranial bleeding
  - Massive cephalhematoma
  - Subcapsular hematoma, ruptured liver or spleen, adrenal or renal hemorrhage, fracture femur
- Exteriorized bleeding
  - Bleeding from the umbilicus due to tearing or cutting of the umbilical cord
  - Gastrointestinal bleeding: NEC and trauma by NG catheter

Iatrogenic causes

From repeated blood samples

Hemolytic anemia

Decreased Hct, increased reticulocyte count, and increased bilirubin level

Immune

Rh, ABO, minor blood group incompatibilities, or maternal disease (e.g., SLE, autoimmune hemolytic anemia)

Hereditary RBC's disorders

Spherocytosis, G6PD deficiency, and α-thalassemia

Acquired hemolytic anemia

Infection, DIC, vitamin E deficiency, and vitamin K (overdose)

Hypoplastic anemia (diminished RBC’s production)

Decreased Hct, decreased reticulocyte count, and normal bilirubin level

- Diamond-Blackfan anemia
- Fanconi anemia
- Congenital leukemia
- Infection (e.g., rubella and parvovirus)

- Suppression by maternal drugs such as chloramphenicol
- Physiologic anemia or anemia of prematurity

Clinical Manifestations

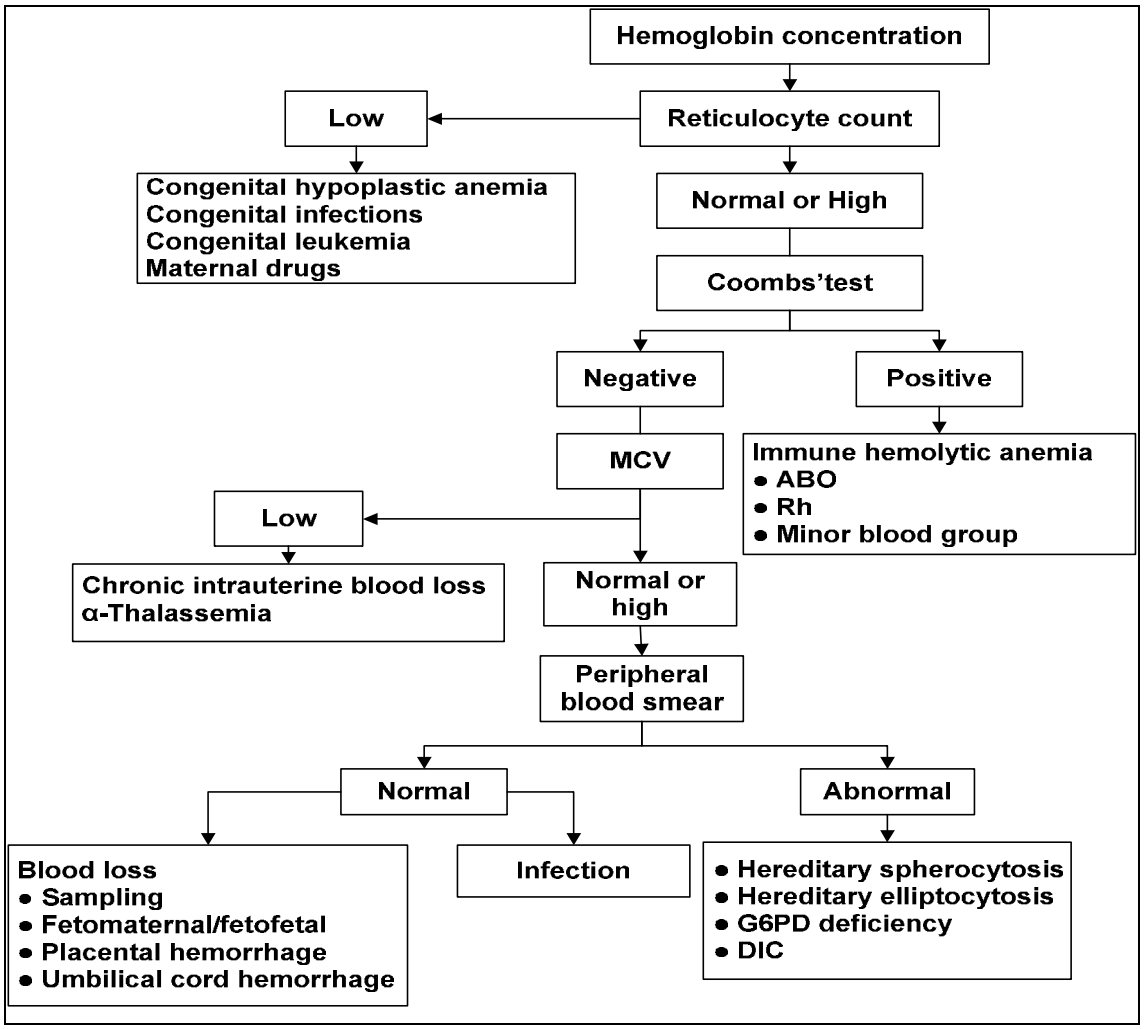
- Pallor may be the only obvious sign.
- In chronic blood loss, there may be mild symptoms such as respiratory distress or irritability.
- The physical findings in neonatal anemia include:
  - Short stature and/or dysmorphic features: Fanconi anemia, and Diamond-Blackfan anemia
  - Blueberry muffin spot and microcephaly: congenital infections
  - Jaundice: hemolytic anemia
  - Petechiae: bone marrow infiltration/failure, DIC, and sepsis
  - Congestive heart failure: chronic anemia causing decompensation
  - Giant hemangioma: Kasabach-Merritt syndrome
- With acute blood loss, symptoms of shock may be observed including low arterial blood pressure, with cyanosis and poor perfusion.

Investigations

- CBC (hemoglobin, hematocrit, and RBC's indices)
- Reticulocyte count

$$\textbf{Corrected reticulocyte count} = \frac{\textbf{Observed reticulocyte count} \times \textbf{Observed hematocrit}}{\textbf{Normal Hct for age}}$$

- Blood smear
- Direct Coomb's test
- Total and direct bilirubin
- Blood group (ABO) and type (Rh)
- Hemolytic profile (hemoglobin electrophoresis, osmotic fragility test)
- Kleihauer-Betke test (on maternal blood to look for fetal red cells as evidence of feto-maternal hemorrhage)
- TORCH screening, if suspected congenital infections
- Ultrasound of the head and abdomen
- Bone marrow examination in cases of hypoplastic anemia or tumor



MCV: Mean corpuscular volume

Figure (34-1): Diagnostic approach to anemia in a newborn infant

Management

Frequent hemoglobin, hematocrit, and bilirubin levels should be drawn to monitor neonatal anemia.

Transfusion

(Refer to Chapter 44)

Indications

- Acute blood loss
- Hct <40% with significant respiratory disease or congenital heart disease (e.g., large left-to-right shunt); fresh blood should be used
- Premature infants, if:
  - Hct <21%: asymptomatic infants but with low reticulocyte count (<2%)
  - Hct <31% and
    - Hood oxygen <36%, or
    - Mean airway pressure (MAP) <6 cmH_2O by CPAP or IMV, or

- >9 apneic and bradycardic episodes per 12 hrs or 2/24 hrs requiring bag and mask ventilation while on adequate methylxanthine therapy, or
- Heart rate >180/minute or respiratory rate >80/minute sustained for 24 hrs, or
- Weight gain of <10 gm/day for 4 days on 100 kcal/kg/day, or
- Having surgery

- Hct <36% and requiring >35% O_2 or MAP 6-8 cmH_2O by CPAP or IMV.

- Infant with ABO incompatibility with excessive hemolysis and who do not have an exchange transfusion

Blood products

Packed RBCs

- The volume of transfusion may be calculated as follows:

$$\text{Volume required (ml)} = \frac{\text{(Blood volume/kg} \times \text{Weight in kg)} \times \text{(Desired Hct} - \text{Observed Hct)}}{\text{Hct of blood to be given}}$$

- Average blood volume in a newborn = 80 ml/kg
- The Hct of packed RBCs = 60-80% (should be checked before transfusion).
- Generally, transfuse ~ 10-15 ml/kg; unless rapid replacement is required for acute blood loss or shock, infuse no faster than 2–3 ml/kg/hr

Whole blood

- 10-20 ml/kg in acute blood loss

Isovolemic exchange transfusion

- With high Hct packed RBC's may be required for severely anemic infants, to avoid circulatory overload.

N.B.: Limiting donor exposures is recommended by assigning the aliquots from a single unit to a single patient. Aging of stored units must then be considered.

Prophylaxis

Nutritional supplementation

- Term infants should be sent home on iron fortified formula if they aren't breast feeding.
- Preterm infants: iron supplementation 2-4 mg elemental/kg/day once full enteral feed is achieved. It is not advised in preterm neonates before 34 weeks' gestation as it enhances lipid peroxidation of red cell membranes due to limited free-oxygen radical scavenger mechanisms in these neonates.
- Give vitamin E 25 IU until the baby is 40 weeks' postconception or is discharged.
- Give folic acid, 1-2 mg/week for preterm infants and 50 μg/day for term infants

Recombinant human erythropoietin (rh-EPO)

- Recombinant human erythropoietin (rh-EPO) is capable of increasing neonatal erythropoiesis. It has been shown to decrease the requirement for late transfusions (past the age of 2-3 weeks).
- Treatment with rh-EPO can be initiated when infants are stable and can tolerate iron supplementation. A practical guideline for the use of rh-EPO is demonstrated in **(Table 34-4).**
- Supplemental oral iron needs to be provided at 2 mg/kg/day as soon as tolerated. The iron dose is increased to 6 mg/kg/day as soon as the infant is tolerating full enteral feeds.

Table (34-4): Guidelines for the use of erythropoietin

- Eligibility criteria:
  - Birth weight ≤1,250 gm and <31 weeks' GA with all of the following:
    - Total caloric intake ≥50 kcal/kg/day with more than 50% enteral
    - Hct <40% or 40%-50% but falling 2% per day
    - Mean airway pressure (MAP) <11 cmH_2O and FiO_2 <0.4
    - Postnatal age >6 days and GA <33 weeks
  - Any infant with birth weight 1,251-1,500 gm and phlebotomy losses >5 ml/kg/week, who meet the previous criteria
- Exclusion criteria: major anomalies, dysmorphic syndromes, hemolytic anemia, and active major infection
- Dosage: 250 units/kg/dose given subcutaneously, three times weekly
- Duration: till infant reaches 34 weeks' postconceptional age
- Monitoring of therapy:
  - Blood pressure (risk of hypertension),
  - Platelet count (risk of thrombocytosis),
  - Hct and reticulocyte count: a base line measurement should be obtained at the time of therapy and followed weekly. Adjust the dose to maintain reticulocyte count >6%
  - Discontinue if Hct reaches 45% without transfusion.

Polycythemia

Polycythemia, or increased total red blood cell mass, is defined as a venous hematocrit ≥65%.

Incidence

The incidence of polycythemia in newborns is increased in SGA and postterm neonates. Average incidence is 0.4-5%.

Pathophysiology

As the central (venous) hematocrit rises, there is increased viscosity and decreased blood flow. When the Hct increases to 60%, there is a fall in oxygen transport. As viscosity increases, there is impairment of tissue oxygenation, decreased glucose in the plasma, and a tendency to form microthrombi. If these events occur in the cerebral cortex, kidneys or adrenal glands, significant damage may occur. Hypoxia and acidosis increase viscosity and the subsequent poor perfusion increase the possibility of thrombosis.

Etiology

Placental red cell transfusion

- Delayed cord clamping
- Cord stripping
- Holding the neonate below the mother at delivery
- Maternal-fetal transfusion (theoretical)
- Twin-twin transfusion
- Forceful uterine contraction before cord clamping

Placental insufficiency and intrauterine hypoxia

- SGA
- Maternal smoking
- Maternal hypertensive disorders
- Postmaturity
- Infant born to a mother with chronic hypoxia (heart disease)
- Pregnancy at high altitudes

Other conditions

- IDM
- LGA
- Beckwith Wiedemann syndrome
- Dehydration
- Trisomy syndromes (particularly trisomy 21)
- Drugs (maternal use of propranolol)

- Congenital thyrotoxicosis
- Congenital adrenal hyperplasia

Clinical Manifestations

As the hematocrit increases, it reaches a point where the viscosity is so high that it interferes with circulation to a variety of tissues and organs.

Infants with polycythemia are either asymptomatic or symptomatic.

Symptoms

Include the following:

- Skin: delayed capillary refill and plethora
- CNS: poor feeding, lethargy, irritability, hypotonia, apnea, seizures, and, in severe cases, cerebral infarction
- Cardiorespiratory: cyanosis, tachypnea, murmurs, congestive heart failure, and cardiomegaly with prominent vascular marking on chest x-ray
- GIT: poor feeding, necrotizing enterocolitis with early feeding
- Renal: hematuria, proteinuria, and, in severe cases, renal vein thrombosis
- Hematological: thrombocytopenia, DIC, and jaundice
- Others: hypoglycemia, hypocalcemia, testicular infarcts

Laboratory Studies

A peripheral venous hematocrit level should be determined in any infant who appears plethoric, who has any predisposing factors of polycythemia, or who has symptoms of polycythemia.

- Central Hct value
- Serum glucose level
- Serum bilirubin level
- Serum calcium level
- Platelet count

Treatment

- Asymptomatic infant with a venous hematocrit between 65-70% can be managed by increasing fluid intake and repeating the Hct in 4-6 hrs.
- Most neonatologists, in the absence of symptoms, will perform an exchange transfusion when the peripheral venous hematocrit is >70%, although this is controversial.
- Symptomatic infant with a venous hematocrit >65% should be managed by performing a partial exchange transfusion. Exchange is usually done with albumin 5% or normal saline to bring the hematocrit level down to 50-60%. Saline is preferred because there is less chance of infection and there is no advantage with the use of albumin. Usually we withdraw blood from the umbilical vein and replace it with saline or albumin 5% in a peripheral vein.

- The following formula is used to calculate the volume of exchange:

$$\textbf{Volume of exchange in ml} = \frac{\textbf{(Blood volume/kg} \times \textbf{Weight in kg)} \times \textbf{(Observed Hct - Desired Hct)}}{\textbf{Observed Hct}}$$

Example:

A neonate weighing 4 kg, and having a hematocrit of 75

$$\text{The volume of exchange in ml} = \frac{4 \times 80 \times (75 - 55)}{75} \simeq 85 \text{ ml}$$

Chapter 35

Neonatal Cardiac Disorders

Neonatal Cardiac Disorders

Congenital Heart Diseases (CHD)

Congenital heart defects account for significant neonatal morbidity and mortality, affecting 0.5-0.8% of full term live-births.

Congenital heart diseases may be encountered in the neonatal care unit. The most common of these lesions is the ventricular septal defect (VSD). Many of these lesions may not be associated with any symptoms at birth, but some may be associated with severe hemodynamic compromise and may be incompatible with life unless treated immediately.

Etiology

- Congenital cardiac malformations may be a result of problems in intrauterine fetal development.
- Factors that might influence this can be classified as:
  - Environmental: viruses (e.g., congenital rubella syndrome) and some medications as anticonvulsants (e.g., phenytoin)
  - Genetic: polygenic inheritance-chromosomal (Down syndrome-Turner syndromes)

Approach to Neonates with Cardiac Disorders

Newborn infants have right ventricular dominance with thick wall and elevated pulmonary vascular resistance secondary to a thick medial layer of the pulmonary arterioles. Thick pulmonary artery smooth muscle gradually becomes thinner and by 6-8 weeks of age resembles that of adults. Premature infants in general, have less right ventricular dominance and a lower pulmonary vascular resistance than do full-term neonates.

Abnormal findings suggesting cardiac disorders

Abnormal physical findings

- Cyanosis, particularly when it does not improve with oxygen administration.
- Pulse:
  - Decreased or absent peripheral pulses in the lower extremities suggest coarctation of aorta.
  - Generally weak peripheral pulses suggest hypoplastic left heart syndrome or shock.
  - Bounding peripheral pulses suggest PDA.
- Heart murmur. However, innocent murmurs are much more frequent than pathologic murmurs.
- Irregular rhythm and abnormal heart rate suggest arrhythmia
- Hepatomegaly, may suggest heart failure.

Abnormal chest x-ray films

- Cardiomegaly
  - Congenital heart defects, such as ventricular septal defect (VSD), PDA, transposition of the great arteries (TGA), Ebstein's anomaly, and hypoplastic left heart syndrome
  - Myocarditis or cardiomyopathy
  - Pericardial effusion
  - Metabolic disturbances such as hypoglycemia, severe hypoxemia, and acidosis
  - Overhydration or overtransfusion
- Abnormal cardiac silhouette **(Refer to Appendix 9)**.
  - Boot-shaped heart (coeur en sabot) is seen in tetralogy of Fallot and tricuspid atresia
  - Egg-shaped heart with a narrow waist may be seen in TGA.
- Dextrocardia **(Refer to Appendix 9)**
  - The heart is located predominantly in the right side of the chest.
- Pulmonary vascular markings
  - Increased pulmonary vascularity
    - Cyanotic newborn infant: transposition of great arteries (TGA), persistent truncus arteriosus, or single ventricle
    - Acyanotic newborn infant: VSD, PDA
  - Decreased pulmonary vascularity
    - Pulmonary atresia, tricuspid atresia, or tetralogy of Fallot

Manifestations of Cardiac Disorders in Neonates

Neonatal cardiac disorders may be easily under-diagnosed and they need a high index of suspicion as well as thorough knowledge and experience on the physician's part to detect them. They are often confused with respiratory disorders.

The most common manifestations in neonate with common cardiac problems are:

- Heart murmurs
- Cyanosis
- Congestive heart failure
- Systemic hypoperfusion or shock
- Arrhythmia

Heart murmurs

Innocent murmurs

- More than 50% of full-term infants have innocent systolic murmurs at some time during the first week of life.
- Pulmonary flow murmur of the newborn is the most common innocent heart murmur in this age group. This murmur is a grade 1-2/6 systolic ejection murmur and characteristically radiates well to the sides and the back of the chest.
- Other innocent murmurs in the newborn period are transient systolic murmur of patent ductus arteriosus (PDA), transient systolic murmur of tricuspid regurgitation (TR), and vibratory innocent systolic murmur.

Pathologic murmurs

- Murmurs of stenotic lesions (e.g., aortic stenosis, pulmonary stenosis, coarctation of aorta): systolic ejection murmur tend to be noted shortly after birth.
- Murmurs of left-to-right shunt lesions (e.g., VSD): pansystolic murmur may not be heard until the 2^{nd} to 3^{rd} week of life when the pulmonary vascular resistance has decreased and left-to-right shunt has increased.
- Continuous murmur of PDA may appear early in preterm infants.

N.B.: Murmur of an ASD usually appears late in infancy with an insidious onset.

Cyanosis

- Early detection of cyanosis in a newborn is crucial. The tip of the tongue is a good place to look for central cyanosis.
- Clinical apparent cyanosis is usually not visible until there is >3 gm/dl of desaturated hemoglobin in the arterial system; therefore, the degree of visible cyanosis depends on the severity of hypoxemia (% O_2 saturation) as well as hemoglobin concentration.
- Cyanosis is usually recognized when arterial oxygen saturation is <85%. However, cyanosis may occur at oxygen saturation as high as 90% in this age group (because the hemoglobin level is high and the peripheral circulation is often sluggish in newborns).
- Hyperoxia test is a method of distinguishing cyanotic congenital heart disease from pulmonary disease. However, it should be done in all neonates with suspected critical congenital heart disease (not just those who have cyanosis). In this test, PaO_2 should be measured in room air (if tolerated), followed by repeat measurements with the patient receiving 100% O_2 through an oxyhood for at least 10 minutes (pulse oximetry cannot be used for documentation).
  - PaO_2 >250 mmHg in both upper (preductal) and lower (postductal) extremities eliminates critical structural cyanotic heart disease.
  - PaO_2 of <100 mmHg is diagnostic of cyanotic congenital heart disease (failed hyperoxia test).
  - Patients who have paO_2 between 100-250 mmHg may have structural heart disease with intracardiac mixing and greatly increased pulmonary blood flow or may have severe pulmonary disease (equivocal results).

- The neonates who fail a "hyperoxia test" or have equivocal results with other cardiac signs are very likely to have congenital lesions that include anatomic features with:
  - Duct-dependent systemic blood flow (left sided obstructive lesions)
    - Critical aortic stenosis
    - Coarctation of aorta
    - Interrupted aortic arch (i.e., complete atresia of a segment of aortic arch)
    - Hypoplastic left heart syndrome
  - Duct-dependent pulmonary blood flow (right-sided obstructive lesions)
    - Critical pulmonary stenosis or pulmonary atresia
    - Tricuspid atresia
    - Tetralogy of Fallot (with severe right ventricular outflow tract obstruction)
    - Ebstein anomaly
  - Lesions with complete intracardiac mixing
    - Truncus arteriosus
    - Total anomalous pulmonary venous return
  - Lesions with parallel circulation
    - Transposition of the great arteries (TGA)
- In these infants, prostaglandin E_1 IV infusion should be started, as soon as possible, until anatomic diagnosis is accomplished by a pediatric cardiologist.

Table (35-1): Differential diagnosis of central cyanosis in a neonate

Central nervous system depression

Causes

- Perinatal asphyxia
- Heavy maternal sedation
- Intrauterine fetal distress

Findings

- Shallow irregular respiration
- Poor muscle tone
- Cyanosis disappears when the patient is stimulated or oxygen is given

Pulmonary disease

Causes

- Parenchymal lung disease (e.g., RDS, atelectasis)
- Pneumothorax or pleural effusion
- Diaphragmatic hernia
- Persistent pulmonary hypertension of the newborn (PPHN)

Table (35-1): Differential diagnosis of central cyanosis in a neonate (continued)

Findings

- Tachypnea and respiratory distress with retraction and expiratory grunting.
- Crackles and/or decreased breath sounds on auscultation.
- Chest x-ray film may reveal the cause.
- Oxygen administration improves or abolishes cyanosis.

Cardiac disease

Causes

- Cyanotic congenital heart defect with right-to-left shunt

Findings

- Tachypnea, usually without retraction.
- Lack of crackles or abnormal breath sounds unless congestive heart failure supervenes.
- Heart murmur (may be absent in serious defects).
- Chest x-ray: may show cardiomegaly, abnormal cardiac silhouette, increased or decreased pulmonary vascular markings.
- Little or no increase in PaO_2 with oxygen administration.

Heart failure

Definition

Congestive heart failure (CHF) is a clinical syndrome in which the heart is unable to pump enough blood to the body to meet its needs, or to dispose venous return adequately, or a combination of the two.

Etiology (Table 35-2)

Clinical manifestations

Clinical diagnosis can be made on the basis of the existence of certain symptoms and signs rather than on radiographic or laboratory findings. A neonate with heart failure may present with these symptoms.

- Feeding difficulties and growth failure
- Tachypnea and tachycardia
- Pulmonary crackles or rhonchi
- Hepatomegaly
- Weak peripheral pulses
- Delayed capillary refill
- Cardiorespiratory collapse in severe cases
- Hydrops fetalis, an extreme form of intrauterine congestive heart failure

Table (35-2): Causes of congestive heart failure in neonates

Structural heart defects

At birth

- Hypoplastic left heart syndrome
- Severe tricuspid regurgitation (Ebstein anomaly)
- Pulmonary regurgitation (e.g., absent pulmonary valve syndrome)
- Large systemic arteriovenous fistula

First week of age

- Transposition of great arteries (TGA)
- Premature infant with large patent ductus arteriosus
- Total anomalous pulmonary venous return below diaphragm

1-4 weeks of age

- Critical aortic or pulmonary stenosis
- Coarctation of the aorta
- Common atrioventricular (AV) canal

Myocardial diseases

- Myocarditis
  - Infectious:
    - Viral (e.g., coxsackie, rubella, varicella)
    - Bacterial and fungal
  - Non infectious: Autoimmune diseases.
- Transient myocardial ischemia (with or without birth asphyxia)

  Elevated serum creatine kinase-MB fraction or cardiac troponin levels may be helpful to identify myocardial damage
- Cardiomyopathy (e.g. infants of diabetic mothers)

Disturbances in heart rate

- Supraventricular tachycardia
- Atrial flutter or fibrillation
- Congenital complete atrioventricular (AV) block (associated with congenital heart defect (40%) and neonatal lupus)

Non-cardiac causes

- Birth asphyxia resulting in transient myocardial ischemia
- Metabolic: hypoglycemia, hypocalcemia
- Severe anemia (as seen in hydrops fetalis)
- Overtransfusion or overhydration
- Neonatal sepsis

N.B.: Large left-to-right shunt lesions (e.g., VSD and PDA) do not commonly cause CHF before 6-8 weeks of age (as the pulmonary vascular resistance does not fall low enough to cause a large left-to-right shunt until this age). The onset may be earlier in premature infants.

Systemic hypoperfusion or shock

- Neonates who present with shock within the first 3 weeks of life are likely to have congenital heart defects with duct dependent systemic flow. These babies present with cardiovascular collapse as the ductus arteriosus closes with resultant systemic hypoperfusion.
- In these cases, it is appropriate to begin an infusion of prostaglandin E_1, even if before a precise anatomic diagnosis can be made by echocardiography.

Arrhythmia

- Arrhythmia (also known as dysrhythmia) refers to any change from the normal sequence of electrical impulse of the heart. The heart rate may be too fast or too slow, and may be regular or irregular.
- Examples:
  - Supraventricular tachycardia (SVT)
  - Congenital heart block

Cardiac Evaluation of a Neonate with Suspected CHD

Clinical evaluation

- Physical examination (CHF, cyanosis, respiratory work, shock)
- Four-extremity blood pressure assessments (manual /automated)
- Systolic pressure >10 mmHg in upper limbs > lower limbs suggests:
  - Coarctation of the aorta, or
  - Interrupted aortic arch
- Pulse oximetry for preductal/postductal O_2 saturation:
  - Preductal > postductal O_2 saturation (differential cyanosis) = normally related great vessels + PDA flow from pulmonary artery to descending aorta, such as PPHN or critical left-sided obstructive lesions.
  - Post-ductal > pre-ductal O_2 saturation (reverse differential cyanosis) = abnormally related great vessels + PDA flow from pulmonary artery to descending aorta, such as TGA (with coarctation of aorta or interrupted aortic arch) or TGA (with supra systemic pulmonary venous return).
- Hyperoxia test

Laboratory and imaging evaluation

- Arterial blood gases to detect hypoxemia and metabolic acidosis.
- Chest radiography for distinctive radiological signs.

Confirmation of the diagnosis of CHD

- Electrocardiography (ECG): for distinctive signs (e.g., axis deviation and chamber enlargement).
- Echocardiography is the gold standard of diagnosis, as it is a non-invasive technique that identifies cardiac anatomy, and gives information about flow patterns.
- Cardiac catheterization is presently used to:
  - Visualize anatomy not identified by the echocardiography
  - Obtain hemodynamic information
  - Perform therapeutic intervention; such as:
    - Balloon atrial septostomy for TGA
    - Balloon pulmonary valvuloplasty
    - Balloon aortic valvuloplasty
    - Balloon angioplasty for coarctation of the aorta

Management of a Neonate with a Cardiac Problem

Neonates with cyanosis or shock

Once the diagnosis of critical CHD is made or suspected, the attention should be focused on the basic life support of the infant with maintenance of a patent ductus arteriosus:

- Maintain a stable airway as well as adequate ventilation and oxygenation: if severe respiratory distress, profound cyanosis or apnea, immediately intubate the infant and initiate mechanical ventilation. Administration of sedation or neuromuscular blockade is recommended, in order to reduce overall systemic oxygen consumption.
- Obtain vascular access including arterial line, better through umbilical vessels.
- Maintain the adequate volume status; volume resuscitation for low cardiac output. However, excessive volume expansion may be potentially harmful.
- Correct the metabolic acidosis.
- Initiate inotropic support: IV infusion of a combination of low-dose dopamine, up to 5 μg/kg/minute and dobutamine, 5-10 μg/kg/minute:
  - Minimize peripheral vasoconstriction induced by high dose of dopamine.
  - Maximize the dopaminergic effect of dopamine on the renal circulation.
  - Produce a desirable inotropic support supported by dobutamine.
- Initiate prostaglandin E_1 infusion:
  - For the neonate who fails a hyperoxia test or who has an equivocal result, as well as the neonate who presents in shock within the first 3 weeks of life.
  - Dose: 0.05-0.1μg/kg/minute by continuous IV infusion, start with 0.05 μg/kg/minute, and if no improvement increase the dose to 0.1μg/kg/minute.
  - Adverse effects of prostaglandin E_1: hypotension, flushing, tachycardia, apnea, fever, and seizures.

- Once the infant has been stabilized, it is necessary to refer the infant to a higher level neonatal care unit specialized in management of CHD.

Neonates with congestive heart failure

General measures

- Maintain adequate oxygenation.
- Restrict fluid intake: infants with CHF usually require fluid restriction (-30 ml/kg/day).
- Measure the infant's weight daily.
- Correct the predisposing factors, such as fever, anemia, and infection. For anemia, packed cell transfusions are given to raise the hematocrit to 35% or higher.

Drug therapy

Three major classes of drugs are used:

- Diuretics (e.g. furosemide IV 1 mg/kg/dose every 12 hrs).
- Afterload-reducing agents (captopril 0.1-0.4 mg/kg/dose, orally, 1-4 times a day) can increase cardiac output without increasing myocardial oxygen consumption.
- Inotropic agents:
  - Digoxin is used in non-critically ill infants. The use of digoxin is contraindicated in hypertrophic cardiomyopathy, complete heart block, or cardiac tamponade.

N.B.: Supplemental oxygen should be given with caution in cyanotic infants in whom CHD is suspected, as O_2 accelerates duct closure. Therefore, some physicians recommend holding O_2 administration in such cases, until prostaglandin infusion is initiated. Others recommend minimizing O_2 administration while keeping infant's O_2 saturation as low as 75% until a definitive diagnosis is established.

Structural Heart Defects with Left-to-Right Shunt

Ventricular Septal Defects (VSD)

- VSD is the most common congenital cardiac anomaly, either alone or associated with other lesions, and also the most common cause of congestive heart failure (CHF) after the initial neonatal period.
- It is an abnormal opening in the ventricular septum that is usually located in the membranous portion**,** but may occur in the muscular portion of the septum.

Clinical manifestations

- Ninety percent of VSD's are hemodynamically insignificant.
- Small VSD is often asymptomatic which may present with a harsh systolic murmur that appears 2-3 days onward at the left sternal border.
- In moderate to large defects, the left to right shunting of blood is greater and results in increased right ventricular pressure and right ventricular hypertrophy leading to increased pulmonary blood flow. The patient usually presents with:
  - Tachypnea interfering with feeding
  - Excessive diaphoresis (sweating)
  - Superimposed pulmonary problems as pneumonia and atelectasis leading to CHF
  - Growth failure is the most common symptom of CHF

Investigations

- Chest x-ray shows enlarged cardiac shadow with plethoric lung.
- ECG reveals a left axis deviation.
- Echocardiography demonstrates the defect size and location.

Management

- Neonate is often followed-up for a period of time as even large defects may close spontaneously.
- Give diuretics, captopril and inotropes with caloric supplementation to control CHF.
- Failure to thrive is an indication for surgical repair of the defect.

Patent Ductus Arteriosus (PDA)

- In term infants, functional closure of the ductus arteriosus occurs during the first day of life. Persistence of patency of the ductus arteriosus, alone or in association with other cardiovascular and/or respiratory problems, may be asymptomatic or associated with severe hemodynamic and respiratory complications, depending on its size and the clinical condition of the infant.
- The ductus arteriosus remains patent frequently in preterm infants, especially in association with primary respiratory disease and fluid overload. If managed appropriately, significant improvement in the respiratory status can be observed.
- PDA is not common in full-term infants. Incidence in preterm infants is inversely related to gestational age.

- Clinical evidence of PDA appears in 45% of infants <1,750 gm birth weight, and in about 80% of infants <1,000 gm birth weight.

Clinical manifestations

- This condition is associated with shunting of blood from the aorta (systemic circulation) to the pulmonary artery (pulmonary circulation) which becomes flooded with the additional volume load, leading to pulmonary edema and eventually to signs of right-sided heart failure.
- The initial presentation in preterm infants usually starts 2-7 days after birth. Apneic spells or episodes of bradycardia may be the initial signs of PDA in infants who are not on ventilators.
- Typically, a preterm infant with hyaline membrane disease shows some improvement during the first few days after birth. This is followed by an inability to wean the infant from the ventilator or a need to increase ventilator settings or oxygen requirements in 4-7 days old preterm infants.
- The continuous murmur of a large PDA may not appear for 2-3 weeks. Instead, it is a systolic murmur with a slight or no diastolic component; it is best audible at the left infraclavicular area.
- Bounding peripheral pulses, hyperactive precordium, and tachycardia with or without gallop rhythm are present. There is wide pulse pressure (the difference between systolic and diastolic pressure).
- Symptoms and signs of CHF may develop.
- There is poor weight gain.

Investigations

- The chest x-ray shows an enlargement of the cardiac shadow, pulmonary plethora/ edema, a prominent main pulmonary artery, and left atrial enlargement.
- The ECG reveals left ventricular hypertrophy (left axis deviation).
- Echocardiography demonstrates the ductus size and the direction of the flow.

Management

- Initial management is usually conservative: adequate oxygenation, fluid restriction and diuretics (furosemide). This may help to minimize the effects of PDA, but should not be given to the point of dehydration.
- In more symptomatic cases: indomethacin (prostaglandin antagonist) may be needed for nonsurgical closure of PDA in premature infants (dose: 0.2 mg/kg over 20 minutes every 12 hrs for 3 doses). Adverse reactions include transient oliguria, decreased platelet functions, and electrolyte disturbances. Follow serum creatinine during therapy.
- Intravenous or oral ibuprofen has been recently approved for use in the newborn. It is as effective as indomethacin but appears to have a better safety profile (more normal urine output, less elevation of BUN and creatinine, less decrease in mesenteric blood flow, and improved autoregulation of cerebral blood flow). The dose of ibuprofen is 10 mg/kg initially, then 2 doses of 5 mg/kg after 24 and 48 hrs.
- If medical treatment is unsuccessful or contraindicated, surgical ligation may be necessary.

Persistent Pulmonary Hypertension of the Newborn (PPHN)

This neonatal condition is characterized by persistence of pulmonary hypertension, which in turn causes a varying degree of cyanosis from a right-to-left shunt through the PDA or patent foramen ovale (PFO). No underlying congenital heart defect is present.

PPHN is discussed in this chapter as it is a common cause of desaturation and cyanosis in newborns and it mimics cyanotic cardiac disorders.

Etiology

Pulmonary vasoconstriction with a normally developed pulmonary vascular bed

- Alveolar hypoxia (e.g., MAS, RDS): hypoxemia, a powerful pulmonary vasoconstrictor
- Birth asphyxia
- Left ventricular dysfunction or circulatory shock
- Infections (GBS infection)
- Hyperviscosity syndrome (polycythemia)

Increased pulmonary vascular smooth muscle development (Hypertrophy)

- Chronic intrauterine asphyxia
- Maternal use of prostaglandin synthesis inhibitors (aspirin, indomethacin) resulting in early ductal closure

Decreased cross-sectional area of pulmonary vascular bed

- Congenital diaphragmatic hernia
- Primary pulmonary hypoplasia

Clinical Manifestations

- The condition starts 6-12 hrs after birth.
- There are cyanosis and respiratory difficulties**.**
- There is prominent right ventricle, single and loud S_2, and soft regurgitant systolic murmur of tricuspid regurgitation**.**
- Systemic hypotension is present.
- PaO_2 gradient between a preductal (right radial artery) and a postductal (umbilical artery) blood >20 mmHg (or >10% difference in O_2 saturation) is highly suggestive of ductal right to left shunt. In severe cases, differential cyanosis (with a pink upper body and a cyanotic lower body) may be seen.

Investigations

- Chest x-ray films are usually normal or demonstrate associated pulmonary parenchymal disease.

- Diagnosis is confirmed by echocardiography.

Management

- Minimize handling, noise level**,** and physical manipulation.
- Administer oxygen 100% to achieve postductal oxygen saturations >95%.
- Initiate mechanical ventilation with FiO_2 1.0, if previous measures fail.
  - The goal is to maintain adequate and stable oxygenation (O_2 saturation >95%) using the lowest possible mean airway pressures.
  - Hyperventilation should, if possible, be avoided and $PaCO_2$ values should be kept >30 mmHg (at 35-40 mmHg) using mild hyperventilation. Complications of hyperventilation include hyperinflation, barotrauma, reduced cardiac output, and decreased cerebral blood flow with later neurodevelopmental deficits (e.g., cerebral palsy and sensory hearing loss).
- High-frequency oscillatory ventilator may be needed in severe cases.
- Sedation and analgesia:
  - Narcotic analgesic, fentanyl infusion (dose 2-5 μg/kg/hr), is a useful adjunct therapy.
  - Rarely, paralysis of the patient with pancuronium may be required so as to accomplish muscle relaxation and full synchronization of the infant with mechanical ventilation.
- Alkalinization with sodium bicarbonate infusion (0.5-1 mEq/kg/hr) may be needed, to increase arterial pH to 7.50-7.55. Serum sodium should be monitored so as to avoid hypernatremia.
- Inotropic therapy, such as dopamine, to support blood pressure and perfusion. Other agents such as dobutamine are helpful in case of myocardial dysfunction.
- Tolazoline (nonselective α-adrenergic antagonist) infusion:
  - Produces pulmonary vasodilatation.
  - Given with both volume support and pressor drugs if systemic hypotension occurs.
- Inhaled nitric oxide (NO): administered by mechanical ventilation in doses of 5-20 ppm. It relaxes vascular smooth muscles and cause**s** pulmonary vasodilatation.
- Sildenafil (phosphodiesterase type-5 inhibitor):
  - It may be administered in cases refractory to inhaled NO and other conventional therapies, and those who are persistently unable to be weaned of inhaled NO, or in situations where NO is not available.
  - Dose 0.3-1 mg/kg/dose every 6-12 hrs orally.
  - Limited data from case reports and small clinical trials.
- Extracorporial membrane oxygenation (ECMO), a life saving therapy in infants with PPHN who fail conventional management and/or inhaled NO.
- Correct hypoglycemia, hypocalcemia, hypomagnesemia in order to provide adequate substrates for myocardial function and appropriate response to inotropic agents.

Chapter 36

Neonatal Shock

Neonatal Shock

Shock

Neonatal shock is an acute, complex syndrome characterized by inadequate circulatory perfusion of the tissues to meet the metabolic demands of the vital organs. Organ dysfunction occurs because of inadequate blood flow and oxygenation. The cellular metabolism becomes predominantly anaerobic producing lactic acid and metabolic acidosis.

Hypotension

The blood pressure is >2 standard deviation below normal for age **(Refer to Appendix 3)**. Systemic hypotension is the key presenting sign of uncompensated shock that eventually progresses to metabolic acidosis.

The lower limit of the mean arterial pressure during the first postnatal day roughly equals the gestational age of the infant. The majority of term neonates have a mean blood pressure of >45 mmHg immediately after birth with a rise to >50 mmHg by the 3rd postnatal day.

N.B.: In ELBW infants, hypotension is more likely due to adrenocortical insufficiency, poor vascular tone, and immature catecholamine responses.

Causes of Shock

Abnormal peripheral vasoregulation

This is the most frequent cause (with or without myocardial dysfunction).

Normal blood volume but poor distribution of this volume leads to inadequate perfusion of the tissues. This may result from increased venous capacity or vasomotor paralysis (e.g., proinflammatory cascades that cause vasodilatation).

Hypovolemia

This may be secondary to antepartum or postpartum blood loss, plasma loss, or excessive extracellular fluid loss.

Blood loss

- Antepartum blood loss:
  - Placental hemorrhage, abruptio placentae, placenta previa or placental incision during cesarean section
  - Fetofetal transfusion
  - Fetomaternal transfusion
- Postpartum blood loss:
  - Bleeding disorders, such as hemorrhagic disease of newborn (HDN) or disseminated intravascular coagulation (DIC)
  - Birth injury, liver laceration or adrenal hemorrhage
  - Massive pulmonary hemorrhage

Plasma loss

- Plasma loss into the extra vascular compartment, as seen in sepsis, and capillary leak syndrome.

Excessive extracellular fluid losses

- As seen in excessive diuresis and skin loss.

Cardiac dysfunction

Conditions that may cause low cardiac output are:

Myocardial dysfunction

- Birth asphyxia
- Infectious agents (bacterial or viral)
- Metabolic abnormalities as hypoglycemia and hypocalcemia (as in IDMs)

Obstruction to cardiac blood flow

- Inflow obstruction (obstruction to venous return)
  - Tricuspid atresia
  - Increased intrathoracic pressure (e.g., tension pneumothorax, excessive ventilator pressures)
  - Cardiac tamponade
- Outflow obstruction
  - Pulmonary atresia or stenosis
  - Aortic atresia or stenosis
  - Hypertrophic subaortic stenosis (as in IDM's)
  - Critical aortic coarctation

Arrhythmias

- If prolonged; supraventricular arrhythmias as paroxysmal atrial tachycardia are most common.

N.B.: Septic shock is a combination of relative hypovolemia, myocardial dysfunction, and peripheral vasodilatation; gram-negative organisms (e.g., *E. coli* and *Klebsiella)* are usually involved. Also it can occur with gram-positive organisms (e.g., GBS and *Staphylococci*)

Clinical Manifestations

- Tachycardia (not always in very premature infants)
- Pallor, poor skin perfusion (prolonged capillary refill time >4 seconds), and skin mottling
- Cold extremities
- Decreased urine output
- Hypotension and weak pulse

- Metabolic acidosis
- CNS signs of lethargy
- In preterm infants, the decrease in brain blood flow and oxygen supply during severe hypotension predisposes to intraventricular hemorrhage and periventricular leukomalacia.

Investigations

- Obtain hematocrit (Hct) level, serum electrolyte levels, blood gases, and serum glucose level as soon as vascular access is obtained.
- Take a chest x-ray: a small heart in volume depletion and a large heart in cardiac disease.
- Specific studies:
  - To identify the cause, for example:
    - Sepsis (CBC, CRP, and cultures)
    - Cardiac lesions (ECG and echocardiography)
  - To detect sequelae, for example:
    - Renal (renal functions and ultrasonography)
    - Liver function tests

Management

General

- Rapidly assess the newborn infant and determine the cause in order to direct treatment accordingly (whether the infant requires volume replacement or administration of inotropic agents). Four useful parameters in making this decision are:
  - History taking: to rule out birth asphyxia and blood loss
  - Physical examination: to reveal which systems are involved
  - Chest x-ray films: to rule out cardiac lesions
  - Central venous pressure (CVP) measurement: if it is low (<3 mmHg), the infant is volume depleted. If it is high (>6-8 mmHg), the infant probably has cardiogenic shock **(Refer to Chapter 16)**.
- With asphyxial shock, treatment of respiratory failure with oxygen and assisted ventilation may be the only therapy needed. Blood and volume expanders, if ever given, should be given with extreme caution, as it will aggravate hypoxic myocardial failure.
- If still unsure of the cause, start empirical volume expansion with crystalloid (e.g., normal saline 10-20 ml/kg IV over 30 minutes).
  - If there is a response, continue volume expansion.
  - If there is no response, an inotropic agent should be started.
- Give respiratory support (supplemental oxygen or mechanical ventilation) as needed**,** based on the results of blood gas analysis and clinical examination.

- CVP measurement may help in the management. CVP at 5-8 mmHg with volume infusion is associated with improved cardiac output. If CVP exceeds 6-8 mmHg, additional volume will usually not be helpful.
- Correction of negative inotropic factors such as hypoxia, hypoglycemia, hypocalcemia, and electrolytes imbalance, if present.
- Correction of metabolic acidosis with a sodium bicarbonate infusion at a dose of 1-2 mEq/kg, when there is significant metabolic acidosis (base deficit ≥10 mEq/L). Be sure the infant is receiving adequate ventilation, and $PaCO_2$ is in the normal range.
- Positive inotropic agents:
  - Dopamine: it is the drug of first choice; high doses (6-30 µg/kg/minute) stimulate α-adrenergic receptors and serotonin receptors, causing vasoconstriction and increased peripheral vascular resistance. High doses are better tolerated in the preterm neonates.
  - Dobutamine: if dopamine fails to improve blood pressure, adding dobutamine is recommended in a dose of 5-15 µg/kg/minute.
  - Epinephrine: it is **not** a first line drug in newborns. It increases myocardial contractility and peripheral vascular resistance. It may be effective in patients who fail to respond to dopamine. The starting dose is 0.05-0.1 µg/kg/minute and can be increased rapidly while dopamine infusion rates are declined.

N.B.: Dobutamine causes peripheral vasodilatation.

Specific situations

Hypovolemia

- Volume expansion: give IV crystalloid. Colloids (e.g., albumin) are to be used with caution (associated with increased risk of mortality in critically ill patients).
- In case of blood loss:
  - Give volume expanders until adequate tissue perfusion is attained as evidenced by good urinary output and central nervous system function.
  - A blood sample should be sent to the laboratory for Hct value.
  - Replace by packed RBCs, whole or reconstituted blood.
- Blood replacement therapy **(Refer to Page 401)**
  - Hct <40%: give packed RBCs, 5-10 ml/kg over 30-40 minutes.
  - Hct >50%: give normal saline, or fresh-frozen plasma (FFP are used if clotting studies are also abnormal).
  - Hct of 40-50%: give alternating transfusions of packed RBCs and normal saline.
- Frequently and carefully monitor the infant's vital signs and general condition.

Septic shock

- Obtain cultures (blood, urine and CSF).

- Start or modify antibiotic therapy. If not already on antibiotics, start empiric therapy with intravenous ampicillin and gentamicin after culture specimens have been obtained.
- Use volume expanders and inotropic agents, as needed.

N.B.: Rapid and effective volume expansion is the most important step in the management of septic shock.

Myocardial dysfunction

- Treat underlying cause:
  - Air leak: immediate air evacuation
  - Arrhythmia
- Inotropic agents: contraindicated in hypertrophic subaortic stenosis.

Corticosteroid therapy

- Corticosteroids rapidly up-regulate cardiovascular adrenergic receptor expression and serve as hormone replacement therapy in cases of adrenal insufficiency.
- Hydrocortisone: a dose of 1 mg/kg every 8-12 hrs for 2-3 days may be useful in extremely preterm infants with hypotension refractory to volume expansion and vasopressors (high dose dopamine or epinephrine).

Chapter 37

Common Congenital Anomalies

Common Congenital Anomalies

Congenital anomalies are malformations in structure, position, or function of an organ or system. They are common causes of disability and mortality in early life.

Causes range from genetic disorders to teratogenic insults to the developing fetus. Any congenital anomaly noted should alert the physician to the possibility of other developmental abnormalities, whether physical, neurological, or mental. The presence of multiple, congenital anomalies may be indicative of a syndrome and requires further testing and/or genetic studies for verification and counseling of the parents.

This chapter reviews some of the important externally apparent malformations**,** which are common and/or life threatening.

Anomalies of the Head and Face

Cleft lip and cleft palate

Cleft lip and cleft palate are the most common congenital anomalies of the head and neck either each one alone or combined.

Clinical manifestations

- The defect may involve the lip, the lip and palate, or only the palate, and may be unilateral or bilateral. Median cleft lip is rare and is usually associated with hypo-telorism, microcephaly, and early death.
- Clefts of the lip are more common in males and on the left side.
- A cleft lip usually affects the upper lip. Sucking problems occur in bilateral cases.
- Cleft palate can be complete or incomplete. It may lead to feeding difficulties, recurrent chest infections, recurrent otitis media, hearing loss, and speech difficulties.
- Malposition of the teeth, usually require orthodontic correction.

Management

- Surgical closure is recommended before phonation.
  - Cleft lip should be closed at 3 months, when the infant has shown satisfactory weight gain and is free of any oral, respiratory, or systemic infection.
  - Cleft palate should be closed surgically before 12 months.
- Breastfeeding should be encouraged in infants with isolated cleft lip.
- Soft artificial nipples with large openings are beneficial in cleft palate. Syringe feeding is an alternative. If repeated life-threatening choking, nasogastric tube feeding should be considered.

Choanal atresia

Choanal atresia is a congenital blockage of the posterior nares caused by the persistence of a bony septum in 90% of the cases and a soft tissue membrane in the other 10% of the cases.

Clinical manifestations

- Female to male ratio is 2:1.

- When the obstruction is unilateral:
  - Inability to pass a catheter into the nasopharynx during routine clinical screening after delivery.
  - The infant may be asymptomatic until the 1st respiratory infection, when unilateral nasal discharge or persistent nasal obstruction may suggest the diagnosis.
- Infants with bilateral choanal atresia present in the delivery room with respiratory distress and cyanosis that resolves with crying.
- May be associated with coexisting anomalies in 50% of cases. The most common anomaly is the CHARGE association:
  - **C**oloboma of the iris, choroid, and/or microphthalmia
  - **H**eart defect such as atrial septal defect (ASD) and/or conotruncal lesion
  - **A**tresia of choanae
  - **R**etarded growth and development
  - **G**enitourinary abnormalities, such as cryptorchidism, microphallus, and/or hydronephrosis
  - **E**ar defects with associated deafness

Management

- Bilateral choanal atresia requires immediate insertion of an oral airway. The infant may be fed by gavage until breathing and eating without the assisted airway is possible.
- Surgical correction should be done as soon as possible.

Anomalies of the Thoracic Cavity

Esophageal atresia (EA) and tracheoesophageal fistula (TEF)

- The esophagus ends blindly and is usually associated with tracheoesophageal fistula (TEF). Esophageal atresia with a distal TEF accounts for up to 85% of the cases, whereas other subtypes are less common **(Figure 37-1).**
- Babies with TEF and EA are often LBW; 20% of these babies are premature and another 20% are small for gestational age.
- They may be associated with coexisting anomalies specifically the VACTERL association: (**V**ertebral anomalies, **A**nal atresia, **C**ardiac defect "most often ventricular septal defect", **T**racheo**E**sophageal fistula with esophageal atresia, **R**enal dysplasia, and **L**imb anomalies, most often radial dysplasia).

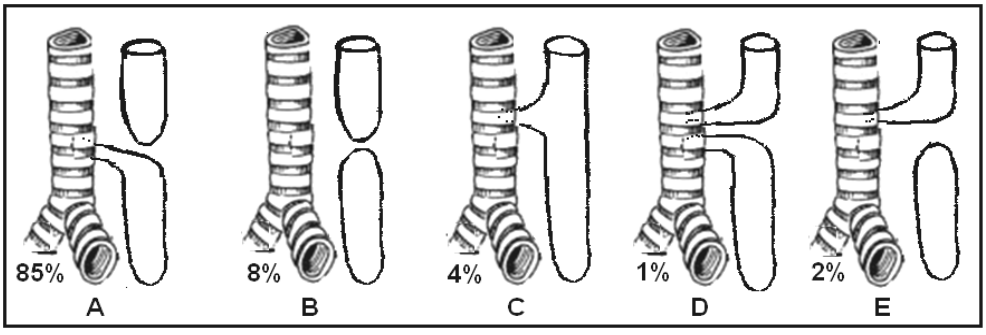


Figure (37-1): Various types of tracheoesophageal fistulas (TEF) with relative frequency (%)

Clinical manifestations

- Maternal polyhydramnios may alert the physician to EA.
- The infant often presents with:
  - Excessive salivation
  - Choking and coughing on feeding
  - Episodes of coughing, cyanosis, and respiratory distress
- TEF without EA (H-type fistula) usually presents after the neonatal period. The diagnosis is suggested by history of recurrent chest infection or respiratory distress related to meals.
- Diagnosis is confirmed by the inability to pass a catheter into the stomach. X-ray studies will show the catheter coiled in the upper esophageal pouch and/or an air-distended stomach, indicating the presence of a co-existing TEF **(Refer to Appendix 9)**.
- If there is no fistula, or if it connects the trachea to the esophagus proximal to the atresia, no GI gas will be seen on x-ray and the neonate will show scaphoid abdomen.
- H-type fistula can be demonstrated with administration of water soluble contrast media (Omnipaque) during cinefluoroscopy.
- Careful search must be undertaken for the commonly associated cardiac and other anomalies.

Management

- Provide basic supportive measures.
- Maintain NPO.
- Suction intermittently the proximal pouch to avoid aspiration of saliva.
- The head of the bed should be elevated 45 degrees to diminish reflux of gastric contents.
- Provide IV antibiotics for possible aspiration.
- Mechanical ventilation is to be avoided, if possible, because it may cause severe abdominal distension compromising ventilation. If mechanical ventilation is required, it should be done using a high rate and low pressure.
- Consult pediatric surgeon for surgical repair: the steps and timing of surgical treatment should be individualized.

Diaphragmatic hernia

- A diaphragmatic hernia is the herniation of abdominal contents into the thoracic cavity through a defect in the diaphragm.
- The most common site is the left hemithorax with the defect in the diaphragm being posterior (foramen of Bochdalek) in 70% of infants.
- Fifty percent of these hernias are associated with other malformations (e.g., cardiac, neural tube, intestinal, skeletal and renal defects).

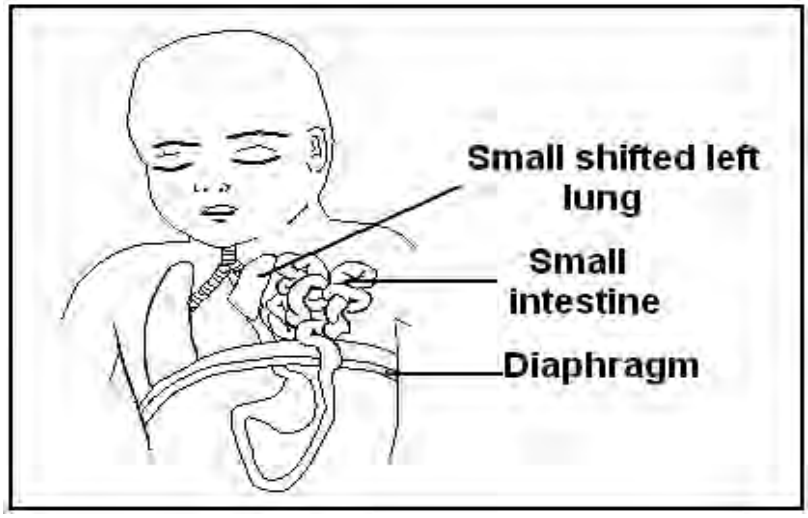


Figure (37-2): Congenital postero-lateral (Bochdalek) diaphragmatic hernia

Clinical manifestations

- Polyhydramnios is a common association.
- Large defects (Bochdalek) usually present at birth with cyanosis, respiratory distress, scaphoid abdomen, decreased or absent breath sounds on the side of the hernia**,** and heart sounds displaced to the side opposite the hernia. Intestinal sounds may be heard on chest auscultation.
- Small hernias, right sided hernias and substernal hernias of Morgagni may have a more subtle presentation, manifested as feeding problems and mild respiratory distress.

Investigations

- Prenatal diagnosis using ultrasonography allows delivery in a well equipped center to increase chances of survival.
- Chest x-ray will reveal loops of intestine in the chest **(Refer to Appendix 9)**.

Management

- All infants should be intubated immediately after delivery.
- Bag and mask ventilation is contraindicated.
- Insert large caliber nasogasteric tube and suction frequently or leave tube open below the level of the baby for continuous drainage to decrease gaseous distention of stomach and intestine.
- Sedate and give analgesia as necessary.
- Measure the preductal and postductal saturations by putting the probe of pulse oximeter on the right hand, then on any limb to detect pulmonary hypertension and ductal shunting.
- Avoid hypoxia and acidosis to avoid pulmonary hypertension.
- Consult pediatric surgeon for surgical repair.

Prognosis

Mortality is related to the associated pulmonary hypoplasia, pulmonary hypertension**,** and congenital heart disease.

Anomalies of the Abdomen and the Back

Omphalocele

- Omphalocele is the herniation of the intestine and/or liver into the base of the umbilical cord.
- The covering sac may be intact or ruptured.
- Immediate surgical repair, before infection has taken place and before the tissues have been damaged by drying (saline-soaked sterile dressings should be applied immediately) or by rupture of the sac, is essential for survival.
- Eighty percent have associated congenital anomalies: Beckwith-Wiedemann syndrome (omphalocele, macrosomia, and hypoglycemia), trisomies 13 and 18, and cardiac anomalies.

Management

- Diagnosis is made by prenatal ultrasonography.
- Cesarean section is indicated if the defect is >5 cm or contains liver.
- Provide continuous nasogastric suction.
- Cover intestinal contents with warm saline soaked gauze without kinking and blocking blood supply.
- Strict attention to the maintenance of core temperature is essential.
- Do not attempt to reduce the sac because it may rupture.
- Start broad spectrum antibiotics.
- Definitive surgical repair, when the baby stabilizes.
- Congenital malrotation of the colon is usually present, and can lead to midgut volvulus presenting as intestinal obstruction after recovery from treatment of omphalocele.

Gastroschisis

- Gastroschisis is a defect in the abdominal wall at the base of the umbilical stalk through which the small or large bowel may herniate. The intestine is eviscerated with no covering sac.
- Ten percent of infants with gastroschisis have intestinal atresia.

Management

- Maintain normal body temperature.
- Correct the hydration status resulting from increased IWL from exposed**,** large surface areas of the intestine.
- Apply protective covering of the intestine by saline-soaked gauze, and dry sterile dressing.
- Start broad spectrum antibiotics.
- Surgical treatment is mandatory.

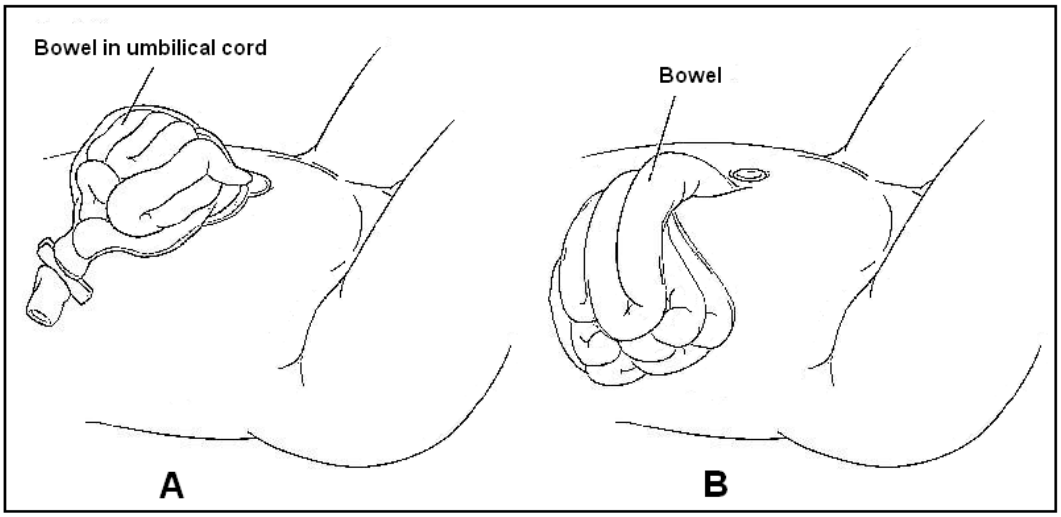


Figure (37-3): Abdominal wall defects

A) Omphalocele, B) Gastroschisis

Imperforate anus

- Imperforate anus means lack of an anal opening at the proper place.
- When a malformation of the anus is present, the muscles and nerves associated with the anus often have a similar degree of malformation. The spine and urogenital sinus may also be involved.
- Fifty percent of affected babies have associated anomalies e.g., VACTERL. Unilateral renal agenesis is the most common non-skeletal anomaly.
- There are two categories of imperforate anus:
  - Low imperforate anus with or without fistula in the perineum. At birth, the opening of the fistula is not always apparent, and an interval of 12-24 hrs may be required until the bowel fills with air or meconium reaches the most distal point in the GI tract.
  - High imperforate anus: this type is never associated with fistula in the perineum, but may be associated with rectovesical fistula in the male and rectovaginal fistula in the female.
- Erect x-ray upside down with a metal coin on the anal opening can help in the diagnosis of the level of imperforate anus. However, it can also be misleading if the distal rectum is filled with meconium, preventing air from reaching the most distal aspect of this pouch. Ultrasonography may be helpful in locating the rectal pouch.
- Surgical treatment is mandatory:
  - In low imperforate anus with a fistula in the perineum, a perineal anoplasty in the newborn period accomplishes decompression of the bowel, and a colostomy is not needed.
  - In neonates with imperforate anus without a perineal fistula, a temporary colostomy is needed for decompression; the definitive pull-through operation is generally deferred until the baby is about 1 year of age.

Myelomeningocele

- Myelomeningocele is a saccular outpouching of neural elements through a defect in the bone and the soft tissues of the posterior thoracic, sacral**,** or lumbar regions, the later compromising 80% of lesions.
- Myelomeningocele represents the most severe form of dysraphism involving the vertebral column.

Clinical manifestations

- Infants with myelomeningocele present with a spectrum of impairments, but the primary functional deficits are lower limb paralysis with sensory loss, bladder and bowel dysfunction, and cognitive dysfunction.
- Motor and sensory deficits are noted below the level of the lesion. The extent and degree of deficits depend on the location of the myelomeningocele, as well as the associated lesions:
  - A lesion in the low sacral region causes bowel and bladder incontinence associated with anesthesia in the perineal area**,** but with no impairment of motor function.
  - Newborns with a defect in the mid-lumbar region typically have a sac-like cystic structure covered by a thin membrane, which may rupture and leak CSF. Examination reveals flaccid paralysis of the lower extremities, absence of deep tendon reflexes, lack of response to touch and pain, and deformities (clubfeet, subluxation of the hips due to in utero hypokinesia). Constant urinary dribbling with retention overflow (neurogenic bladder) and a relaxed anal sphincter may be evident.
- Infants have an increasing neurologic deficit as the myelomeningocele extends higher into the thoracic region.
- Examination of the skull is important, as many cases are associated with hydrocephalus in association with a type II Chiari defect (cerebellar hypoplasia and varying degrees of caudal displacement of the lower brain stem into the upper cervical canal through the foramen magnum). Ocular muscle palsies, swallowing and eating problems**,** and abnormal phonation are signs of cranial nerve dysfunction related to brain stem affection which is also related to Chiari II malformation.
- Myelomeningocele often occurs with multiple system congenital anomalies. Commonly associated anomalies are facial cleft, heart malformations, and genitourinary tract anomalies.

Investigations

- Take chest radiographs to detect rib deformities and cardiac malformations; spine radiographs to detect vertebral anomalies, and x-ray hips to detect hip dysplasia or dislocation.
- Measure serum creatinine, if voiding patterns are abnormal.
- Perform ultrasonography of the urinary tract to assess possible hydronephrosis and/or structural abnormalities
- Take regular bacterial urinary cultures, if urinary tract infection is suspected.
- Perform brain CT, MRI and ultrasonography to detect hydrocephalus.

Prevention

Women of child-bearing age should consume 0.4 mg folic acid/day to reduce the risk of having a fetus affected with neural tube defect. Higher doses are recommended for women with prior affected offsprings.

Management

- Cesarean section improves survival and neuromotor outcome.
- Keep the newborn in prone position with a sterile saline moistened gauze sponge to reduce bacterial contamination and dehydration.
- Administer IV antibiotics: ampicillin and gentamicin to diminish risk of meningitis.
- Refer immediately to the neurosurgeon. Surgical closure of an open meningo-myelocele should be done on the first day of the life and ventriculo perotineal shunt catheter is usually placed. If the defect is covered with skin, elective repair can be done.

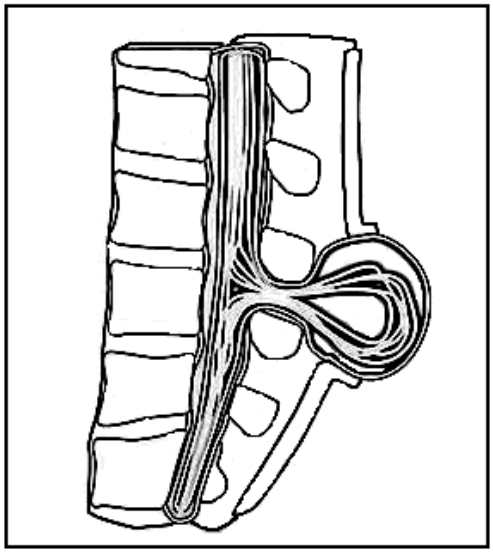


Figure (37-4): Myelomeningocele

Spina bifida occulta

- This anomaly consists of a midline defect of the vertebral bodies without protrusion of the spinal cord or meninges.
- No open skin defect is noted, but a patch of hair, lipoma, discoloration of the skin, or a dermal sinus in the midline of the lower back may be overlying a spinal cord defect.
- Dimples in the coccygeal region are not significant since they do not lie over any spinal cord segment.

Anomalies of the Extremities

Developmental dysplasia of the hip (DDH)

- The spectrum of presentations of DDH:
  - Simple acetabular dysplasia (femoral head may be retained within an inadequate acetabulum).
  - Acetabular dysplasia plus subluxation (femoral head moves slightly away from the acetabular medial wall).

- Dislocation of the hip joint (a complete loss of contact between the femoral head and acetabulum).

- DDH is more common among breech presentations, especially frank breech.
- It occurs more frequently in female infants.
- Any condition that leads to a tighter intrauterine space and, consequently, less room for normal fetal motion may be associated with DDH. These conditions include oligohydramnios, large birth weight, and first pregnancy.
- The dysplasia more often is unilateral with the left hip more frequently affected, but it may be bilateral.
- Diagnosed by Barlow and Ortolani tests:
  - Barlow provocative maneuver:
    - It assesses the potential for dislocation of a nondisplaced hip.
    - The examiner adducts the flexed hip and gently pushes the thigh posteriorly in an effort to dislocate the femoral head. In a positive test, the hip will be felt to slide out of the acetabulum. As the examiner relaxes the proximal push, the hip can be felt to slip back into the acetabulum **(Figure 37-5).**
  - Ortolani test**:**
    - It is the reverse of Barlow test.
    - The examiner attempts to reduce a dislocated hip. He grasps the infant's thigh between the thumb and index finger and, with the 4^{th} and 5^{th} fingers, lifts the greater trochanter while simultaneously abducting the hip. When the test is positive, the femoral head will slip into the socket with a delicate "clunk" that is palpable but usually not audible. It should be a gentle, non-forced maneuver **(Figure 37-5).**

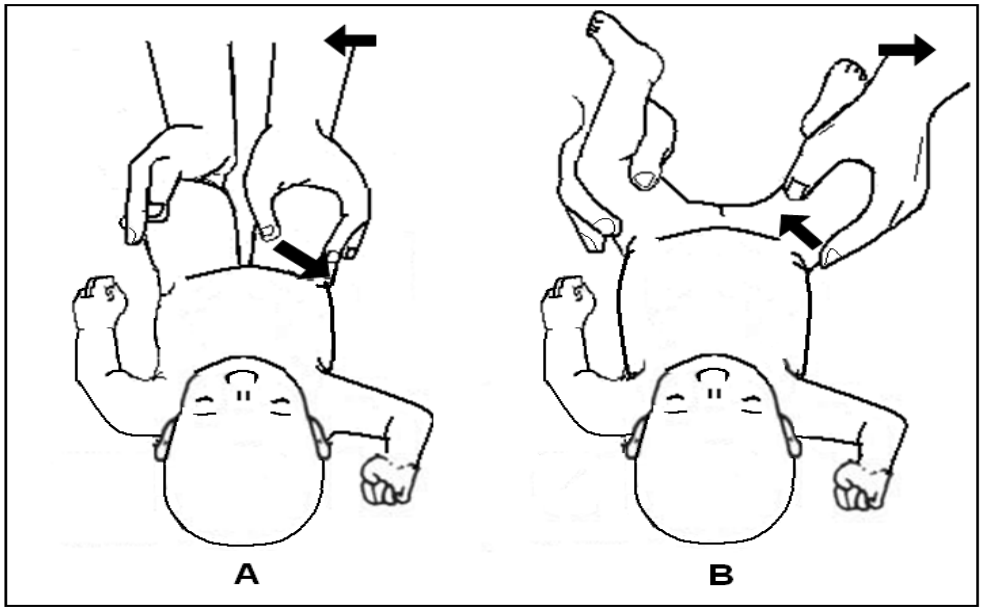


Figure (37-5): Maneuvers for developmental dysplasia of the hip

A) Barlow (dislocation) test, B) Ortolani (reduction) test

- Early diagnosis and treatment are essential to prevent permanent disability. Examination of the hips should be a routine screening test in any neonate.
- Ultrasonography is useful for diagnosis in high risk cases. It should be delayed until one month to avoid high incidence of false positive results.
- Treatment is individualized and includes positioning using a brace applied over the diapers or open surgical correction.

Anomalies of the Genitourinary System

Hypospadias

- This refers to a urethral opening that is on the ventral surface of the penile shaft.
- It is the most common urological anomaly. It affects 1 in 250 male newborns. There is a familial tendency.
- Approximately 60% of cases are distal, 25% are subcoronal or midpenile, and 15% are proximal.
- It presents by curved penis (chorda), deficient ventral prepuce, and abnormal meatal opening.
- It may be associated with undescended testes and hernias.

Management

- Circumcision should be avoided, because the foreskin is often used in the repair.
- The ideal age for repair in a healthy infant is 6-12 months.

Chapter 38

Inborn Errors of Metabolism

Inborn Errors of Metabolism

Inborn errors of metabolism (IEMs) comprise a large class of genetic diseases involving disorders of metabolism. The majority are due to defects of single genes that code for enzymes that facilitate conversion of various substances (substrates) into others (products). In most of the disorders, problems arise due to accumulation of substances which are toxic or interfere with normal function, or to the effects of reduced ability to synthesize essential compounds.

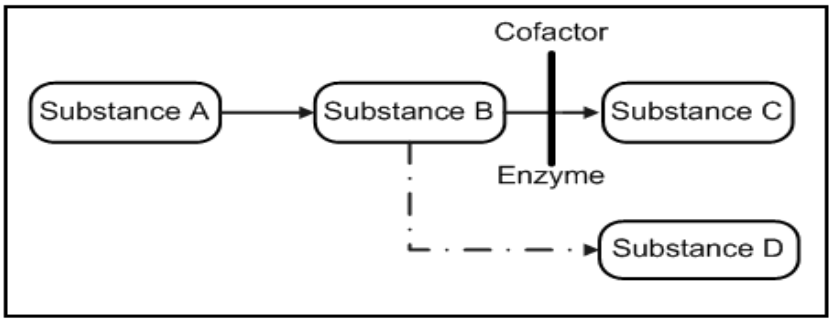


Figure (38-1): Pathogenesis of many IEMs

Incidence and Inheritance

- The overall incidence is as high as 1 in 2,000 live births.
- About 100 IEMs may present in neonatal period.
- Mostly transmitted as autosomal recessive genetic traits. However, some are X-linked (e.g., ornithine transcarbamolase (OTC) deficiency, Lesch-Nyhan syndrome).

Classification

IEM's can be categorized as:

- Disorders of carbohydrate metabolism (e.g., galactosemia, glycogen storage diseases)
- Disorders of amino acid metabolism (e.g., phenylketonuria, maple syrup urine disease)
- Disorders of organic acid metabolism (organic acidemias) (e.g., Isovaleric acidemia, propionic acidemia)
- Disorders of fatty acid oxidation and mitochondrial metabolism (e.g., defects in carnitine cycle, glutaric acidemia type II)
- Disorders of purine and pyrimidine metabolism (e.g., Lesch–Nyhan syndrome)
- Peroxisomal disorders (e.g., Zellweger syndrome)
- Lysosomal storage disorders (e.g., mucopolysaccharidosis, lipid storage disorders)
- Others:
  - Congenital adrenal hyperplasia (CAH)
  - Crigler-Najjar syndrome
  - α_1 antitrypsin deficiency
  - Canavan disease
  - Porphyrias

Clinical Manifestations

Clinical features are usually nonspecific and may simulate several other neonatal conditions, such as infections and cardiopulmonary dysfunctions.

It is important to have a high index of suspicion of IEMs in sick neonates since most of these can be lethal unless diagnosed and treated immediately.

A history of parental consanguinity, and unexplained neonatal deaths in the family should alert the physician to the possibility of IEMs.

IEMs can be divided into two groups on the basis of timing and pattern of presentation in newborn infants.

Time and pattern of onset

Intoxication type

- A newborn infant, who is born healthy and deteriorates clinically, after an initial symptom-free period**,** in an unexpected and "mysterious" manner (e.g., organic acidemias, and urea cycle defects).
- The first signs are poor feeding and vomiting, followed by lethargy, apnea, seizures, and coma.

Energy deficiencies

This is an overwhelming neurologic illness without apparent symptom-free period (e.g., mitochondrial and peroxisomal disorders).

Patterns of presentation

One or more of the following presentations:

Neurological abnormalities

- Coma
- Encephalopathy and seizures
- Seizures
- Hypotonia
- Hypertonia
- Opisthotonus

Disorders of acid-base status

Metabolic acidosis with a high anion gap

Hypoglycemia

Liver dysfunction

- Cholestasis (e.g., galactosemia)
- Hepatomegaly

Dysmorphic features

- Examples include coarse facial features, abnormal skin and hair, abnormal eyes, macroglossia, and macrocephaly.

Cardiac diseases

- Cardiomegaly
- Arrhythmias

Abnormal urine and body odor

- Examples include disorders such as maple syrup urine disease, glutaric acidemia, isovaleric acidemia.

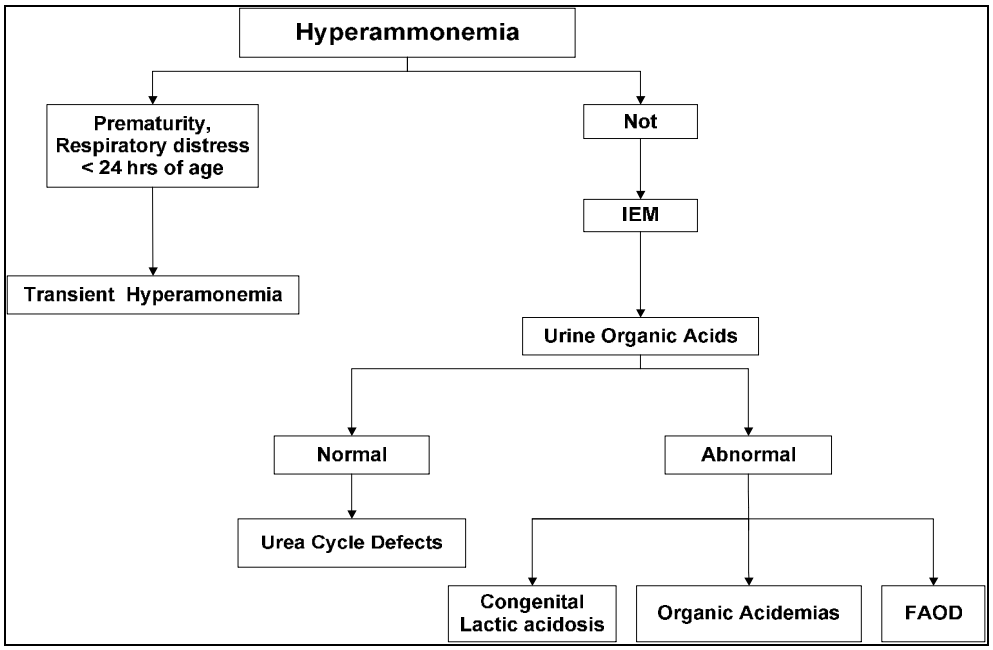
Respiratory abnormalities

- Hiccups
- Apneas
- Irregular breathing
- Hyperpnea

Approaches to Specific Laboratory Abnormalities

Approach to a neonate with hyperammonemia

- The normal plasma ammonia concentration is <50 μmol/L. It may be modestly elevated in cases of high protein intake, struggling or a hemolysed blood sample.
- In a sick neonate, plasma ammonia >150 μmol/L indicates pathological hyper-ammonemia.
- In septic neonates and in cases of perinatal asphyxia, plasma ammonia concentrations may increase to 180 μmol/L. Infants with IEMs presenting in the neonatal period usually have concentrations >200 μmol/L.
- The clinical presentation of hyperammonemia in neonates is that of an overwhelming illness, that rapidly progresses from poor feeding, vomiting, lethargy, or irritability and tachypnea, to fits, coma, and respiratory failure.
- In this condition, the following tests should be done:
  - Blood gases and pH
  - Plasma chemistry: urea, electrolytes, glucose, and creatinine
  - Liver function tests and clotting studies
  - Plasma amino acids
  - Urine organic acids, orotic acid, and amino acids
  - Plasma free carnitine and acylcarnitine

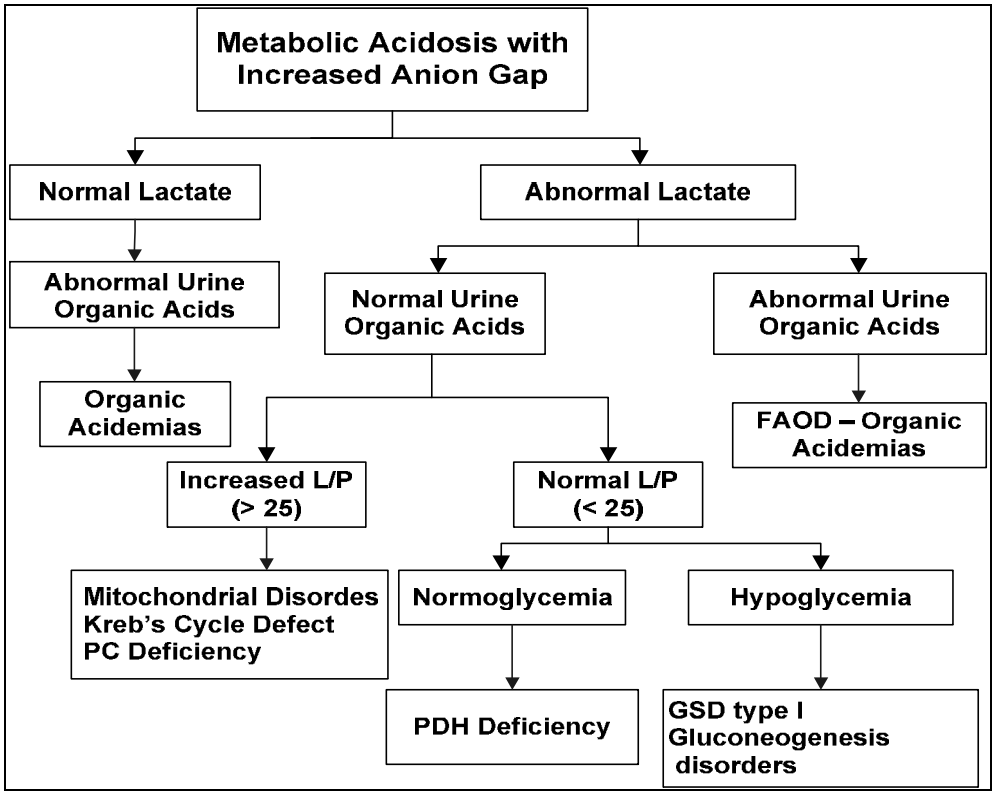


IEM: inborn error of metabolism, FAOD: Fatty acids oxidation defects

Figure (38-2): Approach to neonatal hyperammonemia

Approach to a neonate with metabolic acidosis

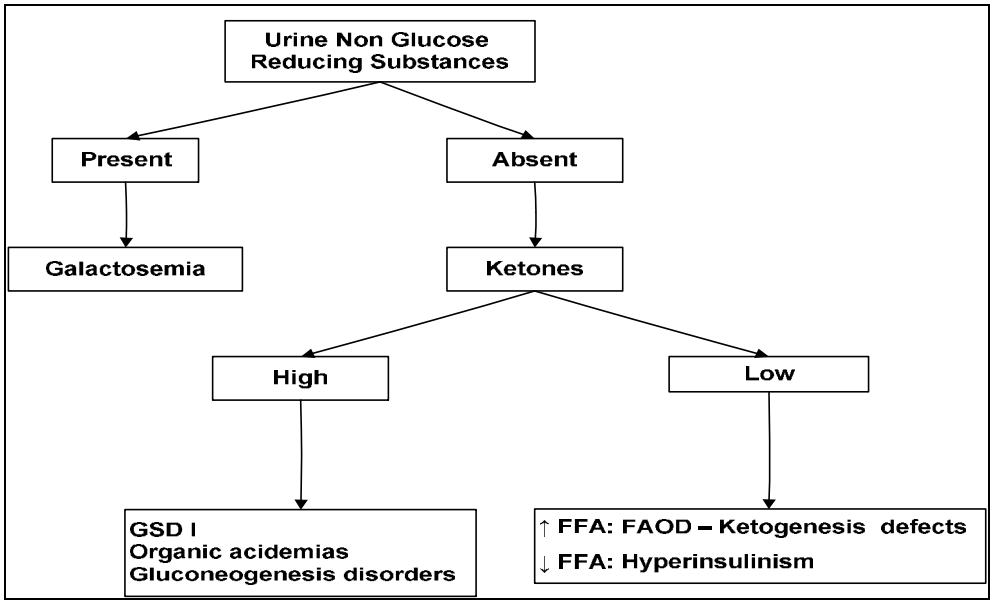
Anion gap is the measurement of the difference between the sum of routinely measured cations minus the sum of the routinely measured anions in the blood or plasma **(Refer to Chapter 23).**



L/P ratio: Lactate/pyruvate ratio, FAOD: Fatty acids oxidation defects, PC deficiency: Pyruvate carboxylase, PDH deficiency: Pyruvate dehydrogenase, GSD I: Glycogen storage disease type 1

Figure (38-3): Approach to neonatal metabolic acidosis

Approach to a neonate with persistent hypoglycemia



FAOD: Fatty acids oxidation defects, GSD I: Glycogen storage disease type 1,
FFA: Free fatty acids

Figure (38-4): Approach to a neonate with persistent hypoglycemia

Investigations

First line laboratory studies

- CBC with differential: to screen for neutropenia and thrombocytopenia in organoic acidemias
- Serum electrolytes, blood gases (calculate anion gap) and plasma urea (low urea in UCD's), and creatinine
- Blood glucose
- Plasma ammonia: use an arterial or uncuffed venous sample (no tourniquet), keeping on ice and assaying promptly
- Plasma lactate and pyruvate
- Liver function tests and coagulation profile
- Urine ketones and reducing substances

Second line laboratory studies

- Plasma amino acid analysis
- Urine organic acid analysis
- Plasma carnitine and acylcarnitine profile: elevated (e.g., FAOD, organic acidemias)
- Plasma uric acid: elevated in GSD type 1 and decreased in xanthine dehydrogenase deficiency
- CSF amino acids: increased CSF to plasma gylcine in non-ketotic hyperglycinemia (NKH)
- Peroxisomal function tests: VLCFA's and phytanic acids

Specific diagnostic tests

- Enzyme assay: e.g. galactose-1-phosphate uridyltransferase (GALT) in galacosemia
- Tissue biopsy
- Skin biopsy and fibroblast cultivation for specific enzyme testing
- DNA analysis for gene mutation

Management

General principles

Rescue treatment

- While the infant is acutely ill, stop oral intake and withhold all protein for 48-72 hrs, and until an aminoacidopathy, organic acidemias and urea cycle defects have been excluded.
- Maintain adequate calorie intake:
  - Maintain at least 20% greater than the ordinary needs. Give glucose 10-15% IV at a rate high enough (8-10 mg/kg/minute, even if insulin is required to keep the blood glucose level normal).
  - IV lipids are given only after ruling out a primary or secondary fatty acid oxidation defect.
- Ringer's lactate should not be used for fluid or electrolyte therapy in a neonate with a known or suspected metabolic disorder.
- Correct dehydration, acidosis and hypoglycemia.
- Eliminate toxic metabolites:
  - L-Carnitine: may be administered empirically in life threatening situations associated with primary metabolic acidosis, hyperammonemia, or organic acidemias. Give dose 25 mg/kg/dose every 6 hrs.
  - Give sodium benzoate for hyperammonemia.
  - Initiate peritoneal dialysis or hemodialysis; in cases of:
    - Coma
    - Hyperammonemia >500 mg/dl
    - Intractable metabolic acidosis
    - Severe metabolic disturbances
- Cofactor supplementation may be useful in cases of vitamin-responsive enzyme deficiencies; these include:
  - Thiamine (200 mg/day)
  - Biotin (10 mg/day)
  - Vitamin C (100 mg/kg/day)
  - Riboflavin (100-300 mg/day)
  - Pyridoxine (50-500 mg/day)
  - Hydroxycobalamin (20 mg/day)

- Treat the precipitating factors (e.g. infection)**.**
- Monitor the infant clinically and biochemically.
- If clinical improvement is observed and a final diagnosis has not been established, some aminoacid intake should be provided after a maximum of 2-3 days of complete protein restriction. Essential aminoacids or total protein can be provided PO or IV at an initial dose of 0.5 gm protein/kg/24 hrs and increased incrementally to 1.0 gm/kg/24 hrs, holding at that level until the diagnostic evaluation is complete and plans can be made for definitive long-term therapy.

Chronic therapy

- Dietary supplementation or replacement (e.g., cornstarch) several times a day helps to prevent infants with glycogen storage disease from becoming hypoglycemic).
- Restrict intake of substrates that increases toxic materials, (e.g., give lactose free milk in galactosemia).
- Administer pharmacologic therapy to increase activity of abnormal cofactor-dependent enzymes, (e.g., thiamine [B1], biotin, riboflavin [B2], cobalamin [B12]).
- Bone marrow or organ transplantation may be needed in some disorders.
- Enzyme replacement or gene therapies may be required.

Postmortem Diagnosis

If an infant is dying or has died of what may be a metabolic disease, it is very important to make a specific diagnosis in order to help the parents with genetic counseling. Specimens that should be collected include:

- Blood, both clotted and heparinized
- Urine, refrigerated
- Spinal fluid, refrigerated
- Skin biopsy
- Liver biopsy samples

Newborn Screening

Many IEMs could be detected by the newborn screening tests using tandem mass spectrometry (TMS) for early diagnosis and treatment which can result in a better outcome.[1]

Classic Two Examples of IEMs

Galactosemia

Inheritance and enzyme deficiency

This is an autosomal recessive trait due to deficiency of galactose-1-phosphate uridyl transferase (GALT).

[1]**This service can be provided in some university hospitals.**

Clinical manifestations

Clinical manifestations develop after ingestion of lactose in a standard formula or breast milk in the form of hypoglycemia, cholestasis, hepatosplenomegaly, vomiting, irritability, seizures, cataract and increased risk of *E-coli* sepsis.

Investigations

- Non glucose reducing substance in urine
- Enzyme assay

Management

Substitute a lactose-free formula for breastfeeding or for the standard formula, and later with a galactose free diet.

Congenital adrenal hyperplasia (CAH)

CAH encompasses a group of autosomal recessive disorders, each of which involves a deficiency of an enzyme required for the adrenocortical synthesis of cortisol from cholesterol resulting in a secondary increase in ACTH. Approximately >90% of cases are due to a deficiency of the enzyme 21-hydroxylase.

CAH is a common cause of ambiguous genitalia that may lead to life-threatening adrenal insufficiency within the first weeks of life.

Clinical manifestations

Two forms are seen in neonates: a simple virilizing form, in which the enzyme deficiency is partial, and a salt-losing form, in which the enzyme deficiency is more complete.

Simple virilizing form

- At birth the spectrum in females ranges from mild clitoromegaly, to complete male differentiation (except that the testes are impalpable).

Salt-losing form

- Female newborns will show ambiguous external genitalia. Male newborns will not appear obviously abnormal, because the genitalia are normal, and may not be diagnosed unless metabolic emergencies occur.
- Salt-wasting adrenal crises are not present at birth and usually do not develop until 5^{th} to 14^{th} day of life (and as late as one month).
- Early manifestations are nonspecific and include lethargy, poor appetite, projectile vomiting, and weight loss.
- Hyperkalemia, hyponatremia, and metabolic acidosis may be seen early.
- Severe manifestations may occur within 1-2 days, including dehydration, azotemia, hypotension, muscle weakness, obtundation, a gray or cyanotic appearance, cold and clammy skin, hyperkalemic cardiac conduction abnormalities, and hyponatremic or hypoglycemic seizures.

Differential diagnosis

- Sepsis
- Congenital heart disease

- Pyloric stenosis (metabolic alkalosis rather than metabolic acidosis)

Diagnosis

Clinical

21-hydroxylase deficiency should be considered in:

- A female infant (with any masculinization of the external genitalia) or a male infant who develops symptoms or signs of adrenal insufficiency or crisis,
- A newborn infant who has a family history of CAH or an unexplained death in infancy.

Laboratory

- Hyperkalemia, hyponatremia, and hypoglycemia.
- Increased level of serum 17-hydroxyprogesterone (the most useful diagnostic test)
- Urinary steroid profile, if available
- Elevation in adrenal androgens and ACTH levels

Prenatal diagnosis

Measurement of 17-hydroxyprogesterone in the amniotic fluid

Management

- If the infant is in shock, give 20 ml/kg normal saline 0.9% to restore intravascular volume.
- Give fluid replacement: continuous IV infusion of 2,500-3,000 ml/m^2/24 hrs normal saline in glucose 5% (1:1).
- Treat hypoglycemia, if present, by IV bolus of 2-4 ml/kg glucose 10%.
- Glucocorticoid therapy: hydrocortisone hemisuccinate 50-100 mg/m^2 (~25 mg) should be given IV bolus immediately, followed by 100 mg/m^2/24 hrs by continuous drip or divided every 6 hrs. Once the clinical condition improves, taper the dose by 1/3 per day to reach the maintenance dose (10-15 mg/m^2/day orally divided in 3 doses). For acute illness, stress doses of hydrocortisone should be given at double or triple the maintenance dose.
- Mineralocorticoid replacement (9 α-fludrocortisone, 0.05-0.2 mg orally every 24 hrs) is needed in severe salt-wasting cases.
- Acidosis, hypoglycemia, and hyperkalemia should be managed, and the patient should be monitored for potassium toxicity.
- Body surface area (BSA) can be calculated using the following the Haycock formula:

$$\textbf{BSA (m}^2\textbf{)} = \textbf{Weight (kg)}^{0.5378} \times \textbf{Length (cm)}^{0.3964} \times \textbf{0.024265}$$

- Average body surface area for a neonate is 0.25 m^2.

Chapter 39

Developmentally Supportive Care

Developmentally Supportive Care

A great number of newborns admitted in the neonatal care units including those with minor and transient illness who displayed normal results in early motor and cognitive tests ultimately prove to have learning disabilities at school age.

The preterm infant's rapidly developing brain is particularly vulnerable to a stressful environment. The detrimental effects of this stress could have short and long term implications for compromised neurobehavioral development.

Developmental care is a philosophy of care that requires rethinking the relationships between the infant, family and healthcare providers in the NICU.

Developmental care is an individual care that is designed to minimize the stress of the NICU environment. It includes regular evaluation of the infant's behavior and providing interventions that support infant's growth and development. This care focuses on the infant as being competent and active in participating in his own care, and in shaping his own development.

Neurobehavioral Assessment

Stress responses

- Autonomic signs: changes in color, heart rate, and respiratory patterns as well as visceral changes such as gagging, hiccupping, vomiting, and stooling.
- Motor signs: facial grimacing, gaping mouth, twitching, hyperextension of limbs, finger splaying, back arching, flailing, and generalized hypertonia or hypotonia.
- State alterations: rapid state transition, diffuse sleep states, irritability, and lethargy.
- Changes in attention or the interactional availability of preterm infants, exhibited by covering eyes/face, gaze aversion, frowning, and hyperalert or panicky facial presentation.

Self-regulating behavior

Preterm infants elicit a number of self consoling behaviors that facilitate their coping responses to stress. These include hand or foot bracing, sucking, bringing hands to face, flexed positioning, cooing, grasping of linens or own body parts.

Chronic Stress in the Neonatal Care Units

Results from:

- Disturbance of procedures
- Noise and bright light
- Inappropriate handling
- Inappropriate positioning
- Pain and stress from diseases

Goal of Developmental Care

The goal is to enhance infant recovery by:

- Reducing infant stress in the NICU.
- Promoting neurobehavioral organization.

- Developing infant's self-regulatory skills.
- Facilitating parent-infant interaction.

Components of Developmental Care

Management of the environment

Limiting noise

- The auditory system functions at 25-27 weeks' gestations.
- NICU infants are exposed to a continuous noise 24 hrs a day for days, weeks, or months. They are more prone to cochlear damage because of concomitant effects of noise and ototoxic medications.
- Neonatal illnesses, drug therapy, and acoustic insults account for the increased risk for sensorineural hearing loss in NICU infants. Preterm infants have 5 times greater risk of developing hearing loss as compared to term babies.
- The NICU environment usually provides sound levels between 80-120 dB.
- The American Academy of Pediatrics (AAP) recommends that noise levels should not exceed 40-45 dB in NICU (<35 dB is needed to allow quiet sleep).

Sources of noise in the NICU

- Telephone ring
- Equipment alarms
- Air compressor
- Carting of equipment
- Bubbling in ventilator circuit
- Tapping incubator with fingers
- Loud talking during the rounds

Consequences of loud sound

- Startle response
- Apnea
- Bradycardia or tachycardia
- Oxygen desaturation
- Sudden elevation of blood pressure possibly leading intraventricular hemorrhage
- Sleep problems and restless, possibly leading to depletion of energy reserves and poor weight gain
- Hearing impairment; with repeated exposure over time

Interventions to decrease noise in the NICU

- Modify behaviors
- Institute quiet hours

- Minimize environmental noise
- Talk softly at the bedside
- Attend to alarms promptly and set alarm volume as low as is clinically safe
- Decrease volume/tone of telephone ring and no radios in rooms
- Close incubator doors quietly
- Do not tap or bang on incubator
- Discourage the use of the top of the incubator as a writing surface and/or storage area
- Ensure CPAP and ventilator tubing is regularly cleared of water

Controlling light

- For ease of observation, most neonatal care units maintain high intensity of day and night illumination ranging between 50-150 foot candles.
- Procedure lights and phototherapy units may provide light intensity between 200-400 foot candles resulting in several adverse consequences.

Adverse consequences of bright light

- Oxygen desaturation
- Damage of developing optic structures by constant light exposure, and squint
- Increased incidence of retinopathy
- Poor circadian rhythms; possibly leading to decreased release of growth hormone and leading to poor weight gain
- Altered sleep patterns and prolonged rapid eye movement sleep leading to apnea

Interventions to control light in the NICU

- Individual lighting system is recommended.
- The windows of NICU should be covered with screens.
- Minimize light levels, where appropriate.
- Protect infant's eyes from bright light during care giving procedures.
- Reduce exposure to light in incubators by using a cover and attach the infant to a vital sign monitor.
- Provide eye protection for infants receiving phototherapy and shield light from infants in adjacent incubators/cots.
- The light should be dimmed at night to simulate day-night pattern to promote hormonal surge and physical growth.

Positioning and nesting

- Neuromuscular immaturity, weak muscle tone and the effects of gravity on the preterm infants can lead to positioning disorders such as widely abducted hips (frog-leg position), retracted and abducted shoulders, increased trunk extension with arching of back and ankle and foot eversion. These complications may lead to difficulties with normal development of body movement and control in childhood.

- Research promotes the use of a variety of positions for preterm infants:
  - Prone positioning in some infants may enhance oxygenation and promote quiet sleep.
  - Side lying positioning, with the back well supported in a nest, provides opportunities for limb and trunk flexion and hand to mouth contact.
  - The less favored position is the supine position that requires 'nesting' with close but flexible boundaries around the infant's body.
- A soft blanket rolled into a nest encourages flexion of lower limbs, brings shoulders forward, and offers containment boundaries.
- Use a hip roll to provide flexion when infant is in prone position.
- Maintain hands positioned near the mouth to provide the infant with midline orientation and to facilitate hand to mouth activities which are self soothing.
- Swaddling simulates in-utero feeling of lack of space and it makes the infant less jittery and less prone to startle. Always swaddle infant when transferred to and from incubator.
- During positioning or doing procedures (e.g., suctioning) "containment" should be provided (holding the arms and legs of the infant close to the midline and supporting his head and buttocks).
- A change in position is recommended every 4 hrs or at the infant's physiological status.

Figure (39-1): Nesting

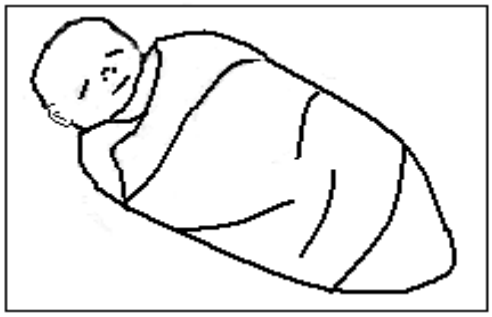


Figure (39-2): Swaddling

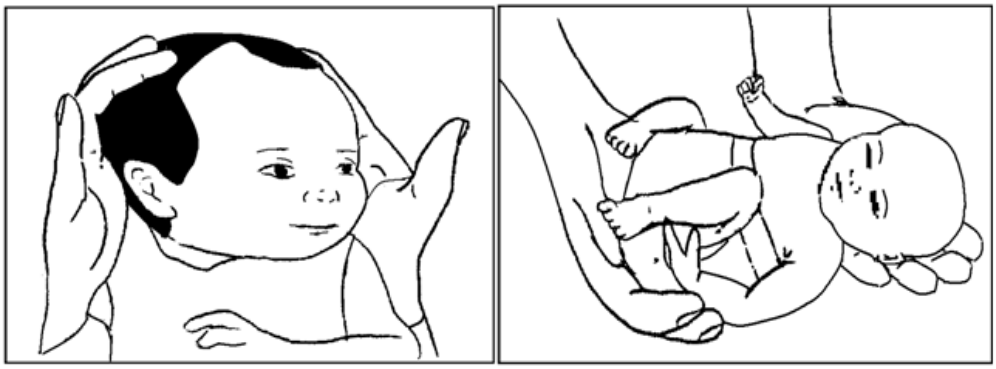


Figure (39-3): Containment

Figure (39-4): Light touch, and resting a hand

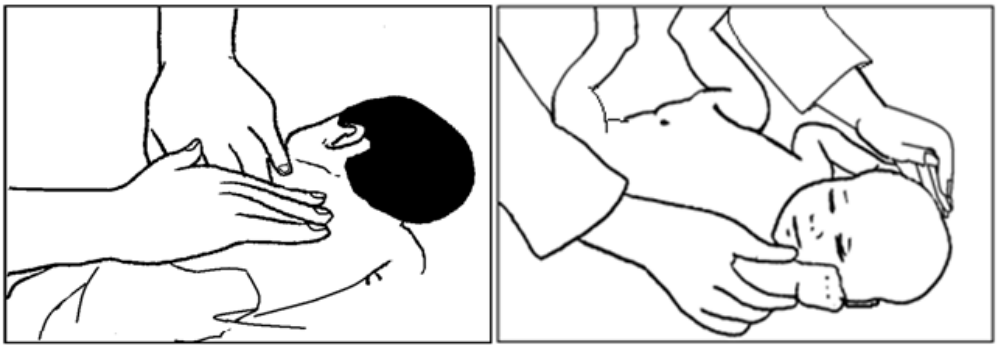


Figure (39-5): Massage

Benefits of optimum positioning

- It reduces complications
- It maintains better oxygenation and temperature control and sleep pattern
- Prone position, compared to supine, is associated with more quiet sleep and less active sleep or crying. Quiet sleep, in turn, is associated with improved lung volume, more stable respiration, less apnea, and improved oxygenation
- Prone position or right lateral position is associated with improved gastric emptying
- It improves neurobehavioral development
- It assures unobstructed venous return to the head

Handling and clustering of care

- Handling is a source of continuous bombardment and results in physiologic instability. Care giving represents a significant stress to the infant.

- Rough handling results in the infant crying, squirming and recoiling his arms and legs. Also, it may lead to hypoxemia and sudden elevation of blood pressure with risk of development of intraventricular hemorrhage.
- Excessive handling of preterm or sick neonates results in significant consequences, such as:
  - Blood pressure changes
  - Alteration of cerebral blood flow
  - Hypoxemia

Interventions

- Provide opportunities for undisturbed rest. Cluster care but avoid completing a number of potentially distressing interventions at the same time.
- Prepare infant for handling with a soft voice or gentle touch to help promote physiological stability and state organization.
- Gently handle the infant to avoid stressful reactions (e.g., oxygen desaturation, arching) and enable the infant to become calm and rest between care-giving.
- Identify signs of stress before physiologic compromise. If an infant indicates signs of stress during handling, stop and provide 'time out' for the infant to recoup from that intervention.
- Observe for 5-10 minutes after care.
- Painful procedures should be minimized to those absolutely indicated. During those necessary procedures, it is essential to provide containment and adequate pain relief **(Refer to chapter 40).**
- To soothe infant during uncomfortable procedures contain infant-head and hands in midline, shoulders forward, lower limbs flexed and adducted towards the midline.
- When clinically possible, consider day/night patterns for interventions (e.g., weigh infant and change bedding in the daytime).
- Nonpainful light touch such as stroking (the head, trunk, or hands) of a physiologically stable preterm infant during care is associated with increased activity and alertness, more rapid weight gain, less crying and apnea and enhanced developmental status.
- Hand placement (on the head, lower back, or abdomen) without stroking has a soothing effect (increase quite sleep, decrease behavioral distress).
- Massage: the touching and stroking of massage stimulate nerve pathways and aid in myelination. Researchers found that applying massage therapy for medically stable preterm growers, for 15-minutes periods during three consecutive hours every day for 10 days, was associated with more rapid weight gain, better motor activity, and fewer stress behavior in these babies.

Co-bedding of multiples

- Co-bedding means the practice of placing medically stable twins, and higher-order multiples together in the same warmer, incubator, or crib.

- Postulated advantages of co-bedding are:
  - Improved stability of temperature, heart rate, and respirations
  - Improved rate of growth and development
  - Co-regulation of sleep-wake cycles
  - Decreased length of hospitalization
- Eligible multiples need to be free of infection, have stable temperature in an open crib, have no indwelling catheters, and be on room air or nasal cannula.
- Color coding of all equipment and monitors is used to ensure proper identification. The parents are required to sign a consent form.

Figure (39-6): Co-bedding of multiples

Non-nutritive sucking (NNS)

- Non-nutritive sucking (NNS) is the sucking activity in which no fluid or nutrition is delivered to the infant.
- It can be applied by making the infant suckles on his/her mothers' emptied breast or a pacifier during gavage tube feeds.
- NNS is associated with:
  - Increased readiness (decrease time) to nipple feeding, fewer gavage feedings, and acceleration of the sucking reflex, therefore facilitating transition to oral feedings.
  - Increased insulin and gastrin secretions that stimulate digestion and storage of nutrients.
  - Improved gastrointestinal motility.
  - Better weight gain.
  - Increased oxygenation.
  - Decreased procedural pain and tension due to release of hormones similar to morphine in the brain.
  - Decreased hospital stay.

N.B.: Concerns exist that pacifier use for NNS may impede breastfeeding for preterm infant.

Kangaroo Care

Definition

A universally available and biologically sound method of care for all newborns, but in particular for premature babies, with three components:

- Skin-to-skin contact
- Exclusive breastfeeding
- Support to the mother infant dyad: never separate mother and infant.

It is a form of parental care-giving where the newborn low birth weight or premature infant is intermittently nursed skin-to-skin in a vertical position between the mother's breasts or against the father's chest for a non-specific period of time. The infant's head is turned so that the ear is above the parent's heart.

Benefits of kangaroo care

- Maintaining physiological stability: thermal stability, improved oxygenation, decreased apnea and bradycardia, and lowered energy expenditure.
- Increasing immunity.
- Optimising breastfeeding; longer duration and early initiation.
- Facilitating and enhancing parent-infant bonding and parental satisfaction.
- Enabling parents to become sensitive care givers.
- Helping babies sleep more restfully.
- Improving weight gain.
- Relieving pain.
- Cuddling to stimulate pressure receptors that reduce levels of the stress hormone cortisol, lowering heart rate and blood pressure, and improves digestion.
- Shortening hospitalization period.
- Possibly reducing the neonatal mortality rate.

Criteria to suggest that the mother adopts kangaroo mother care (KMC)

- Willingness: mother must be willing to provide KMC.
- Full-time availability to provide care: other family members can offer intermittent skin-to-skin contact but they cannot breastfeed.
- General health: if the mother is ill, she should recover before initiating KMC.
- Being close to the infant: she should either be able to stay in hospital until discharge or return when her infant is ready for KMC.
- Supportive family to deal with other responsibilities at home.
- Supportive community to enable families to adopt KMC.

Infants appropriate for kangaroo care

- The ability to feed (to suck and swallow) is not an essential requirement. KMC can begin during tube-feeding. Once the infant begins recovering, discuss KMC with the mother.
- Infants should be physiologically stable with a body temperature of 36°C or higher.
- If apnea or bradycardia is a problem, it must be self-resolving or require only minor stimulation to correct.
- Infants receiving phototherapy can be removed from phototherapy for short periods.
- Short KMC sessions can begin during recovery when infant still requires medical treatment (IV fluids, low oxygen). In special situations, infants requiring CPAP or even assisted ventilation have received this care successfully.

Initial management guidelines

- Physicians and nurses should decide which infants are appropriate for KMC and provide parents with sufficient information describing the advantages of the technique.
- Once the decision has been made, the infant's temperature should be assessed at 36°C or greater and documented on the flow sheet.
- A skin temperature probe can be left on and all other monitoring wires, intravenous lines and respiratory support tubes should be secured.
- The infant can be undressed except for a diaper. A hat is generally not necessary unless the infant weighs less than 1,000 gm.
- Preparation of the mother includes encouraging her to wear a front-opening shirt or cover gown and providing as much privacy and quietness as possible. Fathers can also hold an infant this way.

Kangaroo positioning

- Place the infant between the mother's breasts in an upright position.
- Secure him/her with the binder firmly enough so that when the mother stands up the infant does not slide out. The head, turned to one side, is in a slightly extended position (keeps the airway open and allows eye-to-eye contact between the mother and the infant). The top of the binder is just under infant's ear.
- The hips should be flexed and extended in a (frog) position; arms should also be flexed.
- Make sure that the tight part of the cloth is over the infant's chest. Infant's abdomen should not be constricted and should be somewhere at the level of the mother's epigastrium.

Monitoring the neonate

- Once the infant has been successfully transferred to the parent, the infant's vital signs and oxygenation status should be monitored, and adjustments made based on the infant's status.

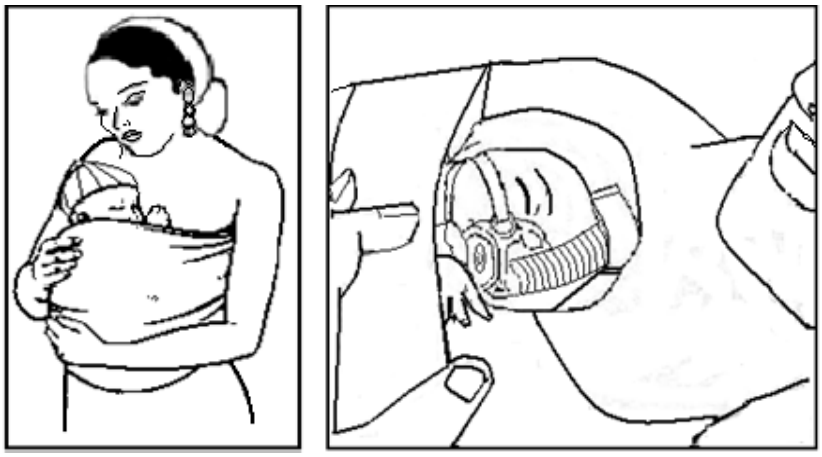


Figure (39-7): Kangaroo mother care

Signs of stress

- The infant should be returned to the incubator if any persisting signs of stress are identified, including tachypnea, tachycardia, temperature instability, or oxygen desaturation.
- The length of time for holding is individually based and depends on the neonate's status and parental comfort.

Family centered care

- Family centered care is becoming a standard of care in NICUs. It includes involvement of parents, as much as possible, in the care of their infants in NICUs, and promoting infant parent bonding.
- Family-centered neonatal care should be based on open and honest communication between parents and physicians.
- Parents and physicians should work together to:
  - Develop policies that promote parenting skills, to encourage maximum involvement of parents with their hospitalized infants.
  - Ensure safety and efficacy of neonatal treatments.
  - Promote long-term follow-up for all high-risk NICU survivors.

Benefits of Developmental Care

- Reduce length of stay.
- Reduce days on ventilator and oxygen.
- Increase daily weight gain.
- Allow earlier nipple feeds.
- Reduce incidence of IVH and ROP.
- Reduce need for sedation.
- Improve infant/parent interaction.
- Yield a favorable long-term developmental outcome.

Chapter 40

Neonatal Pain Management

Neonatal Pain Management

Stress is defined as a physical, chemical, or emotional factor that causes bodily or mental tension and may be a factor in disease causation. Pain is always stressful, but stress is not necessarily painful.

Prevention of pain in neonates is important not only because it is an ethical expectation but also because repeated painful exposures can have deleterious consequences. These consequences include altered pain sensitivity (which may last into adolescence) and permanent neuroanatomic and behavioral abnormalities.

Principles of Neonatal Pain and Stress Management

According to the initial management guideline of the Committee on the Fetus and Newborn of the American Academy of Pediatrics (AAP), principles of pain management include:

- Neuroanatomic components and neuroendocrine systems of the neonate are sufficiently developed to allow transmission of painful stimuli.
- Exposure to prolonged or severe pain may increase neonatal morbidity.
- Infants, who have experienced pain during the neonatal period, respond differently to subsequent painful events.
- Severity of pain and effects of analgesia can be assessed in the neonate using validated tools.
- Newborn infants usually are not easily comforted when analgesia is needed.
- A lack of behavioral responses (including crying and movement) does not necessarily indicate the absence of pain.

Evaluation

- Because neonates cannot verbalize their pain, they depend on others to recognize, assess, and manage their pain. Gestational age must be considered as the stress response of the preterm infant is less competent than that of the more mature infant.
- Reliable pain measures used to assess acute pain in neonates:
  - Physiologic indicators: include changes in heart rate, respiratory rate, blood pressure, oxygen saturation, vagal tone, palmer sweating, and plasma cortisol or catecholamine concentrations.
  - Behavioral indicators: include changes in facial expressions, body movements, and crying (these may be absent in some neonates who are neurologically impaired or pharmacologically paralyzed).
- Recommended assessment tools:
  - Premature Infant Pain profile (PIPP): the only validated method for pain assessment among preterm infants
  - Behavioral Pain Score (BPS)
  - Neonatal Infant Pain Scale (NIPS)

Table (40-1): Premature infant pain profile (PIPP)

Indicator	Finding	Points
Gestational age	≥36 weeks	0
	32 weeks to 35 weeks/6 days	1
	28 weeks to 31 weeks/6 days	2
	<28 weeks	3
Behavioral state	active/awake eyes open facial movements	0
	quiet/awake eyes open no facial movements	1
	active/sleep eyes closed facial movements	2
	quiet/sleep eyes closed no facial movements	3
Heart rate maximum	0-4 beats per minute increase	0
	5-14 beats per minute increase	1
	15-24 beats per minute increase	2
	≥25 beats per minute increase	3
Oxygen saturation minimum	0-2.4% decrease	0
	2.5-4.9% decrease	1
	5.0-7.4% decrease	2
	7.5% decrease or more	3
Brow bulge	none (≤9% of time)	0
	minimum (10-39% of time)	1
	moderate (40-69% of time)	2
	maximum (≥70% of time)	3
Eye squeeze	none (≤9% of time)	0
	minimum (10-39% of time)	1
	moderate (40-69% of time)	2
	maximum (≥70% of time)	3
Nasolabial furrow	none (≤9% of time)	0
	minimum (10-39% of time)	1
	moderate (40-69% of time)	2
	maximum (>70% of time)	3

Scoring instructions

- Score gestational age before examining infant.
- Score the behavioral state before the potentially painful event by observing the infant for 15 seconds.
- Record the baseline heart rate and oxygen saturation.
- Observe the infant for 30 seconds immediately following the painful event. Score physiologic and facial changes seen during this time and record immediately.

Premature infant pain profile = Sum (points for all 7 indicators).

Interpretation:

- Minimum score: 0 (Scores of ≤6 indicate minimal or no pain)
- Maximum score: 21
- The higher the score the greater the pain behavior.

Stevens et al: Premature Infant Pain Profile: Development and initial validation. Clinical Journal of Pain, 1996; 12: 13-22.

Table (40-2): Neonatal infant pain scale (NIPS)

Pain Assessment		Score
Facial expression		
Relaxed muscles	Restful face, neutral expression	0
Grimace	Tight facial muscles; furrowed brow, chin, jaw, (negative facial expression-nose, mouth and brow)	1
Cry		
No Cry	Quiet, not crying	0
Whimper	Mild moaning, intermittent	1
Vigorous Cry	Loud scream; rising, shrill, continuous (Note: Silent cry may be scored if baby is intubated as evidenced by obvious mouth and facial movement	2
Breathing Patterns		
Relaxed	Usual pattern for this infant	0
Change in Breathing	Indrawing, irregular, faster than usual; gagging; breath holding	1
Arms		
Relaxed/Restrained	No muscular rigidity; occasional random movements of arms	0
Flexed/Extended	Tense, straight legs; rigid and/or rapid extension, flexion	1
Legs		
Relaxed/Restrained	No muscular rigidity; occasional random leg movement	0
Flexed/Extended	Tense, straight legs; rigid and/or rapid extension, flexion	1
State of Arousal		
Sleeping/Awake	Quiet, peaceful sleeping or alert random leg movement	0
Fussy	Alert, restless, and thrashing	1

Neonatal infant pain scale = Sum (points for the 6 parameters)

Interpretation:

- Minimum score: 0
- Maximum score: 7

Limitations:

- A falsely low score may be seen in an infant who is too ill to respond or who is receiving a paralyzing agent.

Lawrence J et al: The development of a tool to assess neonatal pain. Neonatal Network. 1993; 12 (6 September): 59-66.

Painful Procedures in the NICU

- Diagnostic (e.g., arterial puncture, venipuncture, heel prick, lumbar puncture)
- Therapeutic (e.g., umbilical catheterization, chest physiotherapy, dressing change, removal of adhesive tape, nasogastric tube insertion, peripheral venous catheterization, tracheal intubation/extubation and tracheal suctioning)

- Surgical (e.g., circumcision, drainage of an abscess, PDA ligation)

Pain Management (Prevention and Treatment)

Nonpharmacological approaches

(Refer to Chapter 39)

Environmental modification

- Decrease bright lights
- Avoid loud noises
- Cluster nursing activities
- Allow undisturbed rest
- Gently manipulate lines and tubes
- Limit painful and stressful procedures

Positioning

- Swaddling
- Containment
- Facilitated tucking (i.e., holding the arms and legs in a flexed position)

Touch

- Stroking, caressing
- Massaging
- Holding
- Kangaroo care

Distraction

- Music
- Rhythmic rocking
- Soft, soothing voice

Nonnutritive suckling

- Pacifier
- Nonlactating nipple

Sucrose

- 24-50%, 0.1-2 ml orally; 2 minutes before procedure via syringe or pacifier

Glucose

- 30%, 0.3-1 ml orally; 1-2 minutes before procedure

Pharmacologic approach **(Table 40-3)**

Table (40-3): Analgesic, sedative, and local anesthetic agents

Agent	Dose	Side effects
Opioid analgesics		
Morphine sulfate	• IV bolus: 0.05-0.1 mg/kg • IV infusion: 0.01-0.03mg/kg/hr	• Respiratory depression • Hypotension • Urinary retention • Decreased GI motility
Fentanyl citrate	• IV bolus: 0.5-3 µg/kg • IV infusion:0.5-2 µg/kg/hr	• Respiratory depression • Hypotension • Hypothermia • Muscle rigidity
Anesthetic agents		
Lidocaine	• 2-5 mg/kg subcutaneously • 0.5-1 mg/kg endotracheally	• Hematoma at injection site • Seizures • Heart block
EMLA*	0.5-2 gm under occlusive dressing, 1hr before procedure	• Redness, blistering • Petechial rash • Methemoglobinemia
Ketamine	• IV bolus: 0.5-2 mg/kg • IV infusion: 0.5-1 mg/kg/hr	• Respiratory depression • Apnea
Thiopental sodium	2-5 mg/kg IV	• Increased secretions • Hypotension
Sedatives/Hypnotics		
Midazolam	• IV: 0.05-0.15 mg/kg IV • IV infusion: 0.01-0.06 mg/kg/hr	• Respiratory depression • Hypotension • Seizure like myoclonus
Chloral hydrate	• 0.25 mg/kg oral versed syrup • 25-75 mg/kg per dose orally or rectally	• Gastric irritation • Respiratory depression • Myocardial depression • Cardiac arrhythmias • Ileus • Indirect hyper-bilirubinemia
Phenobarbital	• Loading: 5-15 mg/kg • Maintenance: 3-4 mg/kg (PO, IV)	• Respiratory depression • Apnea
Nonopioid analgesics		
Acetaminophen	• 10-15 mg/kg orally • 20-30 mg/kg rectally	None reported in therapeutic doses

*Topical EMLA: EMLA, eutectic mixture of local anesthetic should be limited to a single dose per day and it must be removed within 2 hrs.

Table (40-4): Analgesia for procedural pain in neonates

Procedures	Management
Heel prick	Sucrose with pacifier, swaddling, containment, skin-to-skin contact with mother and use of mechanical lancet
Venipuncture	Sucrose with pacifier, swaddling, containment facilitated Tucking, EMLA cream at the site (when not urgent)
Arterial puncture	Sucrose with pacifier, swaddling, containment, facilitated tucking, EMLA cream at the site, consider local subcutaneous lidocaine locally
Lumbar puncture	Sucrose with pacifier, EMLA cream at the site, consider sub-cutaneous lidocaine locally
Intubation	Combination of opioid analgesics, sedatives, and muscle relaxants, consider topical lidocaine spray (if not urgent)
Injection	Avoid subcutaneous/intramuscular injections, prefer intra-venous route, sucrose with pacifier, swaddling, containment, EMLA cream
Chest tube	Sucrose with pacifier, subcutaneous lidocaine, consider opioid analgesics or short-acting anesthetic agents
Umbilical catheter	Sucrose with pacifier, swaddling, containment, facilitated tucking, avoid sutures or hemostat clamps on the skin around the umbilicus
Central line	Sucrose with pacifier, swaddling, containment, facilitated tucking, EMLA to the site, subcutaneous lidocaine, opioid analgesics
Endotracheal suction	Sucrose with pacifier, swaddling, containment, facilitated tucking, consider opioid analgesics
Nasogastric tube	Sucrose with pacifier, swaddling, containment, facilitated tucking, gentle technique, apply lubrication
Circumcision	Sucrose with pacifier, EMLA cream to the site, dorsal nerve block or penile ring block using lidocaine, consider acetaminophen for postoperative pain
Eye examination	Sucrose with pacifier, local anesthetic eye drops
Mechanical ventilation • First 24 hrs (unless extubation is anticipated in 4 hrs) • >24 hrs	• Fentanyl or morphine IV/4 hrs and as needed, or fentanyl infusion 0.2-2 µg/kg/hr (start at low rate) • Fentanyl or morphine IV every 4 hrs and as needed

N.B.: Naloxone reverses the adverse effects of opioids. It can be given in increments of 0.05 mg/kg until the side effects are reversed.

- The American Academy of Pediatrics (AAP) guideline on pain management does not recommend routine continuous narcotic infusions in mechanically ventilated newborns because of concern about short-term adverse effects and lack of data on long-term outcomes.

Chapter 41

Discharge Planning and Follow-up

Discharge Planning and Follow Up

Greater survival rates for preterm infants have created a population with unique long term health care needs.

Effective discharge planning insures continuity of care from hospital to home.

Delay in discharge can be costly and increases risk of hospital acquired morbidity. Readmissions can be traumatic to the infant and the family.

Discharge Orders

Discharge orders are a physician's responsibility. In most situations, the neonate will need only primary care or health maintenance and the parents should know where this will be provided. When the management of problems is necessary, it is the responsibility of the unit doctors and nurses to arrange protocols for the neonate and parents.

Discharge Criteria

An infant is ready for discharge when the infant exhibits:

- Stable vital signs and temperature in an open crib for 24-48 hrs, particularly important when discharging LBW babies to their home in the winter
- An adequate weight gain
- A minimum discharge weight of 1,600-1,800 gm attained
- Ability to take all feeds by breast or bottle without any respiratory compromise
- Tolerating oral feedings or if long term plan is tube feedings (NG tube), tolerating feedings and family has been trained
- Tolerating all medication administered orally
- Normal activity observed
- Normal laboratory values
- No apneas or bradycardias for 5 days
- Parents demonstrated ability to care for infant
- Arrangements made for primary and continuing care

Discharge Plan

Criteria of a good discharge plan

- Begins early, i.e., soon after an infant is admitted to the NICU and updated regularly during hospitalization
- Individualized to meet infant and family needs and resources
- Clearly identified goals
- Decreases fragmentation and duplication of services
- Decreases delay in assessing care

- Anticipates potential delays in development and directs care towards prevention and early intervention
- Decreases the possibility of readmission.
- Increases the quality of care

Components of discharge plan

- Family assessment and dynamics
- Discharge screening, monitoring, and examination
- Review of the hospital course
- Discharge documentation

Family assessment and dynamics

- Involving the family in developing the discharge plan optimizes its success by individualizing the plan and adding to the parents' feeling of control.
- The transition to home can go smoothly with early planning, ongoing teaching, and attention to the family's needs and resources.
- The following should be considered when assessing the family's readiness for discharge:
  - Willingness to assume responsibility for care
  - Previous experiences with infant care
  - Complexity of the skills required to care for infant
  - Family structure
  - Financial concerns
  - Home setting
  - Coping skills
  - Supports (e.g., family support programs, relatives)
  - Medical history (ongoing illness may impact the caretaking needs)
  - Cultural beliefs
- Preparing the family for discharge
  - Alter medication schedules to fit the family's schedule. Eliminate unnecessary medications. Formulas and additives can be changed to less expensive or more easily obtained products.
  - Begin teaching early to allow the parents adequate time to process information, practice skills, and formulate questions. Include written information for the family to take home to use as reference. Include several family members in the learning process so that the parents can get needed support.
  - Encourage parents to have rooming in with the infant in the NICU, maximizing parental confidence and competence and helping to strengthen the parent-infant bond.

- Retro (reverse) transfer to a level II neonatal care unit in the community. This may allow the family to spend more time with the infant, and facilitate learning in a less acute environment.

Discharge screening, monitoring, and examination

Hearing screening

- The preferred screening method for hearing evaluation is auditory brain stem responses (ABR). It is done for all at risk babies.
- Technique is reliable after 34 weeks' postmenstrual age. Abnormal results prior to this age may reflect immaturity.
- Tests with abnormal results should be repeated after 1 month and at 3 months.
- Most NICU graduates are screened for hearing loss prior to discharge; hearing screen should be repeated at 5-6 months corrected gestation age or sooner if there are concerns about hearing impairment. If an abnormal hearing screen is present, formal audiologic assessment should be performed.
- Infants at risk are those with:
  - Family history of childhood hearing loss
  - Birth weight less than 1,500 gm or babies less than 32 weeks' gestation
  - Central nervous system insult:
    - Hypoxic ischemic injury
    - Intracranial hemorrhage
    - Neonatal seizures
    - Infection (e.g., meningitis, encephalitis)
  - Otologic damage occurring in cases of:
    - Hyperbilirubinemia
    - Ototoxic drugs (e.g., aminoglycoside)
    - Persistent pulmonary hypertension.
    - Respiratory alkalosis and hyperventilation
  - Malformation of the ear
  - Craniofacial anomalies

Eye examination

- Retinopathy of prematurity (ROP) is a multifactorial vasoproliferative retinal disorder that increases in incidence with decreasing gestational age **(Refer to Chapter 27).**
- Eye examination should be done for:
  - Very low birth weight infants (birth weight <1,500 gm).
  - Preterm infants <32 weeks' gestation
  - Infants born >32 weeks' gestation, birth weight 1,500-2,000 gm whose clinical course places them at increased risk (e.g., those requiring cardiorespiratory support).

  - Infants exposed to oxygen therapy for long periods.
- Timing:
  - Examination should be done 4 weeks after birth with additional examinations at intervals of 1-2 weeks until the retinal vessels have fully matured.

Cranial ultrasonography

- Cranial ultrasonaraphy should be done prior to discharge to screen for IVH or periventricular leukomalacia for:
  - Infants with birth weight <1,500 gm, <32 weeks' GA, or at any gestational age and at any time if thought to be clinically indicated.
  - Infants >32 weeks' gestation with risk factors, (e.g. perinatal asphyxia, mechanical ventilation, or pneumothorax) or who present with abnormal neurologic signs.
- Timing:
  - On or around days 3, 7, 30, 60 (or just before discharge)

Thyroid function tests

- Screening for congenital hypothyroidism (CH) should be performed from third to seventh day of life **(Refer to Chapter 3)**.

Vaccination

- Infant should receive all vaccines according to his/her postnatal chronologic age regardless of his gestational age.
- Hepatitis B vaccine
  - All infants should be vaccinated against hepatitis B at the age of 2 months. Hepatitis B vaccine and hepatitis B immune globulin (HBIG) are administered as soon as possible after birth if the mother is known to be HBsAg-positive.
- Educate parents about vaccination schedule.

Discharge examination

- Heart: murmurs and femoral pulse
- CNS: activity and fullness of fontanelles
- Abdomen: urine output, stools, masses and hernias
- Skin: jaundice
- Cord: infection
- Infection: signs of sepsis.
- Feeding: vomiting, weight gain, abdominal distension.
- Joint: limited mobility, dislocations

Review of hospital course

- For infants with a complicated hospital course and ongoing health issues, a thorough review of the hospitalization will facilitate the discharge and help make the transition of care to the outpatient setting.

- The results of diagnostic studies, such as cranial ultrasound examinations and echocardiograms, including those that require outpatient follow-up, should be reviewed.
- Subspecialty consultants, who will provide follow-up care, should see the infant prior to hospital discharge.

Discharge documentation

- All patients discharged from hospital must have:
  - Follow up card
  - A plan for follow up clearly documented in the case notes
- Follow up card should include the following:
  - Name
  - Age
  - Diagnosis
  - Responsible physician
  - Date of admission
  - Date of discharge
  - Period of hospital stay
  - Birth weight
  - Discharge measurements (weight, length, and head circumference)
  - Medications on discharge
  - Feeding
  - Immunization
- Follow up dates should be fixed.
- Instructions given to the mother should be clear and precise.
  - Discharge medications:
    - Make a list of medications with proper doses and route of administration.
    - Educate the parents about medication.
  - Infant/mother bonding: keep the infant with mother in the same room.
  - On demand breast feeding.
  - Adjust temperature in infant's room.
  - Avoid taking the infant to crowded indoor places.
  - Avoid contact with anyone who has a cold, flu, or other active infection.
  - Do not allow anyone to smoke around the infant.
  - Encourage anyone who comes into close contact with the infant to wash their hands.
  - Care for umbilical cord **(Refer to Chapter 5).**

- When to call your infant's doctor?
  - Any changes in infant's usual patterns of behavior (increased sleepiness, irritability or feeding poorly).
  - Any of the following:
    - Breathing difficulties
    - Blueness around lips
    - Fever
    - Vomiting or diarrhea
    - Dry diaper >24 hrs
    - No stool >48 hrs
    - Black or red color seen in stools
  - Alarming signs of the umbilical stump
    - Redness around umbilicus
    - Unpleasant smell
    - Discharge
    - Bleeding

Follow-up of High Risk Infants

Each neonatal care unit, especially level III, should provide follow-up care for babies who need special care after birth, who are at risk for developmental delays, or who have ongoing medical problems. This occurs through the neonatal follow up clinic.

Goals of the neonatal follow-up clinic

- Early identification and appropriate intervention of developmental disability
- Parent counseling
- Identification and treatment of medical complications
- Feedback for neonatologists, obstetricians, and pediatrics surgeons

Staff of the clinic

- Follow-up is a multi-disciplinary process involving neonatologist/pediatrician, nurse, physical therapist, speech therapists, audiologists (hearing specialists), and other sub-specialties as indicated.

Infants requiring special follow-up

Infants with any of the following:

- Birth weight <2,000 gm
- Gestational age <34 weeks
- IUGR
- Neurological problems (e.g., asphyxia, seizures, IVH, periventricular leukomalacia, microcephaly)

- Congenital infection and meningitis
- Respiratory problems (e.g., prolonged ventilation >7 days, or BPD)
- Others (e.g., hypoglycemia, polycythemia, and congenital anomalies)

Parameters to be checked during follow-up

- Growth: weight, length, and head circumference - plotted on growth charts
- Respiratory system for apnea, and evidence of distress (BPD)
- Vision, hearing, and language development
- Neurodevelopmental assessment

Chapter 42

Medical Records and Data Collection

Medical Records and Data Collection

- Egyptian neonatal units must collect and maintain two forms of data. One involves care of the individual neonate and the other involves populations served over time**,** e.g., the number of neonates admitted in the NICU each month. Individual and population data must be analyzed to assess quality, determine need, and plan for the future.
- The Egyptian National Neonatal Care Program (ENNCP) has established a data collection system that is standardized for all units. Each unit has the responsibility of collecting and maintaining accurate data of the activity within the unit and submitting monthly reports to a central office.
- These system reports are very important. For example, using birth weights as a basic parameter for comparing groups of neonates allows the evaluation of unit outcomes and provides information for national planning. If data are available on births within a region where a unit is located, then an estimate of the need for neonatal care can be made**,** and the potential demand for neonatal services projected.
- The leadership of each neonatal unit is responsible for identifying, with the system leader, what data must be collected for reporting and for supervising this process. The quality of data is very important and can be maintained only with constant attention. There are three areas of responsibility that require regular supervision: individual patient records, the unit admission book**,** and monthly report forms.

Individual Patient Records

- An accurate patient record documents findings and communicates care plans.
- It should be located in the unit and immediately available to all care providers.
- The unit leadership is responsible for ensuring the quality of the medical records.
- Standardized recording forms are recommended.
- There should be daily notes in the record, with more frequent notes if the clinical condition is unstable.

Unit Admission Book

- Unit admission book maintains a record of every neonatal admission in the NICU.
- The ENNCP has developed a form for this purpose with specific items to be completed.
- For every admitted newborn, the following information are registered: infant's name, parents' names, address and telephone number.
- The nursing staff is responsible for the admission book.

Monthly Report Form

- These forms should be completed monthly and submitted to the ENNCP office through the government health information center with copies to other places, such as the hospital administrator's office, as requested or required.
- The director of neonatal services is the appropriate person responsible for this report and he/she must work closely with the nursing staff members who maintain the admission book.

- An updated summary of monthly activities help make strong presentations in support for proposals for new resources, e.g., equipment and personnel.
- This form is completed and submitted to the ENNCP office every month.

Individual Medical Records

Accurate medical records

Accurate medical records are very important to:

- Assure high quality care
- Improve outcomes
- Help plan for improvements in the future through analysis of data
- Facilitate patient referral
- Provide statistics which help identify organisms implicated in nosocomial infections
- Help following and evaluating nursing care

The following should be included in the infant's medical record

- Infant's data
- Parents' data
- Mother's obstetric history
- Resuscitation data
- **Initial assessment on admission**
  - Measurement
    - Weight, length, and head circumference
    - Daily weight - plotted on the growth chart, following the infant's growth
  - Vital signs
    - Temperature
    - Heart rate: counted in one minute
    - Respiratory rate: counted in one minute
    - Blood pressure **(Refer to Appendix 3)** and capillary refill time
  - Full physical examination
  - Gestational age assessment
    - Using the new Ballard score, document the timing of examination and infant's name as found in the relevant section.
    - Plot the growth parameters on the relevant curve (weight, length, and head circumference) against calculated gestational age and determine the infant's percentile.
  - Impression
    - Document the calculated gestational age.

- Write provisional diagnosis.

- **Progress sheet**
  - Vital signs
  - Activity
  - Measurements
    - Weight (measured daily and expressed as + ve or –ve grams from yesterday's recording), weight is measured and documented twice daily if infant <1,000 gm.
    - Head circumference and length are measured weekly.
    - Abdominal circumference is measured when needed.
  - Color
    - Pallor, cyanosis, jaundice, plethora, or mottling
  - Skin
    - Cleanliness, rash, petechiae or ecchymotic patches, edema, sclerema, or any other abnormal signs
  - System assessment
    - Respiratory system; examined for and commented on:
      - Downes' score: recorded daily for every infant suffering from respiratory distress
      - Bilateral air entry auscultated
      - Apnea, bradycardia and desaturations: recorded frequency, duration, and measures needed to resume breathing
      - Oxygen saturation checked, if indicated
    - Cardiovascular system**:** examined for and commented on:
      - Activity of the precordium
      - Heart sounds and murmurs
      - Peripheral pulsations
    - Abdominal system; examined for and commented on:
      - Masses, or organomegaly
      - The umbilicus.
      - Signs of feeding intolerance
    - Neurological system; examined for and commented on:
      - Lethargy or irritability
      - Fontanelles
      - Neonatal reflexes (Moro and suckling reflexes)
      - Tone
      - Seizures: type and frequency

- Check for bleeding from any orifice
- Hydration status assessment:

  Hydration status assessed daily (twice daily if infant <1,000 gm) and baby classified as well hydrated, dehydrated or overloaded via interpretation of the following data:

  - Weight change from yesterday
  - Clinical data**,** e.g., vital signs, eyes, fontanelles, skin turgor and tongue
  - Urine volume, specific gravity and presence of glucosuria
  - Serum Na^+ level
  - Hematocrit value
- IV cannula site checked for cleanliness, skin infection, sloughing**,** or extravasation.
- Investigations
  - CBC with differential, CRP, serum glucose, Ca^{++}, BUN & creatinine
  - Serum Na^+, K^+
  - If indicated, serum bilirubin, blood gases and liver enzymes
  - Chest x-ray for every baby suffering from respiratory distress
  - Cranial sonar or echocardiography**,** if indicated
  - Assessment of feeding and growth parameters: serum Ca^{++}, pH, alkaline phosphatase weekly**,** and serum albumin monthly
- Infection data
  - Infant's temperature
  - Clinical findings: poor activity, poor Moro and suckling reflexes, or mottling
  - CBC, CRP
  - CSF analysis
  - Culture and sensitivity
- Treatment sheet

  The following items should be clearly stated:
  - Total fluids …..ml/kg/day, giving …... kcal/kg/day
  - Enteral fluids…… ml/kg/day, giving...…kcal/kg/day
    - Documented: type, route, amount/feed and frequency
  - Parental nutrition……. ml/kg/day, giving..….. kcal/kg/day (via peripheral IV line or UVC)
    - Na^+….. mEq/kg/day
    - K^+….. mEq/kg/day
    - Ca^{++}….. mg elemental calcium/kg/day
    - GIR….. mg/kg/minute
  - Incubator temperature referring to NTE ranges in the protocol

- Oxygen mode and flow in liter/minute:
  - Whether incubator or box or nasal prongs is used.
  - If the baby is on CPAP or mechanical ventilation, the relevant flow sheet should be filled.
- Drugs
  - Start first line antibiotic treatment: Ampicillin and gentamicin.
  - Write generic and trade names.
  - Prescribe the dose accurately based on actual weight.
  - Mention frequency and route of administration.
  - State precautions, if needed.
- Nursing care
  - Suction
  - Physiotherapy
  - Checking feeding intolerance signs
- Instructions to the parents

Chapter 43

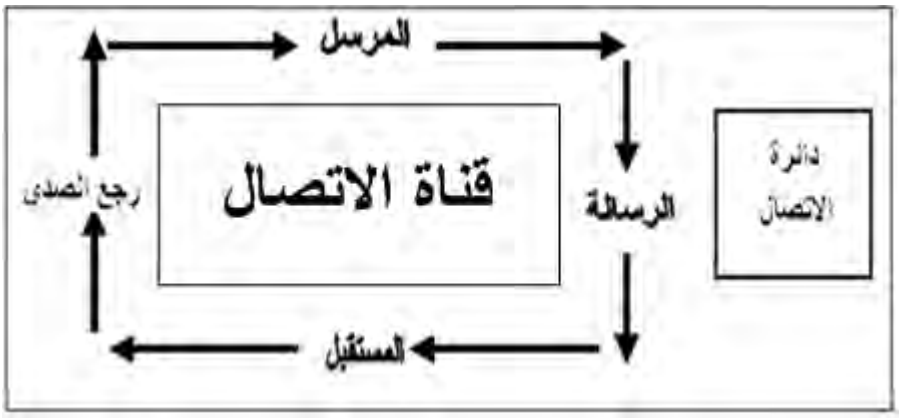
Interpersonal Communication and Counseling

مهارات الاتصال الشخصي و المشورة

مهارات الاتصال الشخصي والمشورة

عملية الاتصال والمشورة

الاتصال هو عملية تبادل الأفكار والمعلومات والمعاني بطريقة فعَّالة بين شخصين أو أكثر (المُرسِل والمُرسَل إليه).



شكل (٤٣–١): عملية الاتصال والمشورة

أهداف الاتصال

- العمل على معرفة اتجاهات وأفكار الآخرين.
- تكوين العلاقات بين الناس بعضهم البعض.
- العمل على نقل وتبادل الأفكار، والآراء، والمعاني بسهولة وبطريقة فعَّالة بين الناس.
- التأثير في تفكير الآخرين، مشاعرهم، سلوكهم، واتجاهاتهم.
- التشجيع على تغيير أو تعديل سلوك ما.
- توليد الاحتياج إلى خدمات ذات جودة.

طرق الاتصال

هناك طريقتان أساسيتان للاتصال وهما:

طريقة الاتصال اللفظي

- الاتصالات الشفهية: مثل المقابلات الشخصية، جلسات المشورة، والندوات
- الاتصالات الكتابية: مثل النشرات والرسومات

طريقة الاتصال غير اللفظي

يؤدي حُسن استخدامها إلى تقوية الروابط بين مقدمي الخدمة الصحية وأهل الوليد والعكس. أما سوء استخدامها فيعوق عملية الاتصال. وتشمل طريقة الاتصال غير اللفظي:

- تعبيرات الوجه والاتصال البصري
- تعبيرات بحركات اليد، والجسم، والرأس
- نبرات الصوت

الأساليب الفعَّالة في عملية الاتصال (مهارات الاتصال)

أ. الإنصات الجيد

وهو يشجع أهل الوليد على الاسترسال في التعبير عن شعورهم، ويعطي لهم الفرصة لتنظيم أفكارهم. ويجب على مقدم الخدمة أن يظهر اهتمامًا بما يقوله الأهل، وأن يحسن الإصغاء لهم بغرض فهم احتياجاتهم واستفساراتهم جيدًا. ويمكن لمقدم الخدمة أن يستخدم تعبيرات الوجه وحركات الجسم المختلفة لإظهار مدى تفهمه وموافقته على ما يقوله الأهل.

طرق تحسين مهارات الإنصات

- الإبقاء على التقاء النظرات مع المتحدث، حسبما تسمح بذلك الأعراف الثقافية.
- إعطاء الاهتمام للمتحدث؛ بأن لا ينشغل المستمع بأعمال أخرى خلال الحديث، لا يتحدث لأناس آخرين في نفس الوقت، لا يقاطعه، ولا يسمح للآخرين بمقاطعته.
- الجلوس باسترخاء وبشكل مريح، والابتعاد عن الحركات التي تشتت التفكير، دون اللجوء إلى لف الأيدي أو الأرجل على بعضها.
- الإصغاء الدقيق للمتحدث عوضًا عن التفكير في أمور أخرى، أو عما سيقوله لاحقًا والطريقة التي يعبر بها عما يريد قوله، مع ملاحظة لهجة صوته، واختياره لكلماته وتعبيرات وجهه وإيماءاته.
- وضع النفس مكان الأهل طيلة فترة الاستماع إليهم.
- إعادة صياغة الحديث وتضمين ما قيل في مناقشات لاحقة.

ب. الشرح والتفسير

وذلك لتوضيح مدى تفهم مقدم الخدمة لملاحظات أهل الوليد ومحاولة وضع أفكارهم في جملة من تكوينه. كما أن الشرح يحث الأهل على توضيح مقاصدهم ويشجعهم على الاستمرار في الحديث.

ج. انعكاس المشاعر

وهي توضح مدى القبول أو الرفض لأفكار وكلام أهل الوليد، والتفاعل معها باهتمام.

د. استخدام الأسئلة

وذلك بتوجيه أسئلة مباشرة ومرتبطة بما يقال، ويمكن استخدام الأسئلة ذات الإجابات المستفيضة والجمل المفتوحة التي تساعد الأهل على الاستمرار في الحديث، ويجب تجنب الأسئلة التي تكون إجابتها "نعم أو لا" لأنها قد تعوق الاتصال.

هـ. إعطاء المعلومات وتبسيطها

يجب إعطاء الأهل المعلومات التي يحتاجونها بصورة مبسَّطة، وذلك بعد تقييم احتياجاتهم، واستفساراتهم. وحتى يتمكن أهل الوليد من اتخاذ خيارات حكيمة، لا بد أن تتوافر لديهم معلومات مفيدة ومفهومة، دون أن تختلط معها آراء وأحكام خارجية، ويجب أن تتضمن هذه المعلومات الخيارات العديدة المتاحة أمامهم، والتوضيحات الخاصة بنتائجها. ولابد أن تتم صياغة المعلومات بشكل يتماشى مع ثقافة واحتياجات الأهل، وأن يتم شرحها بطريقة بسيطة وسهلة تساعدهم على اتخاذ قرارات صائبة للحفاظ علي صحة الوليد.

و. استخدام التعبيرات الغير لفظية واللفظية المناسبة

على مقدم الخدمة أن يظهر مدى قبوله للأهل باستخدام حركات الجسم وتعبيرات الوجه والكلمات المناسبة.

ز. الإيضاح

يجب على مقدم الخدمة أن يوضح الكلمات والمعاني الغامضة أو غير الواضحة وذلك لمساعدة الأهل في التعبير عن مشاعرهم وأفكارهم.

ح. إعادة الصياغة

العمل على إعادة صياغة ما قاله الأهل بالنسبة لمشاعرهم واتجاهاتهم، ووضعها في كلمات وجمل من صياغة مقدم الخدمة للتأكد من فهمها الجيد.

ط. تلخيص محتوى الاتصال

يجب تلخيص المحتوى في نقاط رئيسية مبسطة ومترابطة، وذلك للتأكد من وصول المعلومات بدقة، والتأكد من نجاح عملية الاتصال.

ي. التعليقات المناسبة

يجب إعطاء تعليقات مناسبة وبناءة أثناء الحديث، لأن هذا يعطي أهل الوليد الانطباع بمدى إهتمام مقدم الخدمة بهم، ويشجعهم على مواصلة الحديث والتعبير عن مشاعرهم.

ك. التشجيع

التشجيع هو إعطاء الشجاعة، الثقة، والأمل. ويعني التشجيع بالنسبة لأهل الوليد، أن مقدم الخدمة يؤمن بإمكانياتهم في التغلب على مشاكلهم، وأنه يعمل على مساعدتهم لإيجاد الطرق المناسبة للتغلبّ على تلك المشاكل.

ل. استخدام الوسائل البصرية

الهدف الرئيس من استخدام الوسائل البصرية والمطبوعات هو شرح المعلومات بطريقة جذابة تسهل فهم المعني المقصود، وذلك من خلال حث المزيد من الحواس مثل السمع والبصر.

التعامل مع المفاهيم الخاطئة والشائعات

- **المفاهيم الخاطئة**

هي حالة من سوء الفهم تبين أن الرسالة اللفظية قد وصلت إلى أسماع المتلقي بشكل منقوص، أو تحليلها بطريقة مغايرة لما قصد منها أصلاً، وهذا بحد ذاته يؤدي إلى عدم فهم الرسالة.

- **الشائعات**

تنشأ الشائعة عندما يقوم عدد من الأفراد بترديد رسالة منقوصة أو قصةٍ ما، أو أفكار خاطئة نشأت عن سوء الفهم. وكلما كثر ترديد مثل هذه الأمور، كلما كثرت احتمالات تغير فحواها.

أسباب نشوء المفاهيم الخاطئة

- الأخطاء غير المقصودة التي يرتكبها الشخص وهو ينقل ما سمعه.
- الاعتقادات التقليدية السائدة عن الجسم والصحة.
- المبالغة بهدف جعل القصة أكثر إثارة وتسلية.
- التفسيرات غير الواضحة التي يقدمها مقدمو ا الخدمة، أو عدم إعطائهم المعلومات بلغة بسيطة ومفهومة.
- الأخطاء العلمية أو المبالغات التي قد ترد في التقارير التي تقدمها وسائل الإعلام.
- محاولة الإساءة لخدمات الرعاية الصحية أو لمقدمي الرعاية الصحية.
- ميل الناس للاستماع فقط لما يحبونه أو يريدون سماعه.

أسلوب التعامل مع المفاهيم الخاطئة

- سؤال الشخص عمَا سمعه، وما هي المخاوف التي تتملكه.
- محاولة معرفة مصدر هذه الشائعات، أو كيفية حصوله على هذه المفاهيم الخاطئة.
- شرح سبب أن هذه الشائعة أو هذا المفهوم الخاطئ غير صحيح.
- التعرَف على ما يريد هذا الشخص معرفته (كي تتكون لديه الثقة)، والتعرَف على الشخصية التي يمكن أن يثق بها وتؤثر عليه.
- إعطاء المعلومات الصحيحة، والعلم بالمعتقدات المترسخة في الأذهان عن الصحة، فهذه المعرفة تساعد على فهم الشائعات، وتفسير الأمور الصحيحة بطرق يستطيع الشخص فهمها.
- تشجيع المستفيدين من الخدمة على استشارة مقدمي الخدمات الصحية، إذا ما أرادوا التأكد من صحة المعلومات التي سمعوها.

الأساليب غير الفعالة في عملية الاتصال

أ. إعطاء النصح في شكل أوامر

إخبار أهل الوليد بما يجب أن يفعلوه وما يجب ألا يفعلوه؛ قد يُفسَر من وجهة نظرهم على أنهم غير قادرين على اتخاذ قراراتهم بأنفسهم.

ب. الطمأنينة الزائفة

طمأنة أهل الوليد بدرجة زائدة عن الحد يمكن أن يعطيهم الإحساس أنه ليس هناك سبب يدعوهم للقلق، وينكر عليهم مشاعرهم، مما يظهر مقدم الخدمة الصحية بمظهر غير المتفهم لدوافعهم وشعورهم. كما أن حالة الوليد قد تتدهور بسرعة.

ج. عدم تقبل ما يقوله أهل الوليد

كذلك عدم التجاوب مع أفكارهم، عدم احترام آرائهم، ووجهة نظرهم، حيث أن ذلك يجعل الأهل يشعرون بأن مقدم الخدمة الصحية يتحكم في سلوكهم، وأنه يجب عليهم أن يقفوا موقف المدافعين ضده.

د. كثرة الأسئلة غير المناسبة

قد يشعر أهل الوليد بأن مقدم الخدمة يقوم بالتحقيق معهم، ويحاول أن يأخذ منهم معلومات لا يريدون الإفصاح عنها، أو يتهمهم بالتقصير.

هـ. اللوم

قد يؤدي لوم أهل الوليد، ومحاولة الحكم عليهم إلى سكوتهم وإحجامهم عن الحديث، مما يؤدي إلى عدم إظهارهم لمشاعرهم وأفكارهم.

و. سرعة التنقل بين الموضوعات المختلفة

قد يؤدي إلى زيادة معدل قلق الأهل.

ز. الصمت المستمر

قد يؤدي إلى فقدان الثقة، والشعور بأنه ليس هناك ما يمكن عمله أو مناقشته مع الأهل، أو عدم اهتمام مقدم الخدمة بما يقولونه.

ح. الدفاع

يجب على مقدم الخدمة ألا يحاول الدفاع عن الشخص الذي يقوم أهل الوليد بانتقاده، لأن هذا يشعرهم بأنه ليس لهم الحق في إبداء آرائهم ومشاعرهم.

الأسباب التي قد تعوق الاتصال الناجح

عوائق تتعلق بالمُرسِل (مقدم الخدمة)

- عدم فهم خصائص أهل الوليد.
- عدم التحضير الجيد للموضوع أو عدم الاقتناع به.
- إختلاف القيم والمبادئ، وعدم تفهم عادات وتقاليد الأهل.
- وجود اتجاهات سلبية؛ كعدم القدرة على الإقناع، عدم الانصات، والرغبة في التحدث طوال الوقت.
- التفاوت الكبير بين المُرسل (مقدم الخدمة الصحية) والمرسل إليه (أهل الوليد) من حيث الخبرة، أسلوب التعامل، واللغة.
- عدم اختيار الكلمات الصحيحة، واستخدامها في المكان المناسب، للشخص المناسب، في الوقت المناسب، وبالطريقة المناسبة.

عوائق تتعلق بالمُرسَل إليه (أهل الوليد)

- عدم وجود استعداد لتقبل الرسالة الصحية، أو التأثر بالمعتقدات السائدة بالمجتمع. فقد تتعارض الرسالة مع معتقداتهم وميولهم، فيكون مصيرها الرفض. كما توجد أيضًا عوامل نفسية مثل القلق أو الخوف، وكذلك الشك في دوافع المُرسل (مقدم الخدمة الصحية) قد يقف حائلاً بينهما.
- عدم فهم المعنى الحقيقي للرسالة أو التأثر بخبرات سيئة سابقة.

عوائق تتعلق بالرسالة

- أن تكون الرسالة غير واضحة، صعبة، وغير مبنية على الخبرات السابقة لأهل الوليد.
- وجود تفاوت بين مستوى أسلوب الرسالة ومستوى الأهل، مثل استخدام ألفاظ علمية تفوق مستواهم.
- عدم اكتمال الرسالة، مما قد يؤدي إلى غموضها.

عوائق تتعلق بالوسيلة

تختلف الوسيلة حسب نوع الرسالة، المرسل إليه، المكان، والزمان. ومن العوائق التي تتعلق بالوسيلة:

- مخاطبة الوسيلة لحاسة واحدة فقط يحد من فاعليتها.
- عرض بيانات غير واضحة أو صور صغيرة.

عوائق تتعلق بعدم وجود تغذية راجعة أو رد فعل للمرسل إليه على الرسالة

يجب على المُرسل أن يعرف ما هو رد فعل المرسل إليه، وما هي استجابته لما قيل، وما إذا كان ذا فاعلية أم لا، لأن الرسالة التي تُستقبل ولا يُبدى فيها رأيًا تعتبر مبتورة.

عوائق تتعلق بظروف وبيئة الاتصال

تتوقف فاعلية الاتصال على اختيار الزمان والمكان الملائمين لاستقبال الرسالة.

المشـــورة

المشورة هي مساعدة مقدمة من شخص له إمكانيات خاصة من المهارات والمعلومات (مقدم الخدمة الصحية) إلى شخص آخر (أهل الوليد) أثناء مناقشتهما وجهًا لوجه، وذلك لمساعدته في إتخاذ القرار السليم المبني على المعلومات الصحيحة، واختيار السلوك المناسب، وممارسة هذا السلوك للحفاظ على صحة الوليد.

أهميـة المشـورة

- العمل على إنشاء علاقة أساسها الثقة المتبادلة بين المنتفع (أهل الوليد) والقائم بالمشورة (مقدم الخدمة الصحية)، كما أنها تشجع المنتفع على التفكير في مشاكلها وأسبابها.
- العمل على مساعدة المنتفع على اتخاذ قراره بحرية.
- العمل على مساعدة المنتفع في أختيار السلوك المناسب والالتزام بحل مشاكله.
- العمل على مساعدة المنتفع على تفهم كيفية المحافظة على صحته وصحة الوليد.

قواعد عامة للمشورة

- القيام بعمل المشورة في مكان به خصوصية.
- الجلوس في مواجهة المنتفع، وتجنب الحركات المفاجئة والتي قد تعوق عملية الاتصال.
- تقبل المنتفع كما هو.
- تبادل الأدوار بينه وبين المنتفع، ومحاولة تخيل موقفه وشعوره.
- إظهار الاهتمام بالمنتفع.
- استخدام مهارات الاتصال غير اللفظي.

- الجلوس في استرخاء.
- المرونة في الحديث والمناقشة.
- استخدام نبرة الصوت التي تظهر الاهتمام بالمنتفع.
- الاتصال عن طريق النظر في عين المنتفع.

خصائص المشورة

إنماء العلاقات الجيدة

يبدي مقدم المشورة اهتمامًا ورعاية بالشخص المعني، حيث أن الناس يكونوا أكثر استعدادًا للتحدث عن احتياجاتهم مع من يثقون بهم.

التعرف على الاحتياجات

يحاول مقدم المشورة فهم الاحتياجات كما يراها الشخص نفسه، ولابد للناس من أن يتعرفوا بأنفسهم على مشكلاتهم واحتياجاتهم، ولا ينبغي أن يحددها لهم مقدم المشورة.

التعرف على المشاعر

على مقدم المشورة أن ينمي إحساسًا بالمشاركة العقلانية (أي تفهمًا وتقبلاً) لا إحساسًا بالمشاركة الوجدانية فقط (أي أسىً وعطفًا) نحو مشاعر من يستشيره.

المشاركة

على مقدم المشورة ألا يحاول أبدًا إقناع الناس بتقبل نصائحه، فإذا ثبت خطأ النصيحة، كانت النتيجة غضب المستشير وانعدام الثقة بينهما بعد ذلك، وإذا ثبتت صحة النصيحة فقد يتواكل ذلك الشخص على مقدم المشورة في حل كل مشكلاته. لذلك يجب على مقدم المشورة أن يساعد من يستشيره على التفكير في كل الأمور التي من شأنها أن تؤثر في المشكلة، ويشجعهم على اختيار أفضل الحلول المناسبة لأوضاعهم.

كتمان الأسرار

تُعرض على مقدم المشورة مشكلات شخصية عديدة قد يكون منها ما يسبب الحرج، ويجب أن تبقى هذه المعلومات سرية ولا يباح بها للآخرين، حتى ولو كانوا من أقارب المستشير ذاته. فعلى مقدم المشورة أن يحترم خصوصيات الناس الذين يساعدهم فلا يكشف مطلقاً عن أي معلومات لديه ما لم يحصل على إذن خاص من صاحب الشأن.

دور مقدم الخدمة في إتمام عملية الاتصال أو المشورة الناجحة

- يجب أن يكون مقدم الخدمة على دراية وكفاءة ودرجة عالية من الفهم للمعلومات التي يقدمها لأهل الوليد، ولديه القدرات والمهارات لكي يقوم بعملية الاتصال أو المشورة بصورة ناجحة.
- يجب أن يعطي مقدم الخدمة المعلومات والآراء بحيث تكون متكاملة ومترابطة وقائمة على الثقة المتبادلة والاحترام الذي ينشأ بينهما.
- يجب على مقدم الخدمة استخدام وسائل الاتصال المناسبة لثقافة وفهم أهل الوليد وإدراكهم وتسهيل عملية الاتصال، وذلك بتوفير الإمكانيات والموارد لإنجاح هذه العملية.
- يجب توفير المكان المناسب الذي يتميز بالخصوصية.

- يجب مراعاة الجو النفسي ومشاعر أهل الوليد أثناء إجراء عملية الاتصال.

طريقة التعامل مع الأخبارالحرجة أو السيئة

يضطر مقدم الخدمة في وحدة رعاية اللأطفال حديثي الولادة لإبلاغ الأهل أخبارًا سيئةً في بعض الأحيان، كوفاة الوليد، أو وجود تشوهات أو إعاقة بالوليد. ويجب على مقدم الخدمة الصحية مراعاة النقاط التالية في حالة إبلاغ الأهل بأي خبر سيئ:

- يفضل أن يقوم بهذه المهام أكثر الأطباء أو الممرضات خبرة، وفي حضور طبيب آخر أو ممرضة أخرى للتعلم.
- اختيار الوقت المناسب والمكان المناسب الذي يتسم بالخصوصية والراحة.
- اختيار الشخص المناسب، ويفضل الأم أو الأب.
- استدعاء دعم من العائلة (الخالة، أو الجدة، أو العمة) لمساندة الأم أو الأب.
- السؤال عن المعلومات التي عند أهل الوليد المريض، حتى يتم التعرف على مدى استعدادهم لتلقي الخبر.
- اختيار الألفاظ والمعاني بعناية وحرص، حتى لا تكون أكثر قسوة على أهل الوليد.
- استخدام مهارات الاتصال غير اللفظي بحرص وعناية، من حيث تعبيرات الوجه الحيادية، نبرات الصوت الواضحة، وتواصل العينين مع الأهل وغيرها.
- إعطاء الأخبار السيئة بتدرج، لتخفيف الانزعاج والذعر لدى الأهل.
- استعمال اللغة العربية بدون مصطلحات طبية، التحدث ببطء وبصوت واضح، ويفضل البدء بإعطاء المعلومات الكاملة عن المشكلة الأصلية والتي أدت إلى تداعيات أو مضاعفات معينة، ولذلك يجب عرض المشكلة مباشرةً بصورة كاملة دون تزييف.
- الاستماع إلى مخاوف أهل الوليد المريض، مع إعطاء الاهتمام الكامل والوقت الكافي لتفهم مشاعر الأهل بعد عرض المشكلة، التعامل معهم من منطق إنساني، والإجابة على كافة الأسئلة والاستفسارات.
- التفاعل مع مشاعر أهل الوليد المريض، ولكن يجب عدم التأثر بدموع أو صراخ الأهل، لأن ذلك قد يؤدي إلى الارتباك ويجعل الأمور أكثر تعقيدًا.
- العمل على تهدئة أهل الوليد، وبث الأمل لرفع الروح المعنوية لديهم ومساعدتهم على التفكير العقلاني واتخاذ القرار السليم في بعض المواقف.
- السماح للأهل بإلقاء نظرة الوداع، في حالة وفاة الوليد؛ إذا طلبوا ذلك.

Chapter 44

Neonatal Procedures

Hand Washing

Hand washing is the most effective method for preventing the transfer of bacteria between personnel and patients within the hospital and health care facilities. It is the single most important means of preventing the spread of infection in the hospital.

Types and Indications

Simple hand washing

- Before and after
  - Direct contact with a patient.
  - Handling in-use patient devices (e.g., catheters and respiratory equipment)
  - Handling used instruments
  - Handling contaminated items such as dressings or urinals
  - Collecting a specimen
- After
  - Any invasive procedure
  - Touching mucus membrane, blood or other body fluids
  - Removing gloves that may have invisible holes or tears
  - Making physical contact with patients under isolation precautions or their equipment
- Before
  - Serving meals
  - Leaving work

Antiseptic hand washing

- Before dressing wounds
- Before caring for susceptible patients
- Before preparing IV fluids and medications

Surgical hand wash

- Any invasive/surgical procedure. All personnel (e.g., doctors, anesthesiologists, and nurses) should perform surgical hand antisepsis before any procedure.

Steps of hand washing

Planning

- Clean all skin surfaces thoroughly.
- Prevent contact with contaminated objects.
- Observe certain basic principles:
  - Nails should be short and nail polish should not be used.

  - Weak detergent can safely be used for hand washing provided there is no skin cut or abrasion.
- A defined method of washing is advised.

Simple hand washing

- Wash with soap or detergent for 30 seconds using effective techniques to remove transient microorganisms (longer if hands are visibly soiled).
- Push wristwatch and long uniform sleeves above wrists.
- Remove jewelry, except a plain band, from fingers and arms.
- Keep fingernails short and filed.
- Stand in front of sink, keeping hands and uniform away from sink surface. Use sinks with easily accessible faucet. If hands touch sink during hand washing, repeat the process.
- Turn on water. Press foot pedals to regulate flow and temperature (warm).
- Avoid splashing water on uniform.

Antiseptic hand washing

- Wet hands and lower arms (2.5 cm below the elbow) thoroughly under running water. Keep hands and forearms lower than elbow level during washing.
- Apply 3–5 ml of the skin disinfectant to the cupped hands and carry out steps 1-6 **(Figure 44-1)** one or more times (for 2-3 minutes).
- Each step consists of 5 strokes backward and forward.
- Rinse hands and wrists thoroughly, keeping hands down and elbows up.
- Dry hands thoroughly with good quality paper towels from fingers up to wrists and forearms.
- Discard paper towel in proper receptacle.
- Turn off water with foot or knee pedals.
- Hold the hands up and away from clothing.

Alcohol hand-rub technique

- An alternative and more effective method is the application of 70% ethanol or 60 - 70% isopropanol with or without added disinfectant.
- The hands and fingers are rubbed together with the preparation until dry, ensuring that all surfaces are covered as described **(Figure 44-1)**.
- This method provides a convenient, rapid and effective alternative to hand washing in situations where there is no gross soiling of the hands, where a sink is not readily available, or during an outbreak of infection.

Surgical hand washing

- This method requires the removal of transient skin-microflora and a substantial reduction and suppression of the resident population.
- It is indicated before any surgical procedure.

- Preparations currently in use: 4% chlorhexidine detergent and a povidone-iodine solution containing 0.75% available iodine.
- Remove any jewelry on hands and wrists.
- Turn on the water and ensure that it is warm and the flow is moderate.
- Wet and lather hands and forearms (5 cm above the elbow) with the selected agent. Keep hands above level of elbows during entire procedure.
- With hands under running water, clean under nails with nailbrush. Discard brush after use.
- The same hand washing steps **(Figure 44-1)** are recommended with the wrist and forearm being included for a period of 3-5 minutes.
- Rinse hands and arms thoroughly under running water. Remember to keep hands above elbows.
- If a brush is used, it is to be used only for the first scrub of the day.

Using the Brush for Scrubbing

- Recent studies revealed that using a brush during surgical scrub provides no greater reduction of microorganisms. A soft, sterile brush or a sponge should be used.
- Discard brush and rinse hands and arms thoroughly. Turn off water with foot pedal.
- Keep hands higher than elbows and away from the body.

Agents (Skin Disinfectants)

Iodophor and iodine-containing compounds such as Betadine (Povidone-iodine)

Requirements

- Disinfectant
- Running water
- Good-quality paper towels

N.B.: Repeated scrubbing tends to damage the skin and may be associated with an increase in the numbers of resident organisms, possibly allowing *Staphylococcus aureus* to colonize on the hands.

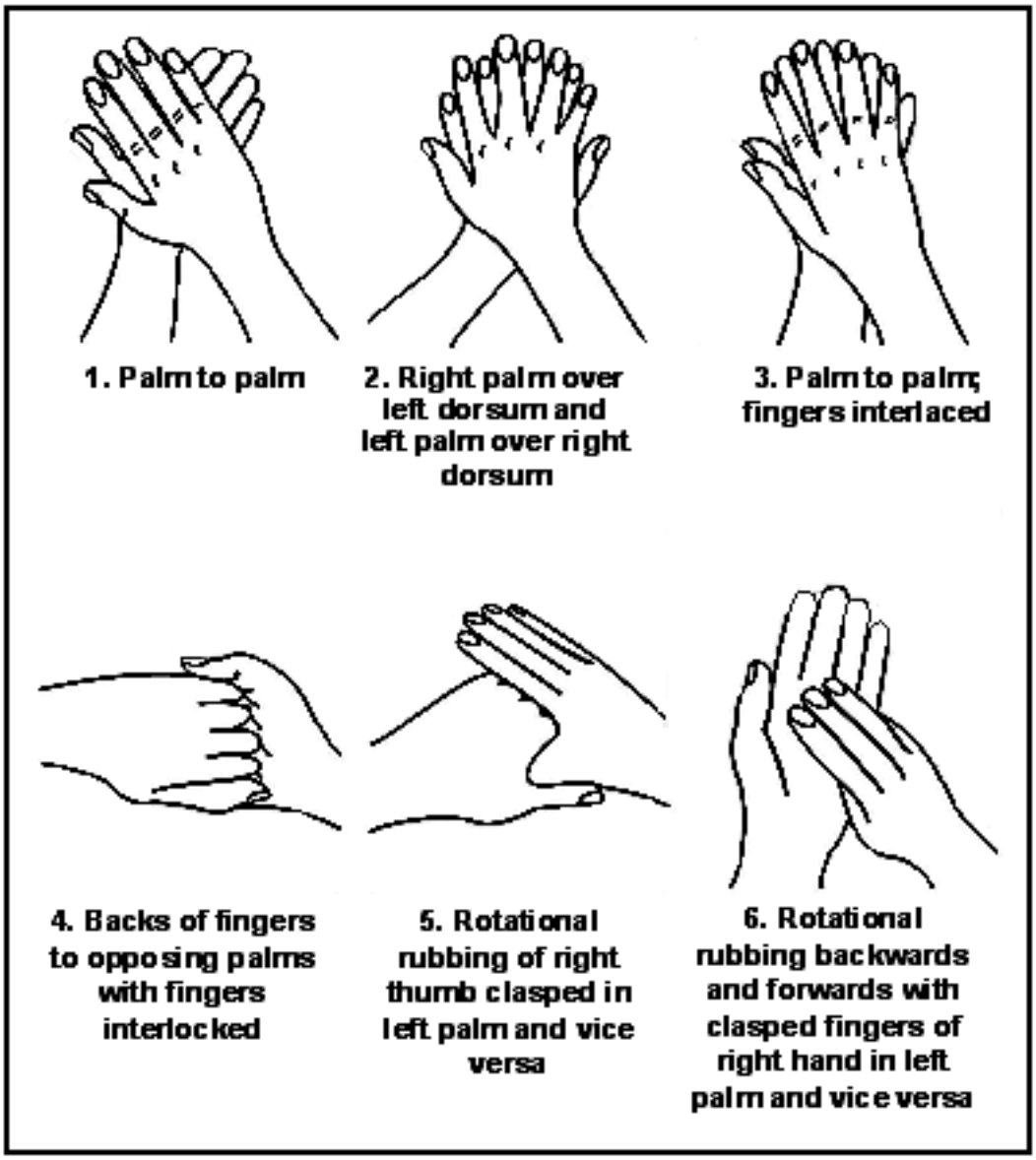


Figure (44-1): Hand washing and Disinfection Technique

Peripheral IV Line Placement

Intravenous therapy is necessary when the administration of fluids and nutritional support is not possible via the gastrointestinal route. It is important that all neonatal care units have the equipment and trained personnel available at all times to start and maintain intravenous therapy.

Preparation for Insertion and Equipment Needs

Preparation for inserting an IV line includes obtaining and preparing all of the necessary equipment, as well as ensuring that there is available help for restraining the infant and taping the IV site. The following equipment is required for inserting a peripheral IV line:

- 70% alcohol swabs
- Tourniquet or elastic rubber band
- Sizes 22 and 24 gauge over-the-needle cannula
- Connection for cannula/IV tubing
- Gauze
- Saline for infusion
- Syringes
- Tape
- Arm-board
- Scissors

Insertion Technique

- When choosing a site, it is important to avoid areas adjacent to injured skin or infection.
- Differentiating veins from arteries can be done by palpating for arterial pulsation and evaluating during occlusion. Limb arteries will collapse and veins will fill; scalp arteries fill from below and veins fill from above.
- **Figures (44-2), (44-3), (44-4), and (44-5)** show schematics of the most common insertion sites.
- Restrain the extremity on an arm-board, or have an assistant help hold the extremity. Apply a tourniquet proximal to the puncture site, if necessary.
- If a scalp vein is to be used, shave the area; a rubber band can be placed around the head, just above the eyebrows.
- Select a straight segment of the vein.
- The site is prepared with alcohol and allowed to dry.
- Attach a saline filled syringe to the needle, fill the needle with flush, then remove the syringe.
- Pull the skin taut to stabilize the vein.
- Hold the needle parallel to the vessel in the direction of blood flow, and introduce through the skin a few millimeters distal to the point of entry into the vessel. Insert

until blood appears in the cannula (note color of blood obtained "arterial blood is bright red and venous blood is darker"); the stylet is withdrawn while the cannula is advanced (if a butterfly needle is inserted, do not advance once the blood return is noted).

- Following removal of the tourniquet, a small amount of saline is infused to confirm the position. Observe for possible blanching of the skin which occurs in arterial vessels or swelling which occurs with venous extravasation.
- Once placement is confirmed, the cannula is secured in place with adhesive tape.
- Write date, time, and cannula size on the piece of tape secured to site.

Intravenous Line Management

- The type of fluid and the hourly rate should be documented. The insertion site should be observed every hour for signs of infiltration and irritation; a check should be placed in the appropriate column on the Daily Neonatal Clinical Record.
- Intravenous tubing and fluids should be changed every 24 hrs to minimize the chance of infection.
- Peripheral cannula should be changed every 3 days to minimize the chance of infection.

Complications

- Hematoma
- Venospasm
- Phlebitis
- Infiltration of subcutaneous tissue with IV solution causing superficial blistering or deep slough
- Infection
- Embolization of a clot with forcible flushing
- Air embolism
- Accidental injection or infusion into an artery with arteriospasm and possible tissue necrosis

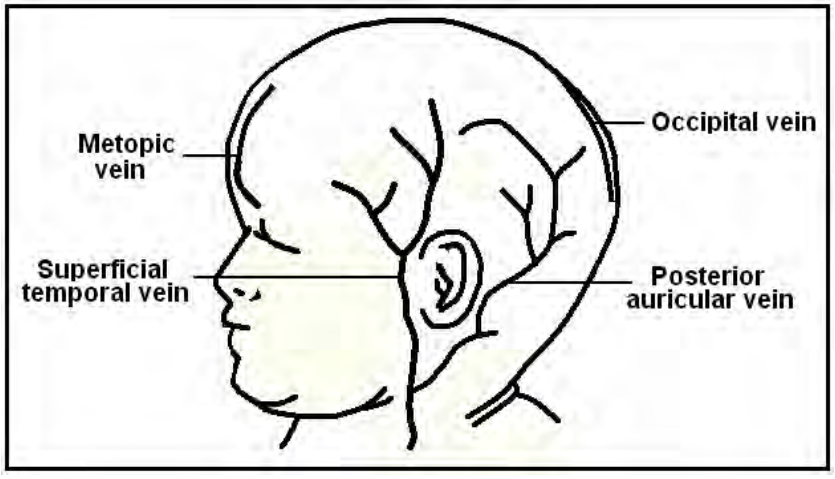


Figure (44-2): Superficial veins of the scalp

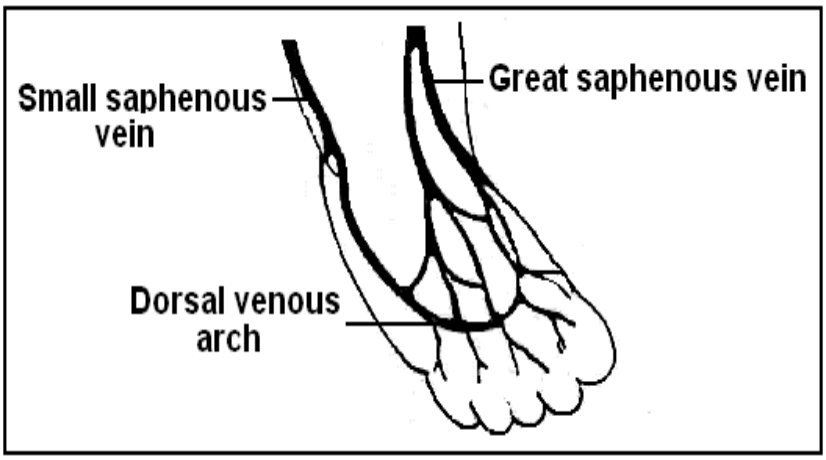


Figure (44-3): Superficial veins of the foot

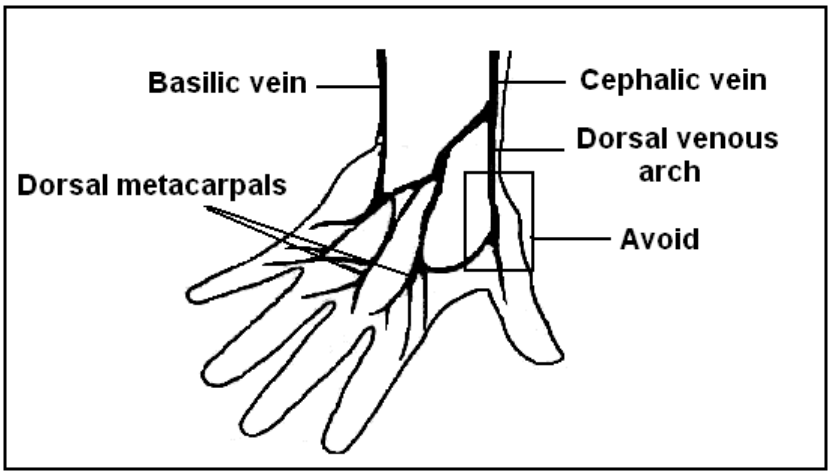


Figure (44-4): Superficial veins of the hand

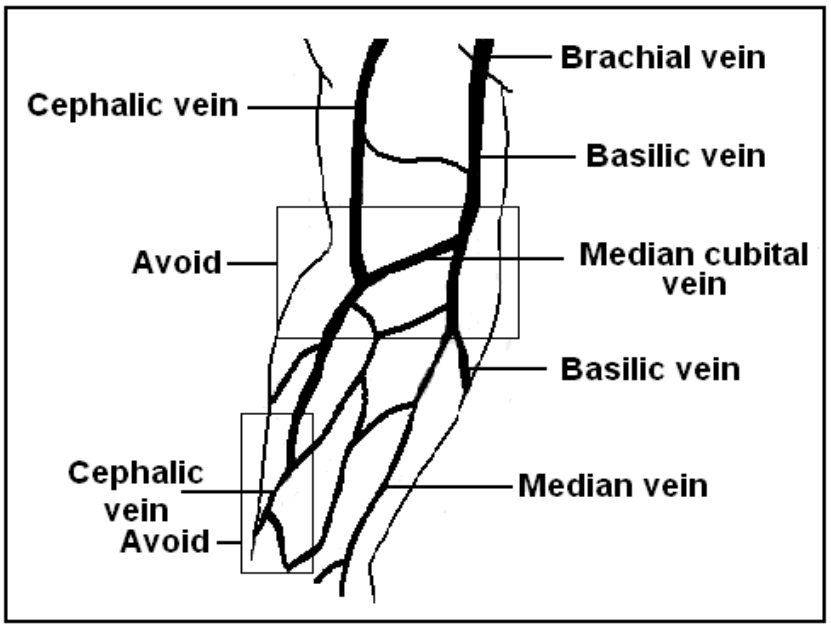


Figure (44-5): Superficial veins of the forearm

Heel Prick and Capillary Blood Sampling

Indications

- Collection of blood samples when only a small amount of blood is needed or when there is difficulty obtaining samples by venipuncture
- Capillary blood gas sampling
- Blood glucose monitoring
- Newborn metabolic screen

Capillary Blood Sampling

Equipment

- Gloves
- Sterile lancet (if a lancet is not available, use a 24-gauge needle)
- Alcohol swabs or cotton-wool ball soaked in antiseptic solution
- Dry cotton-wool ball
- Sterile 2×2 gauze pads
- Heparinized glass capillary tubes

Procedure

- Wrap the foot in a warm cloth (its temperature should not exceed 40º C) for 5 minutes to increase vascularity, making blood collection easier (optional).
- Prepare the skin of the heel using an alcohol swab or cotton-wool ball soaked in antiseptic solution, and allow it to dry.
- Flex the foot up towards the leg and hold it in this position with one hand and encircle the heel with the palm and index finger.
- Squeeze the heel firmly enough to make it flush red (but not so much that it turns white).
- Puncture the skin (about 1-2 mm deep) firmly with a lancet:
  - Aim towards the lateral or medial side of the heel.
  - Avoid the center of the heel because of the risk osteomyelitis.
  - Avoid using previously used sites, if possible.

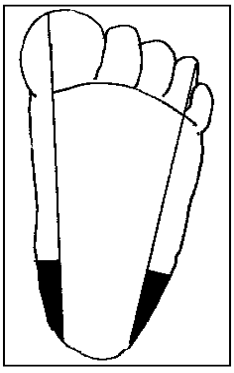


Figure (44-6): Site for heel prick (shaded areas)

- Wipe off the first drop of blood and place the capillary tube at the site of the puncture.
- Squeeze the heel gently and intermittently to enhance blood flow. Avoid excessive squeezing and rubbing of the heel, as this will cause bruising and dilution of blood with tissue fluid, giving inaccurate results.
- One end of the heparinized capillary tube is touched to the drop of blood. The tube is held at about 20° angel from horizontal.
- Allow enough time for capillary refill; both ends of the tube should remain unplugged during the collection. The tube should automatically fill by capillary action. For blood gas sampling, the tube should be filled as completely as possible to minimize exposure to the external air.
- Once the tube is full, the free end is occluded with a gloved finger to prevent air entry when removing it from the site.
- Cap ends of the tube gently with clay.
- Once the blood has been obtained, apply pressure to the puncture site with a dry cotton-wool ball or sterile gauze pad for several minutes to provide hemostasis.

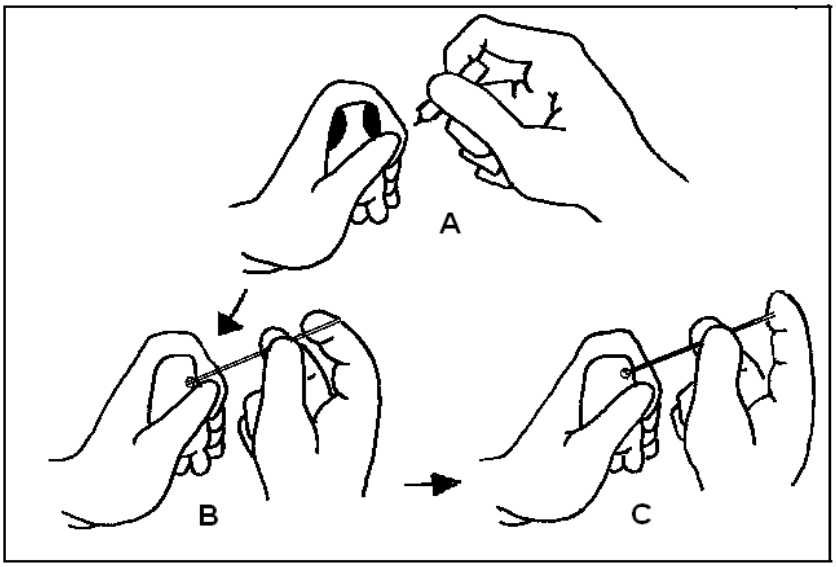


Figure (44-7): Steps for capillary blood sampling

(A) Heel puncture in safe area, (B, C) Collection of specimen

Complications

- Cellulitis
- Osteomyelitis
  - Usually occurring in the calcaneus bone.
  - Avoid the center area of the heel, and do not make the puncture opening too deep.
- Scarring
  - Multiple punctures in the same area causing scarring of the heel.
- Pain

Arterial Blood Sampling

Indications

- To obtain blood for blood gas measurements
- When blood is needed and venous or capillary blood samples cannot be obtained

Equipment

- 23-25 gauge scalp vein needle or 23-25 gauge venipuncture needle
- Syringe (1 or 3 ml)
- Povidone-iodine and alcohol swabs
- Gauze pad (4×4)
- Gloves
- Heparin 1:1000

Procedure

- Draw a small amount of heparin (concentration 1:1,000) into the syringe and then discard any excess heparin.
- Site:
  - Radial artery: the most frequently used.
  - Alternative sites: posterior tibial or dorsalis pedis arteries.
  - Femoral arteries in emergency situations.
  - Brachial arteries not used (minimal collateral circulation and a risk of median nerve damage).
  - Temporal arteries not used (a high risk of neurologic complications).
- Allen test: to check for collateral circulation and patency of the ulnar artery:
  - Elevate the arm and simultaneously occlude the radial and ulnar arteries at the wrist.
  - Rub the palm to cause blanching.
  - Release pressure on the ulnar artery:
    - Adequate collateral circulation: if normal color returns in the palm in <10 seconds.
    - Poor collateral circulation: if normal color does not return in 15 seconds or longer or does not return at all (do not use the radial artery in this arm, and check the other arm).
- Take the infant's hand in your left hand and extend the wrist. Palpate the radial artery with the index finger. Mark the puncture site with a fingernail imprint.
- Clean the puncture site first with a povidone-iodine swab and then with an alcohol swab.

- Puncture the skin at about a 30° angle, and slowly advance the needle with the bevel up until blood appears in the tubing.
- Collect the least amount of blood needed for the test (the volume of blood taken should not exceed 3-5% of the total blood volume).
- Withdraw the needle and apply firm but not occlusive pressure to the site for ≥5 minutes with a gauze pad.
- Expel air bubbles from the sample and tightly cap the syringe.
- Place the syringe in ice, and take it to the laboratory immediately. Note the collection time and the infant's temperature and hemoglobin on the laboratory slip.

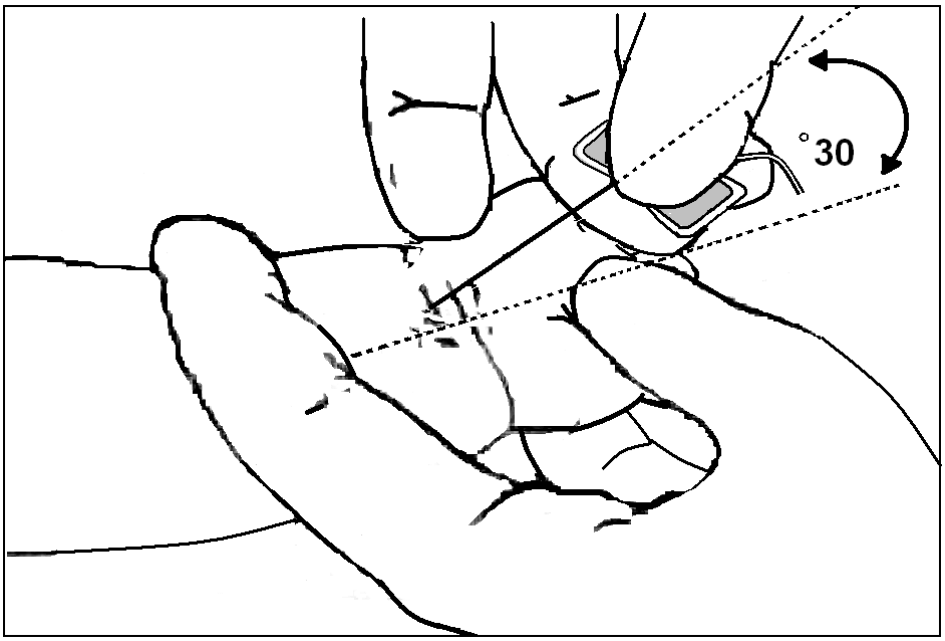


Figure (44-8): Technique of arterial puncture in the neonate

Complications

- Hematoma
- Arteriospasm, thrombosis, and embolism
- Infection
- Inaccurate blood gas results.
  - Excessive heparin may result in a false low pH and $PaCO_2$.
  - Air bubbles may falsely elevate the PaO_2 and falsely lower the $PaCO_2$.

Blood Glucose Monitoring

Blood glucose monitoring should be performed on all infants with risk factors and those who present with symptoms of hypoglycemia.

Arterial blood samples have slightly higher glucose concentrations than simultaneous venous samples, with capillary blood samples being in the intermediate zone. While these differences are of little clinical significance in well babies, capillary blood sample measurements of blood glucose in poorly perfused infants may be misleading.

Indications

Infants at risk for hypoglycemia

Some babies are more likely to have low blood glucose in the first few hours or days of life. The following babies need routine glucose checks:

- Infants of diabetic mothers (IDM)
- Large for gestational age infants (LGA)
- Small for gestational age infants (SGA)
- Preterm and post-term infants
- Sick or stressed infants (RDS, hypothermia)
- Neonates experiencing delayed feeding
- Infants with polycythemia
- Infants with erythroblastosis
- Maternal drugs (e.g., steroids, β-sympathomimetics, and β-blockers)

Infants demonstrating symptoms of hypoglycemia

- A blood glucose screen should be performed immediately.
- In hypoglycemic infants, plasma glucose values should be repeated 1-2 hrs after initiation of treatment if the infant remains asymptomatic, or every 20-30 minutes, if symptomatic.

Infants at risk for hyperglycemia

- Infants may be at risk when receiving a high glucose infusion.

N.B.: Blood glucose screens should be performed according to the physician's orders.

Equipment

All neonatal care units must have adequate equipment and be able to perform blood glucose screenings. The required equipment includes:

- Gloves
- Fresh reagent strips
- Micro lancets
- A container for (sharps), i.e. for lancets

- A clock or watch
- Alcohol swabs
- Cotton wool swab to stop the bleeding
- Sterile 2×2 gauze pads
- Adhesive bandages (optional)

Procedure

- The area should be cleaned thoroughly with alcohol swabs. Be sure to allow the area to dry, because alcohol may alter the reading.
- The person performing the procedure should wear appropriately fitting gloves.
- Heel puncture should be done on the most medial or lateral portions of the plantar surface of the heel. Do not use the center of the heel (increased incidence of osteomyelitis).
- Encircle the heel with the palm of your hand and index finger **(Figure 44-9)**.
- Make a quick, deep (<2.5 mm) puncture with a lancet.
- Remove the first drop of blood with a gauze pad, gently squeeze the heel, and collect the subsequent large drop of blood on the reagent strip.
- Repeated sampling at previous puncture sites should be avoided.
- Maintain pressure on the puncture site with a dry sterile gauze pad until the bleeding stops. Consider using an adhesive bandage if necessary.

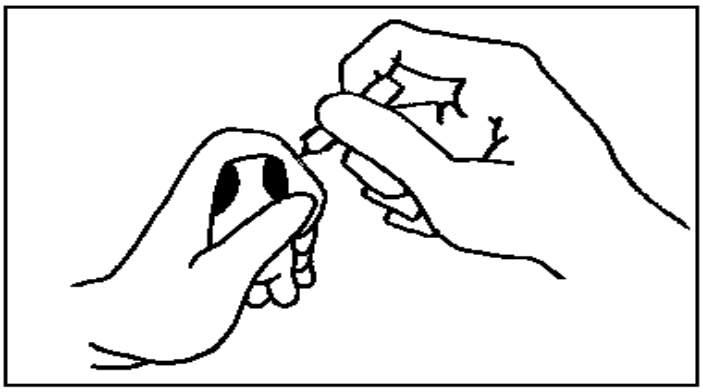


Figure (44-9): Technique of heel prick in a newborn infant

Points to be remembered

- Reagent strips must be:
  - Fresh and stored at room temperature, not in a fridge.
  - Kept away from direct sunlight. Replace the cap immediately after a reagent strip is removed (temperature, humidity or light may cause the reagents to deteriorate, possibly resulting in a false low reading).
  - Discarded if the expiry date on the bottle has been reached.
- The whole reagent area must be covered with blood to prevent difficulty in reading the color change. A large drop of blood is, therefore, needed.

- The blood must be wiped off after exactly 60 seconds. Waiting less than 60 seconds will give a false low reading while waiting too long will give a false high reading. It is advisable to use a watch or clock with a second hand to measure the 60 seconds accurately.
- Do not attempt to wipe, wash off, or rub off any pieces of adherent, dry blood, as excessive washing will give a false low reading.
- A low packed cell volume (PCV) may give a false high reading while a high PCV may give a false low reading.

Umbilical Vessel Catheterization

Umbilical Artery Catheterization

Indications

- When frequent or continuous measurements of arterial blood gases are required
- For continuous arterial blood pressure monitoring
- To provide exchange transfusion (for constant withdrawal of infant blood and not for infusion of donor blood)
- For angiography

Equipment

- Sterile gown and gloves
- Antiseptic solution
- Surgical drape with central aperture
- Size 3.5-5Fr umbilical catheter
- Three-way stopcock
- 10 ml syringe
- Saline flush solution (saline with heparin, 1-2 U/ml)
- Scissors
- Tape measure
- Umbilical tie
- Gauze sponge
- Two curved mosquito hemostats
- Toothed iris forceps
- Two curved, non-toothed iris forceps
- 3-0 silk suture on small, curved needle

Technique

Catheter insertion

- Determine the appropriate length of catheter to be inserted. The tip of the catheter should be above the level of the liver in UVC, between T6-T9 in high position UAC, and between L3-L4 in low position UAC **(Figure 44-10)**. The required length of catheter can be obtained from the umbilical catheter measurements **(Figures 44-12 and 44-14)**.
- Follow sterile technique
  - ► Scrub hands to elbow for 3 minutes.
  - ► Put on sterile gloves, a mask, a hat, and a sterile gown.

- Cleanse the cord and surrounding area with an antiseptic solution. Avoid tincture of iodine because of the potential effect on the neonatal thyroid; other iodine-containing products (e.g., povidone-iodine) can be used.
- Drape the abdomen with sterile towels leaving the feet and head exposed to observe the infant closely during the procedure for vasospasm in the legs or signs of distress.

- Prepare the area **(Figure 44-11)**
  - Place umbilical tape around the base of the cord and tie loosely with a single knot.
  - Cut the cord horizontally with a scalpel to a length of 1 cm from skin.
- Dilate the vessel **(Figure 44-11)**
  - Remove clots with forceps.
  - Identify cord vessels.
    - Vein is identified as large, thin-walled, sometimes gaping vessel. It is most frequently situated at the 12 O'clock position at the base of the umbilical stump.
    - Arteries are smaller, thick-walled, usually located at the 4 and 7 O'clock positions; they are white and may protrude slightly from cut surface.
  - Grasp cord stump to hold it upright and steady, using toothed forceps at point close to (but not on) the vessel to be catheterized.
  - Gently dilate the vessel by inserting iris forceps into the lumen to a depth of 0.5 cm and leave them in place for a minute after the release of tension on the forceps.
- Insertion of the catheter **(Figure 44-11)**
  - A sterile, saline-filled, size 3.5-5 Fr umbilical catheter is threaded into the vessel to the calculated length.
  - Umbilical artery catheter can be placed in one of two positions:
    - Low catheterization: the catheter tip lies between lumbar vertebral bodies **L3 and L4**; this position is below the celiac trunk, the mesenteric arteries, and the renal arteries, and above the aortic bifurcation (L4-L5). Low positioning is associated with more episodes of vasospasm of the lower extremities.
    - High catheterization (preferred): the catheter tip lies above the diaphragm at the level of the thoracic vertebrae from **T6** to **T9**. High positioning is associated with hypertension and an increased risk of intraventricular hemorrhage. It is also associated with a lower incidence of blanching and cyanosis of the extremities.
  - The required length of catheter can be obtained from the umbilical catheter measurements **(Figure 44-12)**. For the high position, the insertion depth could be calculated using the following formula: UAC depth (cm) = (weight [kg] × 3) + 9.
  - A good blood flow should be established through the catheter.
  - The position of the catheter should be verified by x-ray, preferably before use **(Refer to Appendix 9).**

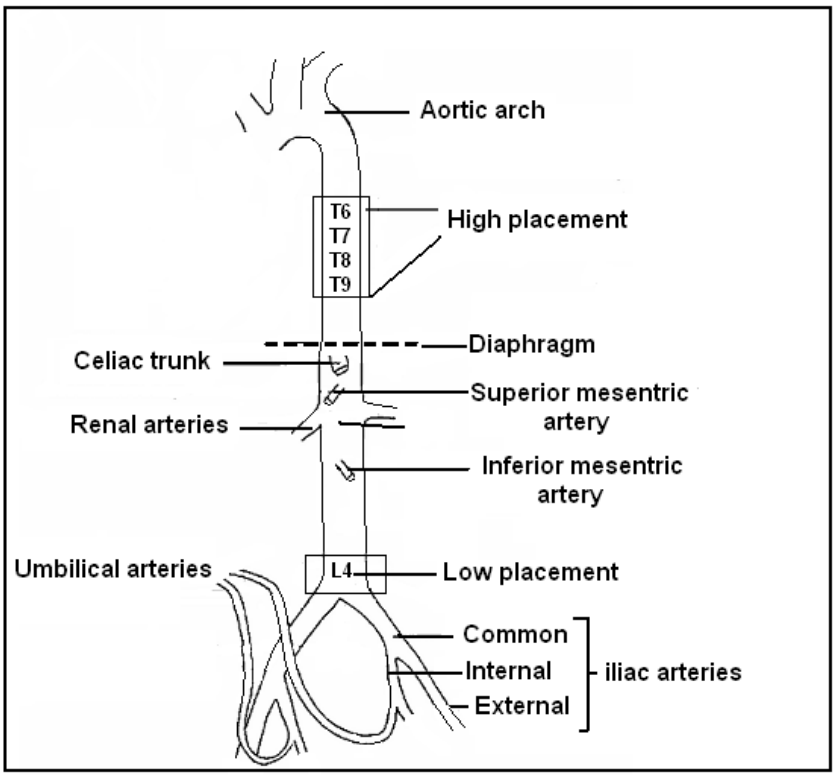


Figure (44-10): Localization of umbilical artery catheter

- If the catheter tip is above required position, measure distance between actual and appropriate position on the radiograph and withdraw equal length of catheter. Then repeat the radiographic study. If the catheter tip is below the required position, remove the catheter. Never advance it once in situ, because this will introduce a length of contaminated catheter into the vessel.

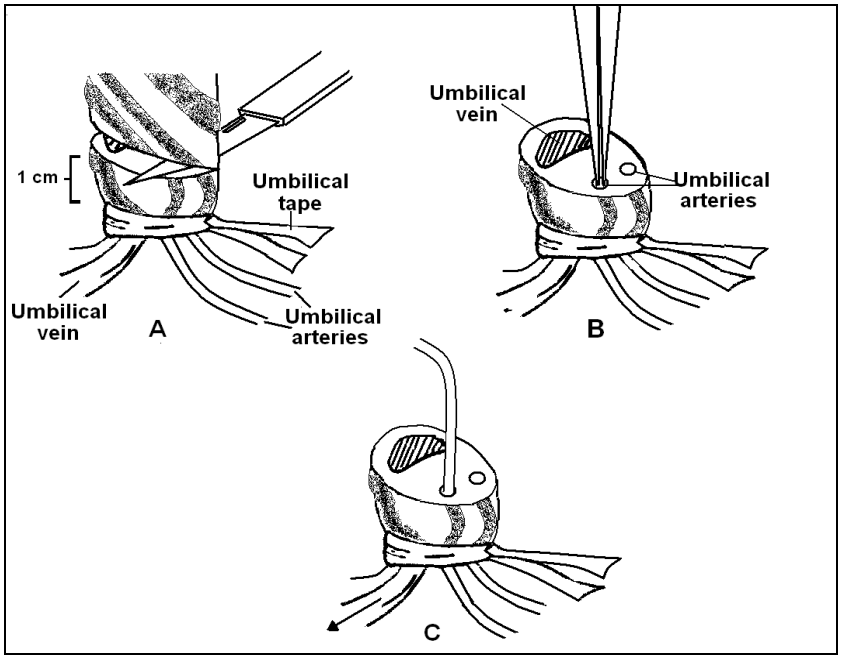


Figure (44-11): Umbilical artery catheter insertion

A) Cutting the umbilical cord leaving a 1 cm stump, B) gently dilate the umbilical artery with a forceps, C) Catheter is inserted into the umbilical artery.

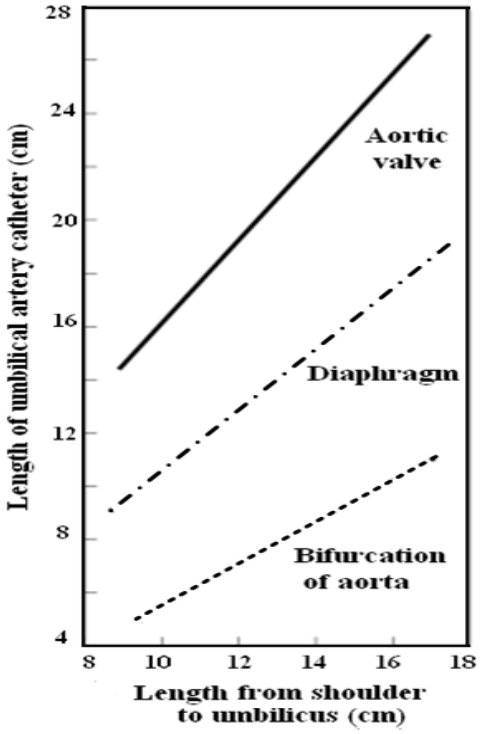


Figure (44-12): The umbilical artery catheter can be placed in one of two positions.

The low catheter is placed below the level of L3 (between L3 and L4) to avoid the renal and mesenteric vessels. The high catheter is placed between the thoracic vertebrae from T6 to T9. The graph is used as a guide to help determine the catheter length for each position. The low line corresponds to the aortic bifurcation in the graph, whereas a high line corresponds to the diaphragm. To determine catheter length, measure (in centimeters) a perpendicular line from the top of the shoulder to the umbilicus. This determines the shoulder-umbilical length. Plot this number on the graph to determine the proper catheter length for the umbilical artery catheter. It is helpful to add the length of the umbilical stump to catheter length. (From Dunn PM: Localization of the umbilical catheter by postmortem measurement. Arch Dis Child 1966; 41:69. Reproduced with permission from BMJ Publishing Group Ltd)

- Fixation **(Figure 44-13)**
  - Place a purse-string suture using silk thread around base of the cord (not through skin or vessels).
  - Add a tape bridge for further stability.

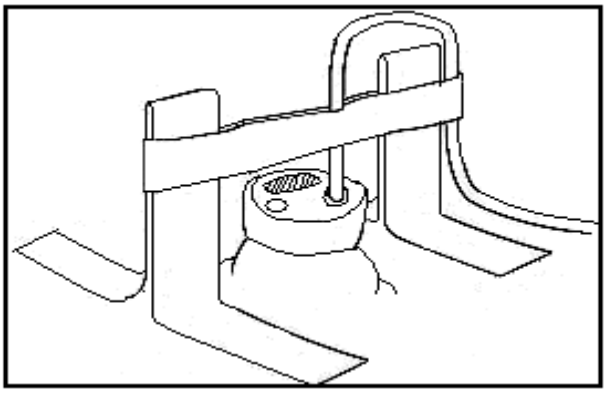


Figure (44-13): Securing the catheter to the abdominal wall using (bridge method) of taping

Catheter care

- Add dilute heparin, 0.25 unit/ml of infusate to prevent clotting.

Catheter removal

- Indications of catheter removal:
  - The infant improves, so that continuous monitoring and frequent blood drawing is no longer necessary.
  - UAC **should not** be left in place for more than 5 days to reduce infectious and thrombotic complications.
  - Complications are noted.
- Slowly remove the catheter over 30-60 seconds to allow the umbilical artery to constrict at its proximal end while the catheter is still occluding the distal end.

Complications

- Bleeding may occur if the catheter or tubing becomes disconnected
- Infection
- Thromboembolic phenomena
- Vessel perforation
- Blanching of a leg due to vasospasm
- Hypertension, a long-term complication, as a result of improper catheter placement near the renal arteries

Umbilical Vein Catheterization

Indications

- Central venous pressure (CVP) monitoring
- Immediate access for IV fluids or emergency medications (e.g., neonatal resuscitation)
- Exchange transfusion or partial exchange transfusion
- Long-term central venous access in extremely low birth weight infants

Equipment

Prepare the same equipment as for umbilical artery catheterization, except using a No. 6Fr catheter for infants weighing <3.5 kg, and a No. 8Fr catheter for those weighing >3.5 kg.

Technique (Figure 44-16)

It is similar to umbilical artery catheterization

- Determine the specific length of catheter needed **(Figure 44-14)**. Another method is to measure the length from the xiphoid to the umbilicus and add 0.5-1 cm (this number indicates how far the venous catheter should be inserted). If the catheter is placed for an exchange transfusion, it should be advanced only as far as it is necessary to establish good blood flow (usually 2-5 cm).
- Occasionally, a catheter will enter the portal vein. This should be suspected if a resistance is met and the catheter can not be advanced to the desired distance, or if a

bobbing motion of the catheter is detected. Several options are available to correct this:

- Try injecting flush as you advance the catheter.
- Pass another catheter (a smaller size) through the same opening and then remove the one in the portal system.
- Apply mild manual pressure in the right upper quadrant over the liver.

- Only isotonic solution is infused until the position of the catheter is confirmed by x-ray films **(Refer to Appendix 9)**.
- Never advance a catheter once it is secured in place.
- Umbilical venous catheters should be removed as soon as possible when no longer needed, but can be used up to 14 days if managed aseptically.

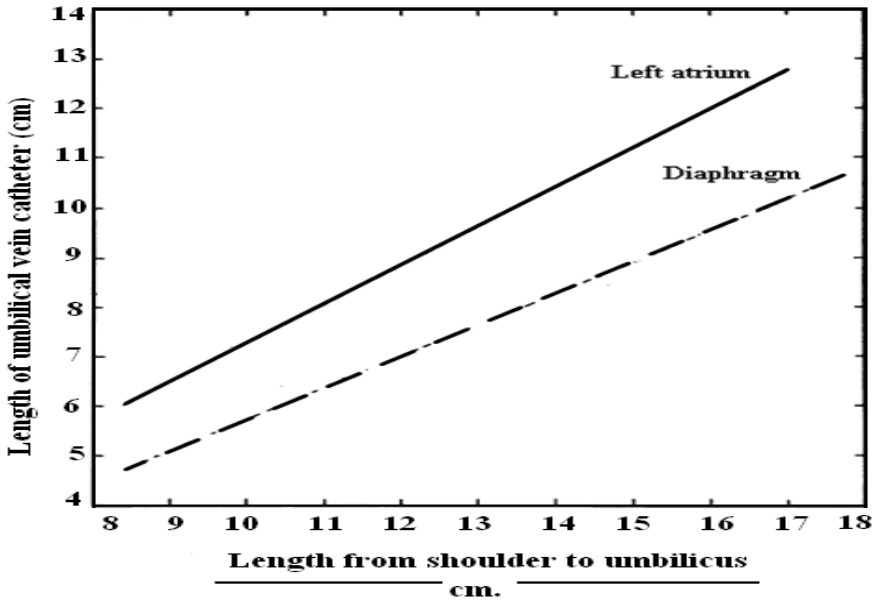


Figure (44-14): The umbilical venous catheter is placed above the level of the diaphragm. Determine the shoulder-umbilical length as for the umbilical artery catheter. Use this number determine the catheter length using the graph. Remember to add the length of the umbilical stump to the length of the catheter.

(From Dunn PM: Localization of the umbilical catheter by post-mortem measurement. Arch Dis Child 1966; 41: 69. Reproduced with permission from BMJ Publishing Group Ltd)

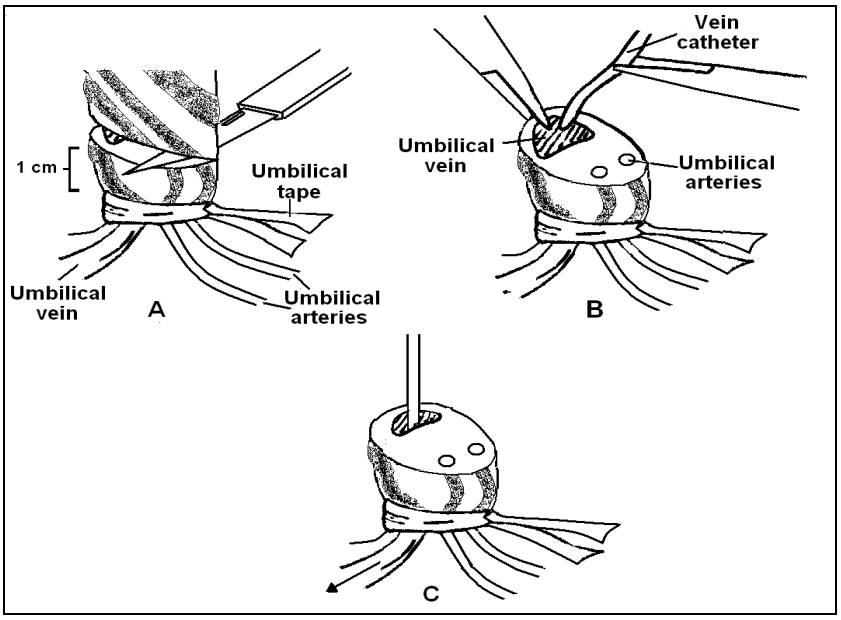


Figure (44-15): Umbilical vein catheter insertion

A) Cutting the umbilical cord leaving a 1-cm stump. B) Umbilical stump is held for catheter insertion. C) Catheter is inserted into the umbilical vein.

Complications

- Infection: the risk of infection can be minimized by following strict aseptic technique, and not advancing the catheter after positioning.
- Thrombolic or embolic phenomenon: do not allow the air to enter the catheter and do not try to flush clots from the catheter end; a nonfunctioning catheter should be removed.
- Hepatic necrosis: do not allow a catheter to remain in the portal system. In case of emergency placement, the catheter should be advanced only 3 cm (just until blood returns) to avoid hepatic infusion.
- Cardiac arrhythmias: by a catheter that is inserted too far and is irritating the heart.
- Portal hypertension: by a catheter that is positioned in the portal system.

Contraindications of Umbilical Vessel Catheterization

- Evidence of local vascular compromise in lower limbs or buttock areas
- Peritonitis
- Necrotizing enterocolitis
- Omphalitis
- Omphalocele
- Acute abdomen etiology

Points to be remembered

- Do not use topical antibiotic ointment or creams on umbilical catheter insertion sites because of the potential to promote fungal infections and antimicrobial resistance.
- Replace umbilical venous catheters if the catheter malfunctions.

- Remove and do not replace umbilical venous catheters if any signs of CRBSI or thrombosis are present.
- Remove and do not replace umbilical artery catheters if there are any signs of catheter related blood stream infection (CRBSI), vascular insufficiency, or thrombosis.
- Remove umbilical catheters as soon as possible when no longer needed or when any sign of vascular insufficiency to the lower extremities is observed.

Exchange Transfusion

Exchange Transfusion Techniques

Two techniques of exchange transfusion are used:

- Pull-push, or intermittent, method involves drawing an aliquot of infants' blood and then replacing it with an aliquot of donor blood.
- Continuous, or isovolumetric, method involves constant infusion of donor blood via the umbilical vein and a constant withdrawal of infant's blood via the umbilical artery. This method provides a more consistent arterial blood pressure and may be tolerated better in small, sick, or hydropic infants.

Indications

- Hyperbilirubinemia, of any etiology, when phototherapy fails to prevent rise in bilirubin to toxic levels **(Refer to Chapter 21).**
- Hemolytic disease of the newborn (ABO and Rh incompatibility) where exchange transfusion aids in removing antibody-coated RBCs, in removing potentially toxic bilirubin, and in providing plasma volume and albumin for bilirubin binding. Early exchange transfusion is usually indicated if:
  - Cord bilirubin level is >4.5 mg/dl and the cord hemoglobin (Hb) level <11 gm/dl.
  - Hemoglobin (Hb) level is between 11-13 gm/dl.
  - Bilirubin increasing >1 mg/dl/hr despite phototherapy.
- Exchange transfusion also corrects anemia and improves heart failure in hydrops fetalis due to hemolytic diseases.
- Partial exchange transfusion is usually indicated in treatment of clinical polycythemia.

Equipment

General exchange transfusion equipment

- Sterile gown and sterile gloves
- Sterile towels
- Radiant warmer
- Equipment for respiratory support and resuscitation (e.g., oxygen or a suctioning device)
- Equipment for monitoring the heart rate, blood pressure, respiratory rate, temperature, PaO_2, $PaCO_2$, and SaO_2.
- Equipment for umbilical artery and umbilical vein catheterization
- Blood filter
- IV tubing between donor blood and stopcock
- IV tubing between stopcock and collection container
- Plastic bag or container to collect exchanged blood

- Two sizes 3-5 ml syringes for pre- and post-exchange laboratory samples
- Appropriate blood product
- Syringes and tubes for pre-and post-exchange blood tests

Methods of Exchange Transfusion

Pull-push method

- One "4-way" stopcock (if not available, two "3-way stopcocks" connected)
- Syringes 5, 10, 20 ml

Continuous method

- Three "3-way" stopcocks
- One 50-60 ml syringe for each 150 ml of blood to be withdrawn
- One 50-60 ml syringe for the infusion of blood
- One 5 ml syringe for a heparinized saline flush

Preparation for Exchange Transfusion

- Send the maternal and infant blood to the laboratory for cross matching.
- Prepare type of blood for exchange transfusion:
  - In neonates with Rh incompatibility, use Rh negative blood that has been cross-matched with the mother's blood if prepared before delivery. It may be also cross matched with the infant if the blood is obtained after delivery.
  - In neonates with ABO incompatibility, use O positive or O negative group and with low-titer anti-A and anti-B blood that has been cross-matched with both the infant's and mother's blood.
  - In other cases, use the infant's group after cross-matching with the infant's blood.
- Use only fresh (<72 hrs old) citrated blood.
- Establish and document baseline vital signs.
- Do not give anything orally for 3-4 hrs prior to the procedure. A nasogastric tube should be passed to evacuate the stomach and should be left in place to prevent regurgitation and aspiration of gastric juices.
- Calculate the volume of blood to be exchanged: usually a double-volume exchange transfusion is performed (i.e., double the volume of the infant's blood). If the infant's blood volume is 80 ml/kg, then a double-volume exchange transfusion requires 160 ml of donor's blood for every kilogram of infant's weight.

Required blood volume (ml) = 80 ml × Infant's weight [kg] × 2

- Once the blood is available it needs to be well-mixed. This can be accomplished by hanging it upside down for approximately 20-30 minutes; this is followed by checking the hematocrit level (Hct should be between 45-55%).
- Use no more than equivalent of one whole unit of blood for each procedure, to decrease donor exposure.

- Warm the blood to a temperature of 37°C, either by placing the tubing in a blood warmer with a precise thermostatic control or by immersing the tubing in a warm water bath of 37-38°C. Excessive heating can cause hemolysis. It is not appropriate to warm the blood under the radiant warmer.
- Exchange is done with the infant under a servo-controlled radiant warmer.
- Resuscitation and monitoring equipment must be available.
- Infant's arms and legs should be properly restrained (snug but not tight).
- A nurse must be available to assist exclusively with the procedure. While the physician performs the procedure, she must constantly monitor the infant's condition; perform any necessary interventions to maintain physiological stability, and record blood volume removal and infusion on the Exchange Transfusion Flow Sheet **(Table 44-1).**
- Sterile techniques should be used.
- Old dried umbilical cord can be softened with saline-soaked gauze.
- If using the pull-push method an umbilical venous catheter (UVC) must be inserted
- If using the continuous method an umbilical arterial catheter (UAC) and a UVC and/or a 23-gauge peripheral IV can be used.
- Obtain an x-ray to determine that the placement of the UVC is at or above the level of the diaphragm and is at the junction of the inferior vena cava and the right atrium. If it is not possible to place the catheter at the level of the diaphragm, the catheter can be inserted only as far as required to permit free blood exchange (2-5 cm). In this case, avoid infusing drugs such as calcium to prevent potential liver damage.

N.B.: A catheter placed in the heart may cause arrhythmias.

- Proper placement of the catheter is indicated by easily aspirating blood through it.
- Depending on the amount of blood to be exchanged, the procedure will take 1-2 hrs.

Pull-Push Method

- Blood is withdrawn or infused in aliquots that are tolerated by the infant. This usually is 5 ml for infants <1,500 gm, 10 ml for infants 1,500-2,500 gm, 15 ml for infants 2,500-3,500 gm, and 20 ml for infants >3,500 gm (smaller aliquots and a slower rate place less stress on the cardiovascular system). Whether withdrawing or infusing, the same amount of blood should always be handled.
- Once the desired amount of blood has been removed, the stopcock is turned off to the infant and opened to the collection bag and the blood is discarded into this bag.
- The stopcock is then turned off to the collection bag and opened to the donor blood and the same amount of blood that has just been removed from the infant is withdrawn from the donor blood bag. The stopcock is then closed to the donor bag and opened to the infant **(Figure 44-16) and (Figure 44-17)**. When injecting the donor blood into the infant, the syringe must be held upright so that air bubbles rise to the top and are not injected into the infant.
- The orientation of the stopcock(s) for infusion and withdrawal must be double-checked by an assistant (usually a nurse).

- The assistant should record the amount of blood removed and infused on the Exchange Transfusion Flow Sheet **(Table 44-1)**.
- Rapid shifts in blood volume are avoided by slowly and steadily removing the infant's blood and infusing donor blood at a rate of approximately one cycle/minute until the desired blood has been exchanged. The recommended time for the exchange transfusion is 1 hour.
- The blood bag should be gently agitated every 10-15 minutes to prevent red cell sedimentation and the transfusion of anemic blood at the end of exchange.

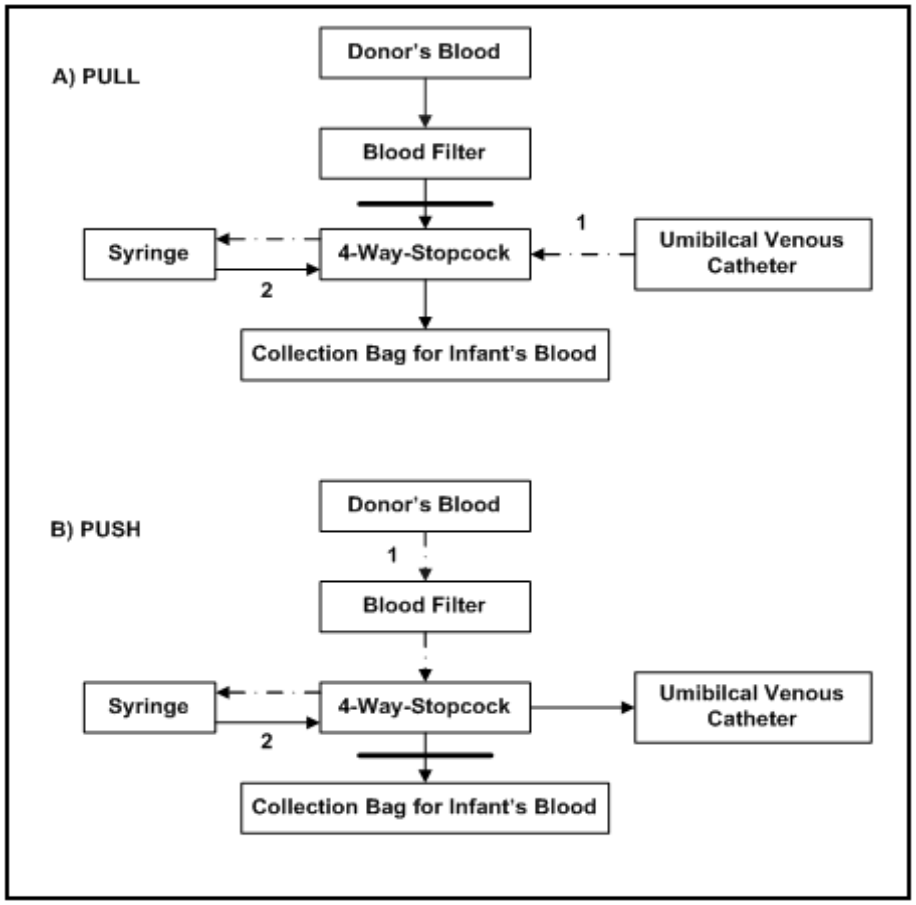
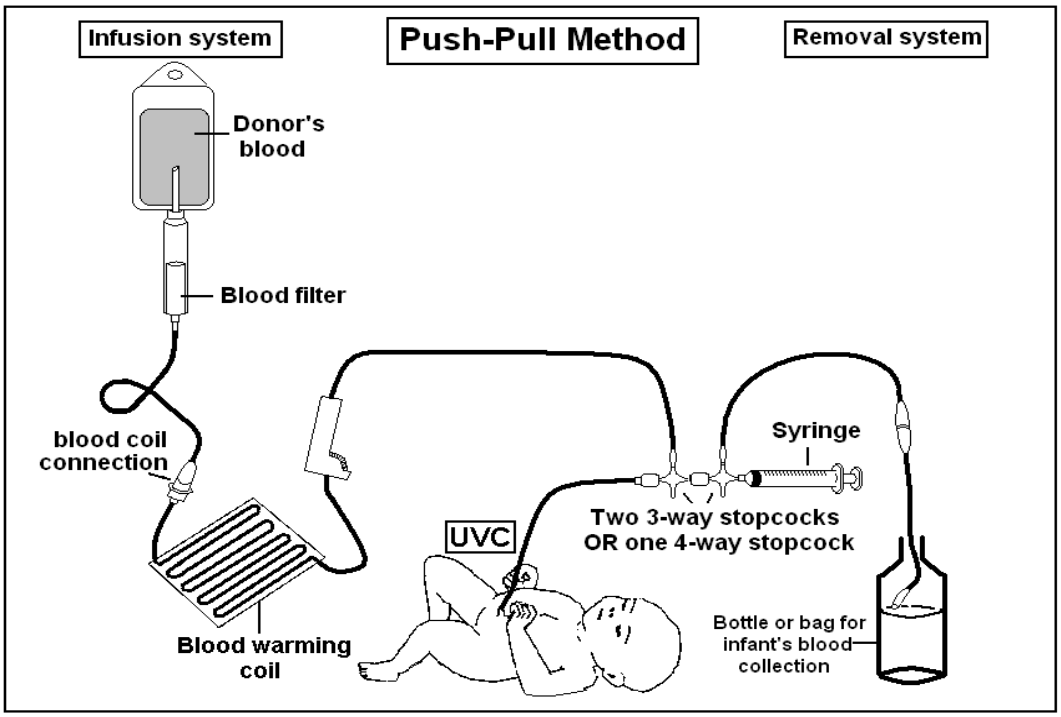


Figure (44-16): Schematic approach to Pull-Push method of exchange

A) Pull: 1) Blood is withdrawn from infant 2) Blood is discarded into collection bag

B) Push: 1) Donor's blood is withdrawn from the blood bag 2) Donor's blood is injected into the infant.

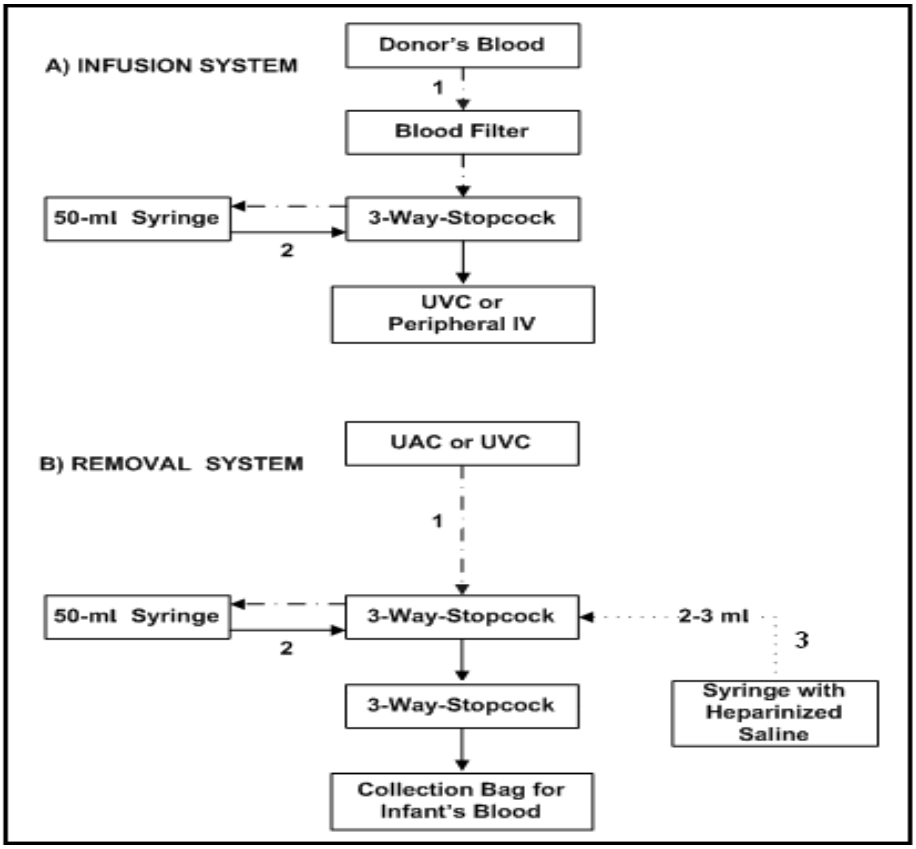


UVC: Umbilical vein catheter

Figure (44-17): Pull-Push method of exchange

Continuous (Isovolumetric) Method

- The blood is infused and withdrawn simultaneously, so that the rate of infusion and withdrawal remains equal and shifts in blood volume do not occur. Once the procedure has begun, it is important to have a third person available to record the blood removed and infused and to maintain a running total so that at the end of the procedure the total amounts are equal **(Figure 44-18) and (Figure 44-19)**.
- The member of the team performing the infusion portion of the exchange opens the stopcock to the donor blood and fills the 50-60 ml syringe, then turns the stopcock off to the donor blood and opens it to the UVC or peripheral IV that is being used for the infusion. The donor blood is then infused at a rate of 2-3 ml/kg/minute. The blood bag should be gently agitated every 10-15 minutes to prevent red cell sedimentation. This procedure is continued until the desired volume of donor blood has been infused.
- The member of the team performing the removal portion opens the stopcock to the UAC or UVC (if not used for infusion) to withdraw the infant's blood and begins to fill the 50-60 ml syringe at a rate of 2-3 ml/kg/minute until 50 ml have been withdrawn. The stopcock is then turned to the collection bag and the infant's blood is quickly discarded into this bag. Periodically change the 50-60 ml syringe with a new one and gently flush the catheter with 1-2 ml of heparinized (5 unit/ml) saline to prevent clot formation. Continue to perform this procedure until the desired amount of infant's blood has been removed.

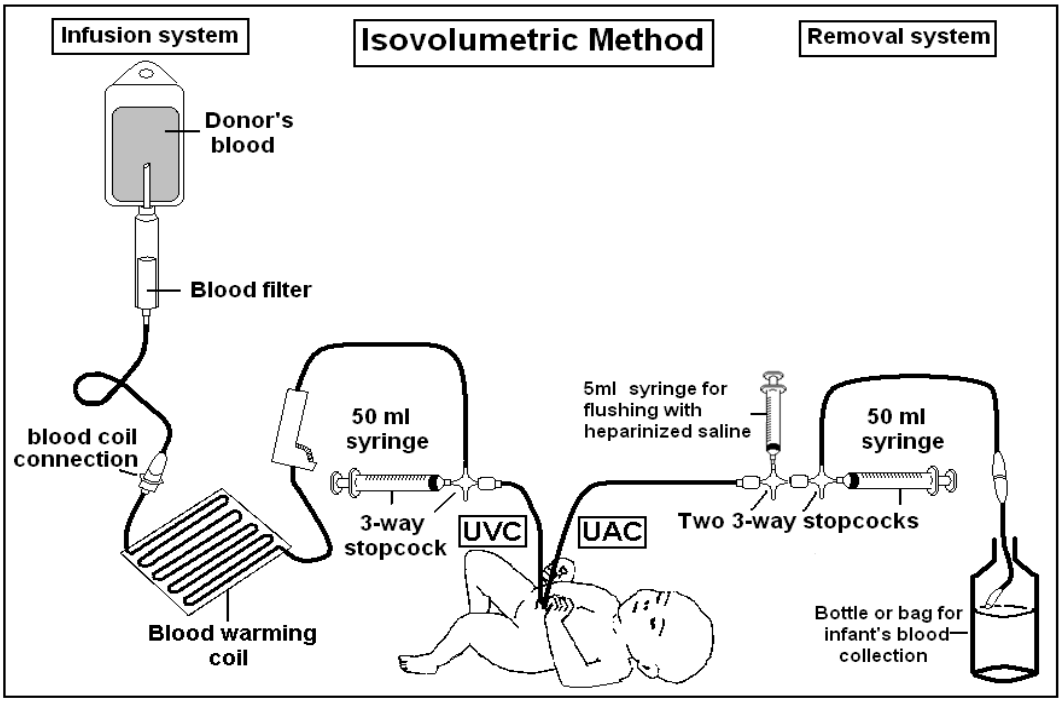


UAC: Umbilical artery catheter, UVC: Umbilical vein catheter

Figure (44-18): Schematic approach to continuous method of exchange

A) Infusion system: 1) Donor's blood is withdrawn from the blood bag, 2) Donor's blood is injected into the infant.

B) Removal system: 1) Blood is withdrawn from infant 2) Blood is discarded into collection bag 3) Periodically flush the catheter with 1-2 ml of heparinized saline.



UAC: Umbilical artery catheter, UVC: Umbilical vein catheter

Figure (44-19): Continuous method of exchange

Management of the Infant During and After Exchange Transfusion

- Before starting the procedure, 5-10 ml of blood should be withdrawn to check bilirubin, hematocrit, electrolytes and calcium levels.
- Infant's temperature, oxygenation and other vital signs should be checked and recorded every 15 minutes and a peripheral glucose value evaluated every 30 minutes. All should be maintained within normal limits throughout the procedure.
- Some physicians routinely administer 1-2 ml of 10% calcium gluconate by slow infusion after 100 ml of exchange donor blood. Others maintain that this treatment has no therapeutic effect unless hypocalcemia is documented by ECG changes.
- The infant should be observed for jitteriness, seizures, or apnea, which may be signs of hypocalcemia. If hypocalcemia is identified as the cause, the catheter should be flushed with normal saline, and 100-200 mg of 10% calcium gluconate should be administered slowly through the UVC or peripheral IV. Calcium **must not** be administered quickly, especially through a UVC, because it can cause cardiac arrest. If the infant's heart rate begins to slow during administration, the calcium should be stopped immediately. Once the calcium has been administered, the catheter should be flushed and the exchange transfusion continued.
- When the desired amount of blood has been exchanged, an infant's blood sample should be sent to the laboratory for glucose, bilirubin, hematocrit, electrolyte and calcium values and cross-matched for possible future exchanges.
- Bilirubin levels should be checked every 4-6 hrs until adequate levels are achieved or an additional exchange transfusion is deemed necessary (a rebound of bilirubin levels is to be expected 2-4 hrs after the transfusion).
- Phototherapy should be reinstituted and vital signs checked every 15-30 minutes for 3-4 hrs, or until stable.
- Oral feedings may be resumed 2-3 hr after the exchange is completed.
- If a dirty cord was entered or there was a break in sterile technique, antibiotic prophylaxis should be considered.

Complications

- Metabolic: Hypocalcemia, hypo- or hyperglycemia, hyperkalemia
- Cardiopulmonary: apnea, bradycardia, hypotension, hypertension, arrhythmias
- Hematologic: thrombocytopenia, dilutional coagulopathy, neutropenia, disseminated intravascular coagulation
- Vascular catheter-related: vasospasm, thrombosis, embolization
- Gastrointestinal: feeding intolerance, ischemic injury and NEC
- Infection: omphalitis, septicemia (usually caused by a *Staphylococcus* organism), HIV, CMV and hepatitis
- Hypothermia and hyperthermia
- Rash with or without graft versus host disease (GVHD)

Table (44-1): Exchange transfusion flow sheet

EXCHANGE TRANSFUSION FLOW SHEET							Pre-exchange		Post-exchange	
Date			Exchange transfusion #				Hematocrit		Hematocrit	
Name of infant			Birth weight				Bilirubin		Bilirubin	
Date of birth			Time of birth				Calcium		Calcium	
Diagnosis							Potassium		Potassium	
							Sodium		Sodium	
Mother's blood type							Chloride		Chloride	
Infant's blood type			Coombs				Time exchange started			
Blood buffered?	Yes		No				Time exchange finished			
If yes, with what?			Amount				Total volume withdrawn from infant			
Donor Blood type							Total volume given to infant			
Donor Blood Hematocrit							Top up blood transfusion		Yes	No / Amount

Time	Blood out		Blood in		Baby's Temperature	Pulse	Resp.	BP	SaO_2	Blood Glucose	Medication Comments
	AMT	Total	AMT	Total							

Suprapubic Bladder Aspiration

Indications

This intervention is used to obtain urine for culture when a less invasive technique is not possible.

Equipment

- Sterile gloves
- Povidone-iodine solution
- 23 or 25 gauge needle with a 3 ml syringe attached
- Gauze pads (4×4)
- Sterile container

Procedure

- Be certain that voiding has not occurred within the previous hour.
- An assistant should hold the infant's legs in the frog-leg position.
- Put on sterile gloves, and clean the skin at the puncture site with antiseptic solution three times.
- Palpate the pubic symphysis and insert the needle 1-2 cm above the pubic symphysis in the midline at a 90° angle.
- Advance the needle while aspirating at the same time. Do not advance the needle once urine is seen in the syringe.
- Withdraw the needle, and maintain pressure over the site of the puncture.
- Place a sterile cap on the syringe or transfer the specimen to a sterile urine cup.

Complications

- Bleeding: check platelet count before aspiration; if low, the procedure should not be performed.
- Infection: minimize the risk by the use of strict aseptic technique.
- Bowel perforation: if occurs, close observation and intravenous antibiotics should be considered.

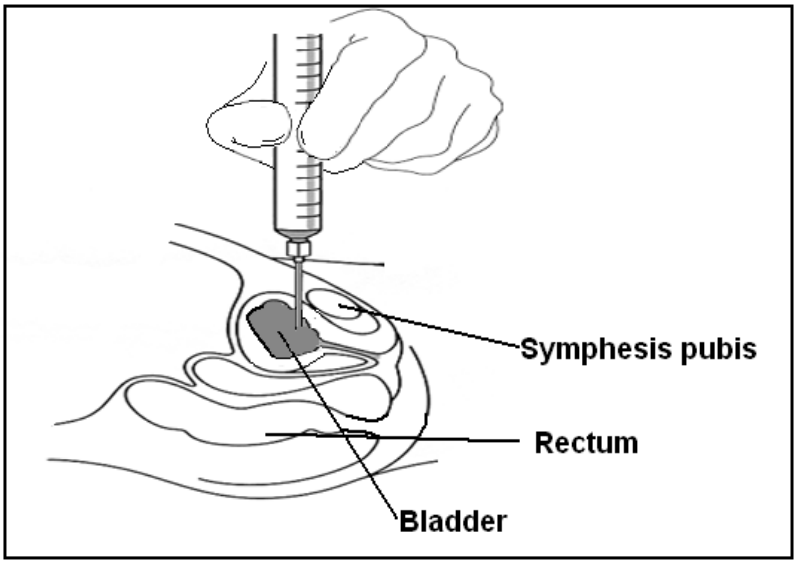


Figure (44-20): Suprapubic bladder aspiration

Lumbar Puncture

Indications

This procedure is used:

- To diagnosis CNS disorders such as meningitis/encephalitis or intracranial hemorrhage.
- To drain CSF in communicating hydrocephalus associated with intraventricular hemorrhage.
- To administer intrathecal medications.

Equipment

- Three sterile specimen tubes
- Sterile drapes
- Gloves
- Sterile gauze
- Lidocaine 1%
- Povidone-iodine solution
- 22-24 gauge spinal needle with stylet
- 1 ml syringe

Procedure

- Positioning: either a sitting or a lateral decubitus position can be used. An intubated, critically ill infant must be placed in the lateral decubitus position. The assistant should hold the infant firmly at the shoulders and buttocks so that the lower part of the spine is curved. Neck flexion should be avoided (not to compromise the airway).
- Supplemental oxygen is used before the procedure or for increasing oxygen if the infant is already on it.
- Site: the space between the 4^{th} and 5^{th} lumbar processes.
- Palpate the iliac crest and slide your finger down to the L4 vertebral body and make a nail imprint at the exact location to mark the site **(Figure 44-21).**
- Put gloves on and clean the lumbar area with antiseptic solution, starting at the selected interspace (a widening circle from that interspace up and over the iliac crest).
- Drape the area with one towel under the infant and one towel covering everything but the selected interspace. Keep the infant's face exposed.
- Inject 0.1-0.2 ml of 1% lidocaine subcutaneously (optional).
- Insert the needle in the midline into the selected site. Advance the needle slowly in the direction towards the umbilicus, withdrawing the stylet frequently to check for the appearance of spinal fluid. Usually a slight “pop” is felt as the needle enters the subarachnoid space.
- Collect ~1 ml of CSF in each of the four sterile specimen tubes by allowing the fluid to drip into the tubes.

- Replace the stylet and withdraw the needle.
- Maintain pressure on the area, and clean off the antiseptic solution.
- For a routine CSF examination, send four tubes of CSF to the laboratory in the following recommended order.
  - Tube 1: for Gram's stain, culture, and sensitivity testing.
  - Tube 2: for glucose and protein levels.
  - Tube 3: for cell count and differential.
  - Tube 4 (optional): for rapid antigen tests for specific pathogens, such as group B streptococcus.
- If a bloody specimen is obtained in the first tube, observe for clearing in the second and third tubes:
  - If bleeding clears, the tap was traumatic.
  - If blood does not clear but forms clots, a blood vessel has probably been punctured. A repeat tap must be done.
  - If blood does not clear and does not clot, the infant probably has had IVH.

Complications

- Infection.
- Intraspinal epidermoid tumor by displacement of a plug of epithelial tissue into the dura.
- Herniation of cerebral tissue through the foramen magnum (not common because of the open fontanelle in infants).
- Spinal cord and nerve damage (avoid by using only interspaces below L4).
- Apnea and bradycardia from respiratory compromise caused by the infant being held too tightly during the procedure.
- Hypoxia prevented by preoxygenation of the infant and increasing the oxygen during the procedure.

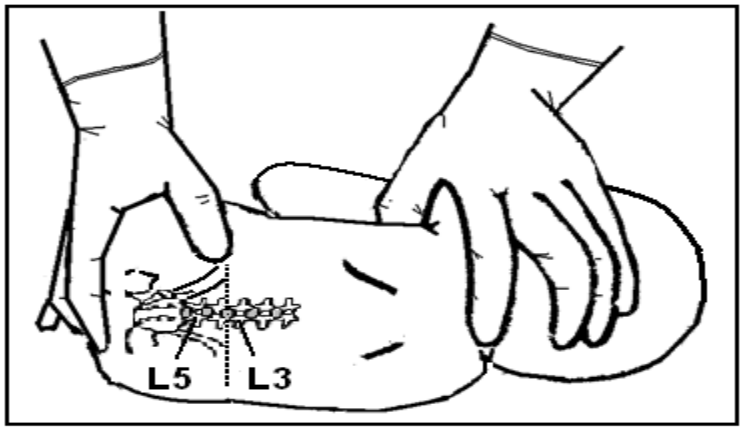


Figure (44-21): Positioning the infant for lumbar puncture, and landmarks used for lumbar puncture, the iliac crest marks the approximate level of L4.

Blood and Blood Products Transfusion

Indications

Red blood cell transfusion

(Refer to Chapter 34)

Fresh frozen plasma transfusion

- Acquired deficiencies in coagulation (e.g., DIC and liver failure) or congenital coagulation factor deficiency when specific factor replacement therapy is not available
- Unspecified hereditary coagulopathy
- Volume expansion in the presence of abnormal coagulation
- Homozygous protein C deficiency if the protein concentrate is not available. Also in protein S deficiency and purpura fulminans

Platelets transfusion

- An otherwise stable healthy term infant with a platelet count as low as 20,000-30,000/μL may be allowed a platelet transfusion.
- Prophylactic platelet transfusions should be considered for ill neonates with platelet count less than 20,000-50,000/μL.
- Infants receiving indomethacin or thrombolytics/anticoagulants should have a platelet count of more than 75,000/μL.
- Therapeutic platelet transfusions (i.e., active bleeding) should be considered for infants whose platelet count is less than 100,000/μL (also those in need for elective invasive procedures).
- Hemorrhage associated with acquired (e.g., uremia) or congenital qualitative platelet abnormalities may be allowed a platelet transfusion even if the platelet count is in the normal range.

N.B.: Platelets are administered in 10 ml/kg aliquots/hr. Infants receive type specific or group O platelets in plasma compatible with the infant.

Cryoprecipitate transfusion

- Bleeding episodes associated with Von Willebrand disease (if a factor VIII product co-purified with VWF is not available)
- Factor XIII deficiency (treatment of choice)
- Congenital afibrinogenemia or severe hypofibrinogenemia associated with DIC
- Infants with volume overload and ongoing coagulopathy

Transfusion Procedure

The following steps apply to all blood and blood-product transfusions. The only blood product exempted from this procedure is albumin.

- The physician must write all transfusion orders.

- Consent from the parents must be obtained after explaining the reason for the transfusion.
- Two nurses or physicians must check the blood together for name, type and Rh, medical record number, and expiration date.
- When a large volume of blood is to be transfused, it must be warmed first. Never submerge the blood bag into warm water or place under a hot light.
- Blood to be administered must be drawn through a blood filter and administered by direct drip or via a syringe pump. Mechanical pumps must not be used under any circumstances for the transfusion of red blood cells.
- FFP, cryoprecipitate, and platelets should be filtered before giving. If using a syringe pump to administer FFP or cryoprecipitate they must be drawn through a filter.
- Place the infant on a cardiac monitor during the transfusion.
- Vital signs should be recorded according to the following schedule:
  - Fifteen minutes before the transfusion
  - Once each hour during the transfusion
  - One hour after the transfusion
- Observe the infant for any signs of a transfusion reaction.
- The blood product bag must be returned to the laboratory following a transfusion reaction.
- Transfusion information should be documented in the infant's chart following the procedure.
- Consider a dose of IV furosemide after transfusion in a fluid sensitive infant (e.g., chronic lung disease, or large PDA).
- If parenteral glucose administration is interrupted during blood transfusion, check blood glucose every hour during transfusion. Temporarily discontinue transfusion to deliver glucose if the blood sugar falls below 45 mg/dl. The blood glucose should be checked for rebound hypoglycemia 30 minutes to 1 hr after transfusion.
- The IV site must be checked every 15 minutes for redness, edema, or discoloration.
- A follow-up hematocrit should be obtained 4-6 hrs after transfusion.

N.B.: Only a certified nurse may hang blood. A student or uncertified nurse can not hang blood.

Preparation for Transfusion

- Obtain a blood sample to cross match the infant's blood
- Take a blood sample for cross match for red and white blood cell products.
  - Send a minimum of 2 ml in an EDTA tube with every request for cross-matched products.
  - Specimens are appropriate for only 72 hrs. If blood is needed after this time, a new specimen should be obtained.

- Other blood products (platelets, fresh frozen plasma, and cryoprecipitate):
  - Call blood bank to check if the infant's blood group and type is on record.
  - If a record of the infant's blood group/type does not exist in the blood bank send 2 ml EDTA blood.

Safety Technique

- Before drawing the specimen, prepare a label with the infant's name and medical record number printed legibly.
- Confirm the accuracy of the name and number on both the label and the infant's chart.
- If any correction is required, write a new label. Alterations should not be done on any labels prepared for transfusions.
- At the bedside, after drawing the blood, attach the label to the tube. Do not leave the infant's bed without attaching the label to the tube. The nurse or physician who drew the blood from the infant should sign the label.

Intravenous Access

- The IV catheter must be at least a size 23 gauge. Small catheters may damage red blood cells.
- Do not transfuse any blood product via arterial lines or umbilical artery catheters.
- Platelets should be administered through a peripheral venous access.
- Do not infuse parenteral nutrition (or any glucose containing fluids) along with the transfusion via the same line. Never add any drug or IV fluid to a unit of blood or blood product.
- Flush the IV with saline after the blood transfusion is completed.
- If the infant's IV rate was changed during the transfusion, check a glucose level every hour during the transfusion.

Donor's Blood

- There is a special consideration regarding the transfusion of donor blood to neonates. Neonates should be transfused only with CMV negative blood (CMV can cause hepatitis and pneumonia in the neonate).
- Blood components should be:
  - The same as the neonate's own ABO and Rh group, or an alternative compatible ABO and Rh D group **(Table 44-2)**
  - Compatible with any ABO or atypical red cell antibody present in the maternal or neonatal plasma

Table (44-2): **Criteria for ABO and Rh compatibility of blood components**

Guidelines for ABO-Compatible Blood Components		
ABO Group (Infant)	**ABO Group (RBC's and Granulocytes)**	**ABO Group (FFP or Platelets)**
O	O	O, A, B, or AB
A	A or O	A or AB
B	B or O	B or AB
AB	AB, A, B or O	AB

Guidelines for Rh-Compatible Blood Components			
Rh Type (Infant)	**Rh Type (RBCs and Granulocytes)**	**Rh Type (FFP)**	**Rh Type (Platelets)**
Positive	Positive or negative	Positive or negative	Positive or negative
Negative	Negative	Positive or negative	Negative

FFP: fresh frozen plasma, RBC: red blood cells.

Adapted from Warkentin PI: Blood component therapy for the neonate. In Fanaroff AA, Martin RJ (eds): Neonatal-Perinatal Medicine: Diseases of the Fetus and Infant, 6th ed, Vol 2. New York, Mosby–Year Book, 1996, p 1258.

Component Volumes to be Transfused

- Packed red cells: 5-15 ml/kg transfused at a rate of 5 ml/kg/hr; this can be adjusted depending on the severity of anemia and/or the infant's ability to tolerate increased intravascular volume **(Refer to Page 401)**.
- Whole blood: 10-20 ml/kg
- Platelet concentrates: 10-20 ml/kg
- Fresh frozen plasma: 10-20 ml/kg
- Cryoprecipitate: 5 ml/kg

Irradiated Blood

- Radiation of the blood prevents lymphocytes from proliferating. This prevents any possibility of graft versus host disease (GVHD). Irradiated blood should be considered in the following populations:
  - Neonates with a birth weight <1,200 gm
  - Neonates with a known immunodeficiency syndrome
  - Neonates receiving blood from direct donor relatives

Transfusion Time

- The optimal duration of neonatal transfusions is indicated in the table below. This timeframe begins when the blood is released from the blood bank refrigerator. The

risk of hemolysis and bacterial contamination of blood increases with prolonged handling at room temperature.

Table (44-3): The optimal duration of neonatal transfusions

Blood Product	Infusion Time	Minimum*	Maximum**
RBCs, whole blood	As tolerated	2 hrs	4 hrs
Platelets	As tolerated	5-15 minutes per unit	4 hrs
Frozen plasma	As tolerated	30 minutes	4 hrs
Cryoprecipitate	As tolerated	2 minutes per bag	4 hr

*4 hrs are needed if the baby has symptoms of volume overload or congestive heart failure. Blood may need to be administered faster for acute blood loss or hypovolemia.
**Measured from the time the blood is taken out of the transfusion medicine refrigerator

Transfusion Reactions

Clinical manifestations

For an immediate reaction to a transfusion, the nurse should check the infant for:

- Fever greater than 38°C
- Tachycardia
- Respiratory distress
- Hypotension
- Facial flushing
- Pain and irritability
- Nausea and vomiting
- Blood in urine (+1 or greater)
- Urticaria and rash
- Localized or generalized, patchy or diffuse erythema of the skin

Managing a transfusion reaction

- Stop the transfusion immediately.
- Clear the IV catheter with a normal saline flush.
- Examine the infant immediately.
- Check and document vital signs every 15 minutes until the infant's condition is stable.
- Inform the blood bank physician about the reaction. Be prepared to give the physician the infant's name and medical record number.
- Send the transfusion bag, syringe, and tubing to the blood bank physician. Do not send needles.
- Obtain the first voided urine specimen and send it for analysis as soon as possible.

- For future transfusions, these infants may require pre-medication with anti-histamine.

Transfusion Complications

Potential complications of transfusion are listed in **(Table 44-4).**

Table (44-4): Potential transfusion complications

Complication	Cause	Prevention and/or Treatment
Sepsis	Blood contaminated with bacteria	• Use the blood within 4 hrs of its release from blood bank. • Obtain cultures if sepsis is clinically suspected.
Hypothermia	A large volume of cold blood is transfused	• Warm the blood before transfusion as indicated above.
Circulatory overload	A large volume of blood is administered rapidly	• Avoid pushing blood fast (except for emergencies). • Consider giving a dose of furosemide if required.
Hypocalcemia (jitteriness, dysrhythmias, and hypotension)	Citrate in the transfused blood may cause hypocalcemia	• Obtain a serum calcium level. • Obtain an ECG. • Consider a calcium infusion.

Decompression of Pneumothorax

Tension Pneumothorax

- It is an emergency (1-2 minutes delay could be fatal).
- If the infant's status is deteriorating, rapidly place a butterfly needle for aspiration, followed by chest tube placement.

Needle aspiration

- Identify the site: 2nd or 3rd intercostal space along midclavicular line.
- Cleanse the area with povidone-iodine solution.
- Connect a butterfly needle 21 or 23 gauge to 10-20 ml syringe with a three-way stopcock attached.
- Palpate the 3rd rib at the midclavicular line. Insert the needle perpendicular to the chest wall and above the rib, and advance it until air is withdrawn from the syringe.
- When the syringe is full of aspirated air, the stopcock then may be closed to the chest while the syringe is emptied.
- Repeat suctioning and emptying of the aspirated air done by an assistant until improvement of color of the baby and oxygen saturation is observed and documented by pulse oximetry. Do not try to aspirate all air in the pleural sac since this will increase the risk of lung injury by the needle or upon the subsequent insertion of the chest tube.
- The needle may be removed before the chest tube is placed if the infant is relatively stable, or it may be left in place for continuous aspiration while the chest tube is being placed.

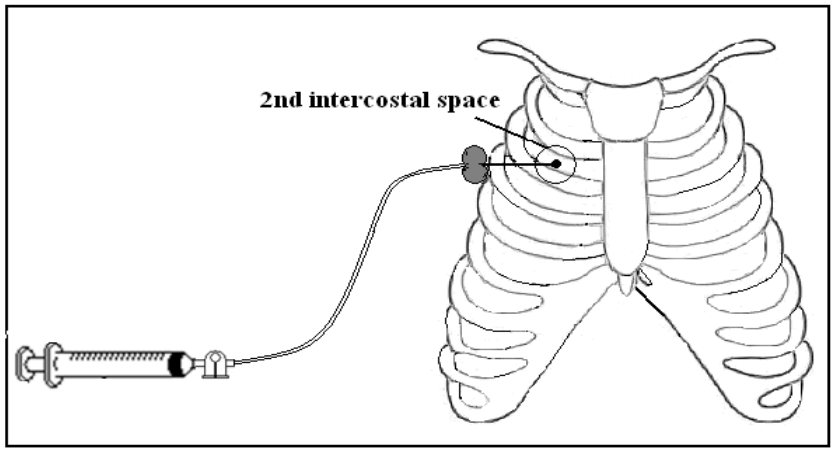


Figure (44-22): Needle aspiration

Chest tube placement

Indications

- Tension pneumothorax
- Pneumothorax causing increased work of breathing, hypoxia, and increased $PaCO_2$
- Pleural effusion

Equipment

Prepackaged chest tube trays typically consist of:

- Sterile towels
- Gauze pads (4×4)
- Silk suture (3-0)
- Needle holder
- Curved hemostats
- Scalpel (No. 15 or No. 11)
- Scissors
- Antiseptic solution, antibiotic ointment, and lidocaine (1%)
- Syringe (3 ml) and 25 gauge needle
- Sterile gloves, a mask, hat, and gown
- A suction-drainage system
- Chest tube:
  - No.10 French catheter for infants weighing <2,000 gm
  - No.12 French catheter for infants weighing >2,000 gm

Procedure

- Positioning: position the infant supine with the arm at a 90° angle or with the affected side elevated 45-60° off the bed, using a towel as back support. This has an advantage of allowing air to rise to the point of entry and of encouraging the correct anterior direction of the chest tube in case of pneumothorax decompression.
- Identify the site:
  - Posterior placement at 4^{th}, 5^{th}, or 6^{th} intercostal space along anterior axillary line, in case of chest tube insertion for fluid drainage **(Figure 44-23).**
  - Anterior placement at 2^{nd} or 3^{rd} intercostal space along midclavicular line, in case of pneumothorax decompression. Risk of injury of the internal mammary artery **(Figure 44-23)**.
- Put on a sterile gown, mask, hat, and gloves. Cleanse the chest area of insertion with povidone-iodine solution then infiltrate the subcutaneous tissue with 0.125-0.25 ml, of 1% lidocaine solution.
- Make a small incision (approximately the width of the tube, usually ≤0.75cm) in the skin over the rib just below the intercostal space where the tube is to be inserted.
- Insert a closed, curved hemostat into the incision, and spread the tissues down to the pleura, grasping the end of the chest tube with the tips of the curved forceps. Apply pressure until the pleural space is entered (just above the rib, to avoid trauma to the intercostal artery). When the pleura has been perforated, a rush of air is often heard. The curve of the hemostat should be aiming anteriorly.
- Advance the chest tube through the opened hemostat. Direct the chest tube toward apex of the lung (midclavicle) and advance it, assuring that side holes are within the

thorax. Observe for cloudiness, vapor, or bubbling in the chest tube to verify intrapleural location.

- The tube is inserted 2-3 cm for a preterm infant and 3-4 cm for a term infant. The length of tube insertion could be determined by measuring the distance between the insertion site and the midclavicle, and then tying a silk suture around the tube the same distance from the tip. Position the tube until the silk suture is just outside the skin.
- Hold the tube steady first, and then allow an assistant to connect the tube to a water-seal vacuum drainage system.
- Secure the chest tube with 3-0 silk sutures and silk tape **(Figure 44-24)**. Close the skin opening with sutures if necessary.
- Obtain a chest x-ray film to verify placement and check for residual fluid or pneumothorax.

N.B.: Do not use the trocar because its use may increase the risk of lung perforation.

Removal of the chest tube

Prior to removal, the chest tube should be clamped for 6 hrs. If there is no re-accumulation of air, the chest tube can be removed.

Complications

- Infection
- Bleeding
- Nerve damage
- Trauma: lung trauma can be minimized by never forcing the tube into position
- Diaphragmatic paralysis
- Subcutaneous emphysema
- Malpositioning

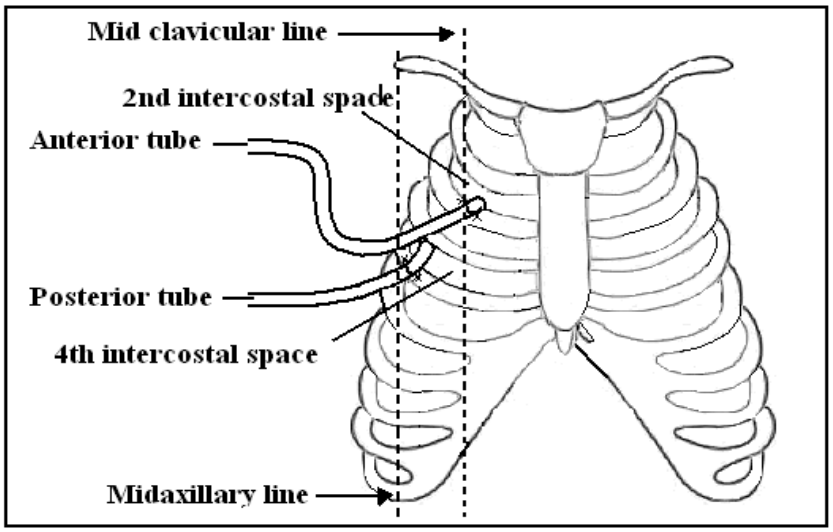


Figure (44-23): Sites for chest tube insertion in neonates

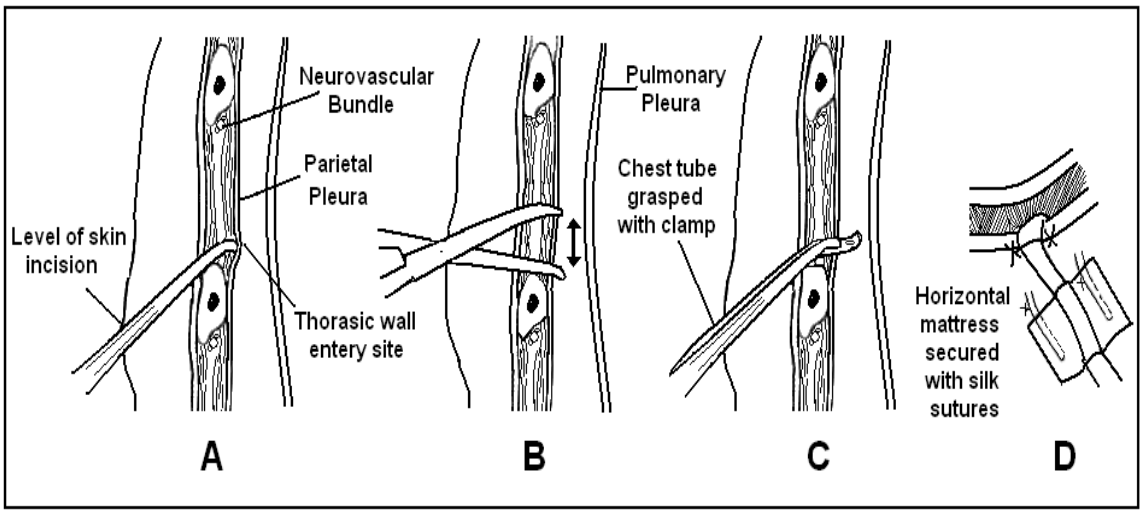


Figure (44-24): Procedures of chest tube insertion

(A) Level of skin incision and thoracic wall entry site in relation to the rib and the neurovascular bundle.
(B, C) Opened hemostat, through which the chest tube is inserted.
(D) Chest tube is then secured to the skin with silk sutures.

Chapter 45

Common NICU Drugs

Common NICU Drugs

The following are commonly used pediatric drugs, their indications for use, recommended dosages and cautions. All physicians are responsible for their choice of medical treatment and drug therapy and should consult the appropriate references for a more in-depth discussion of their chosen regimen.

The renal function and drug elimination are strongly associated with postmenstrual age (PMA) equivalent to gestational age (GA) plus postnatal age (PNA). Therefore, PMA is used as the primary determinant of dosing interval, with postnatal age as the secondary modifier.

Example for drug dosing:

- Calculate ceftazidime dosing for an infant born at 29 weeks' gestation and who is now 14 days old.
- Answer:
  - Infant's PNA is 14 days and PMA = GA (29 weeks) + PNA (2 weeks) = 31 weeks.
  - First go to the row containing PMA of 31 weeks (30-36 weeks), and then his PNA is 14 days (0-14 days), resulting in an interval of 12 hrs.

N.B.: The information contained herein is not intended to cover all aspects of the following drugs. Please refer to the internal pamphlet of each drug for detailed information about available drug preparations, drug interactions, and other possible adverse effects.

Acyclovir

Classification	Antiviral agent
Indications	Treatment of herpes simplex infections including *herpes encephalitis*, and *varicella zoster* infections with CNS and pulmonary involvement
Dosage: 20 mg/kg/dose PO - IV (infuse over 60 minutes)	
• Localized HSV infections	PMA <34 weeks or renal impairment or hepatic failure: IV q12 hrs for 14 days
	PMA ≥34 weeks: IV q8 hrs for 14 days
• Disseminated or CNS infections	PMA <34 weeks or renal impairment or hepatic failure: IV q12 hrs for 21days
	PMA ≥34 weeks: IV q8 hrs for 21days
• Varicella zoster infections	PO q6 hrs (initiated within the first 24 hrs of disease onset) for 5 days
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Infusion solution concentration must be <7 mg/ml - Reduce dosage for impaired renal function - Monitor renal and hepatic function
Adverse effects	Nephrotoxicity, bone marrow suppression, fever, thrombo-cytosis, and transient elevation of serum creatinine, and liver enzymes

Albumin

Classification	Plasma volume expander
Indications	Hypovolemia, hypoproteinemia
Dosage	0.5-1 gm/kg IV (or 10-20 ml/kg of 5% IV bolus) repeated as necessary. Maximum: 6 gm/kg/day
Cautions/Monitoring	- Contraindicated in severe anemia or congestive heart failure - Monitor for signs of hypervolemia, pulmonary edema, and cardiac failure
Adverse effects	- Rapid infusion may cause vascular overload and precipitation of congestive heart failure - Hypersensitivity reactions may include chills, fever, nausea, and urticaria

Amikacin Sulfate

Classification	Aminoglycoside
Indications	Infection with gram-negative organisms
Dosage: IM - IV (infuse over 30 minutes)	
• PMA ≤29 weeks (or significant asphyxia, PDA, treatment with indomethacin or impaired renal function)	PNA 0-7 days: 18 mg/kg/dose q48 hrs
	PNA 8-28 days: 15 mg/kg/dose q36 hrs
	PNA ≥29 days: 15 mg/kg/dose q24 hrs
• PMA 30-34 weeks	PNA 0-7 days: 18 mg/kg/dose q36 hrs
	PNA >7 days: 15 mg/kg/dose q24 hrs
• PMA >35 weeks	All neonates: 15 mg/kg/dose q24 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- For IV administration: dilute with a compatible solution to a concentration of 5 mg/ml - Monitor serum concentration when treating for more than 48 hrs (desirable levels: trough 2-5 µg/ml and peak 20-30 µg/ml) - Monitor renal function before and during therapy - Monitor auditory function after therapy completion
Adverse effects	- Nephrotoxicity is associated with serum trough concentrations >10 µg/ml - Ototoxicity, with serum peak concentration >35-40 µg/ml (more cochlear damage than vestibular)

N.B.: Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose.

Aminophylline

Classification	Bronchodilator, respiratory stimulant
Indications	- Apnea of prematurity - May improve respiratory function and lung compliance and aids in weaning infants from respiratory support in diseases such as BPD
Dosage: PO - IV	
• Loading dose	- 5-6 mg/kg/dose IV (over >20 minutes) or PO
• Maintenance dose	- 1.5-3 mg/kg/dose PO, IV slow push (over >5 minutes) q8-12 hrs - Start 8-12 hrs after the loading dose
• If changing from IV to PO*	- Increase dose by 20%
Compatible solutions	- D5W, D10W, and NS - Dilute 1 ml (25 mg) with 4 ml NS or D5W → 5mg/ml concentration
Cautions/Monitoring	- IM administration causes intense local pain and sloughing - Monitor serum trough levels before the 5th dose - Desired serum levels in apnea of prematurity are 7-12 µg/ml - Monitor heart rate, blood glucose and feeding intolerances and agitation - If heart rate >180/minute, withhold next dose
Adverse effects	GI irritation, vomiting, feeding intolerance, sinus tachycardia, hyperglycemia, diuresis, CNS irritability and seizures

*For theophylline, no adjustment is needed if changing from IV to PO.

Amphotericin B

Classification	Antifungal agent
Indications	Systemic fungal infection
Dosage	
• Initial	- 0.25-0.50 mg/kg IV infusion over 2-6 hrs, diluted in D5W to a concentration of 0.1mg/ml
• Maintenance	- Increase the daily dose by 0.125-0.25 mg/kg/day IV infusion over 2-6 hrs, until a maximum daily or alternate-day dosage of 0.75-1.5 mg/kg has been attained - A total dosage of 30-35 mg/kg should be given over 6 weeks or longer
• Liposomal amphotericin B	- 5 mg/kg/dose q24 hrs IV infusion over >2 hrs - For cases resistant to conventional amphotericin B or in infants with renal or hepatic dysfunctions
Compatible solutions	D5W, and D10W
Cautions/Monitoring	- Do not flush IV or mix with saline solution-precipitation will occur - Avoid additional nephrotoxic drugs - Monitor urine output - Monitor BUN, serum creatinine, electrolytes and AST (every day or every other day until the dose is stabilized then every week) - Monitor CBC every week - Observe for signs of hypokalemia and ECG changes - Observe IV site for irritation - Modify dosage for renal dysfunction if serum creatinine increases >0.4 mg/dl during therapy - Discontinue if BUN >40 mg/dl, serum creatinine >3mg/dl or if liver function tests are abnormal
Adverse effects	- Fever, chills, vomiting, thrombophlebitis at injection sites, renal tubular acidosis, hypomagnesemia, hypokalemia, nephrotoxicity, anemia and thromocytopenia - Liposomal amphotericin has limited toxicity and is well tolerated in neonates including VLBW infants

Ampicillin

Classification	Semi-synthetic penicillinase-sensitive penicillin
Indications	Combined with either an aminoglycoside or cephalosporin to prevent and/or treat infections with group *B streptococci* and *Listeria monocytogenes*
Dosage: IM - IV (infuse over >15 minutes)	
• Meningitis:	PNA 0-7 days: 100-200 mg/kg/day divided q12 hrs
	PNA >7 days: 200-300 mg/kg/day divided q8 hrs (maximum: 400 mg/kg/day)
• Other indications:	PNA 0-7 days: 100 mg/kg/day divided q12 hrs
	PNA >7 days: 100 mg/kg/day divided q8 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Maximum concentration for IV infusion is 100 mg/ml - Dose adjustment required in renal impairment
Adverse effects	- Hypersensitivity, rubella-like rash, abdominal discomfort, nausea, vomiting, diarrhea, eosinophilia - Very large doses may cause CNS excitation or convulsions

Ampicillin/Sulbactam

Classification	Combination β-lactamase inhibitor and β-lactam agent
Indications	Infections covered by the ampicillin spectrum as well as *Staphylococcus aureus*
Dosage: IM - IV	
• Meningitis:	PNA 0-7 days: 100-200 mg/kg/day divided q12 hrs
	PNA >7 days: 200-300 mg/kg/day divided q6-8 hrs
• Other infections:	PNA 0-7 days: 100 mg/kg/day divided q12 hrs
	PNA >7 days: 100 mg/kg/day divided q6-8 hrs
Cautions/Monitoring	See ampicillin
Adverse effects	See ampicillin

Calcium Gluconate 10%

Classification	Electrolyte supplement; calcium salts
Indications	Symptomatic hypocalcemia, exchange transfusions
Dosage: IV infusion	
• Acute	100-200 mg/kg/dose **or** 1-2 ml/kg/dose; infuse IV over 10-30 minutes
• Maintenance	200-800 mg/kg/day **or** 2-8 ml/kg/day IV as a continuous infusion
• Exchange transfusion	100 mg/100 ml **or** l ml/100 ml citrated exchange blood
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Monitor heart rate, and stop if rate <100 beats/minute - Avoid hypercalcemia during treatment - Observe IV infusion site for extravasation
Adverse effects	- Arrhythmias (e.g., bradycardia) and deterioration of cardio-vascular function - Extravasations may cause skin sloughing - May potentiate digoxin-related arrhythmias
Incompatibility	Amphotericin B, ceftriaxone, clindamycin, fluconazole, indomethacin, sodium bicarbonate, and phosphate and magnesium salts when mixed directly

Captopril

Classification	Angiotensin-converting enzyme inhibitor
Indications	Congestive heart failure and hypertension
Dosage	- Initial: 0.01-0.05 mg/kg/dose - PO q8-12hrs - Adjust dose and interval based on response - Maximum recommended dose: 0.5 mg/kg/dose PO q6-24hrs
Cautions/Monitoring	- Use caution in patient with low renal perfusion pressure. Reduce the dose with renal impairment - A low initial dose is used because some infants have experienced a dramatic drop in blood pressure - Monitor blood pressure (particularly after the first dose), BUN, serum creatinine, urine dipstick for protein, CBC, and serum K^+ - It is contraindicated in bilateral renal artery stenosis and unilateral renal artery stenosis in a solitary kidney
Adverse effects	- High initial dose may cause hypotension. - Rash, fever, eosinophilia, neutropenia, GI disturbances, cough, hyperkalemia and acute renal failure

N.B.: Administer on empty stomach, 1 hr before or 2 hrs after feedings, if possible.

Carbamazepine

Classification	Anticonvulsant
Indications	- Partial (especially complex partial), primary generalized tonic-clonic seizures and mixed seizures - Not effective for absence (petit mal) seizures
Dosage	5 mg/kg/day divided q6-8 hrs PO with feeding, can be increased weekly to10 mg/kg/day to a maximum of 20 mg/kg /day
Cautions/Monitoring	- Monitor CBC and liver transaminases before, during, and after use - Perform periodic eye examination - Do not discontinue abruptly, because seizures may result in epileptic infants
Adverse effects	- Nausea and vomiting - Leukopenia, thrombocytopenia, aplastic anemia, and agranulocytosis - Congestive heart failure, heart block, and collapse - Dystonia, drowsiness, and behavioral changes - Scattered punctate cortical lens opacities - SIADH - Hepatitis and cholestasis - Rash and Stevens-Johnson syndrome - Urine retention, azotemia, oliguria, and anuria

Cefepime

Classification	Fourth-generation cephalosporin
Indications	Treatment of serious infections caused by gram-negative organisms, especially *Pseudomonas aeruginosa* that are resistant to third generation cephalosporins, as well as serious infections caused by susceptible gram-positive organisms
Dosage : IM - IV (infuse over 30 minutes)	
• Term and preterm infants	PNA ≤ 14 days: 30 mg/kg/dose q12 hrs
	PNA >14 days: 50 mg/kg/dose q12 hrs
• Meningitis and severe infections	Doses administered q8 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Maximum concentration for IV administration is 160 mg/ml, and for IM administration 280 mg/ml
Adverse effects	Uncommon, but include rash, diarrhea, elevated hepatic transaminases, and eosinophilia

Cefotaxime Sodium

Classification	Third-generation cephalosporin
Indications	Suspected or documented gram-negative meningitis or sepsis. When used empirically, it is combined with ampicillin or aqueous penicillin G for gram-positive coverage
Dosage : IM - IV (infuse over 30 minutes)	
• Meningitis	50 mg/kg/dose q6 hrs
• Gonococcal conjunctivitis	25 mg/kg/dose q12 hrs
• Other infections	PNA 0-7 days: 50 mg/kg/dose q12 hrs
	PNA >7 days: 50 mg/kg/dose q8 hrs
Compatible solutions	- D5W, D10W, and NS - For IV administration: reconstitute the vial with sterile water for injection → 100 mg/ml concentration
Cautions/Monitoring	- Dosage modification is required for impaired renal function - Monitor CBC, BUN, creatinine and liver enzymes
Adverse effects	Hypersensitivity reactions, thrombophlebitis, serum sickness-like reaction with prolonged administration, diarrhea, and, rarely, blood dyscrasias, hepatic dysfunction, or renal damage

Ceftazidime

Classification	Third-generation cephalosporin
Indications	Treatment of neonatal meningitis and sepsis caused by gram negative organisms, especially *Pseudomonas aeruginosa*
Dosage: 30 mg/kg/dose IM - IV (infuse over 30 minutes)	
• PMA ≤29 weeks	PNA 0-28 days: q12 hrs
	PNA >28 days: q8 hrs
• PMA 30-36 weeks	PNA 0-14 days: q12 hrs
	PNA >14 days: q8 hrs
• PMA 37-44 weeks	PNA 0-7 days: q12 hrs
	PNA >7 days: q8 hrs
Compatible solutions	- D5W, D10W, and NS - For IV administration: reconstitute the vial with sterile water for injection → 50 mg/ml concentration
Cautions/Monitoring	- Modify dosage for renal impairment - Monitor CBC, renal, and liver functions
Adverse effects	- Infrequent except for allergic reactions, including: fever, rash, and urticaria - May cause transient leukopenia, neutropenia, and thrombo-cytopenia; a direct positive Coombs' test; and transient elevation in the liver function test

Ceftriaxone Sodium

Classification	Third-generation cephalosporin
Indications	Good activity against both gram-negative and gram positive organisms except *Pseudomonas spp., enterococci*, methicillin-resistant *staphylococci*, and *L.monocytogenes*
Dosage: IV - IM	
• Meningitis	Loading: 100 mg/kg q24 hrs
	Maintenance: 80 mg/kg q24 hrs
• Other indications	50 mg/kg q24 hrs
Compatible solutions	- D5W, D10W, and NS - For IV administration: reconstitute with sterile water for injection to a concentration of 40 mg/ml
Cautions/Monitoring	- Do not use in gallbladder, biliary tract, liver, or pancreatic diseases - Use with caution in infants with hyperbilirubinemia - Monitor CBC, electrolyte, and renal and liver functions - Ceftriaxone should not be reconstituted or mixed with a calcium-containing product *
Adverse effects	- Mild diarrhea and eosinophilia are most common. May also cause neutropenia, rash, thrombophlebitis - Increases free and erythrocyte-bound bilirubin in premature infants with hyperbilirubinemia - Transient formation of gall bladder precipitate - GI tract bacterial and fungal overgrowth - There is a risk of precipitation when ceftriaxone and calcium are administered concurrently via IV route

*The United States Food and Drug Administration (FDA) issued these recommendations:

- Concomitant use of ceftriaxone and IV calcium-containing products is contraindicated in infants ≤28 days of age.
- Ceftriaxone and IV calcium products may be administered sequentially in patients >28 days of age, provided that the infusion lines are thoroughly flushed between infusions with a compatible fluid.
- Ceftriaxone must not be administered simultaneously with IV calcium-containing solutions (e.g., Ringer, parenteral nutrition) via a Y-site in any age group.
- There are no data on interactions between intravenous ceftriaxone and oral calcium-containing products or between intramuscular ceftriaxone and intravenous or oral calcium-containing products.

Clindamycin

Classification	Anaerobic antibiotic
Indications	Treatment of *B. fragilis* sepsis, peritonitis, and NEC
Dosage: 5 mg/kg/dose IV (infuse over >30 minute)	
• <1,200 gm	PNA 0-28 days: q12 hrs
• 1,200-2,000 gm	PNA 0-7 days: q12 hrs
	PNA >7 days: q8 hrs
• >2,000 gm	PNA 0-7 days: q8 hrs
	PNA >7 days: q6 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Infusion concentration: 10 mg/ml (maximum concentration for infusion is 18 mg/ml) - Does not cross the blood-brain barrier; therefore, do not use to treat meningitis - Contraindicated in hepatic impairment
Adverse effects	- Fatal pseudomembranous colitis (treated with oral vancomycin or metronidazole) - Stevens-Johnson syndrome - Rash, glossitis, and pruritus - Serum sickness, anaphylaxis - Granulocytopenia and thrombocytopenia - Increased liver function tests

Dexamethasone

Classification	Adrenal corticosteroids, anti-inflammatory agent
Indications	Refractory hypoglycemia, bronchopulmonary dysplasia, prophylactic use on extubation
Dosage	
• Broncho-pulmonary dysplasia	0.2-0.3 mg/kg/day divided q12 hrs for 48 hrs, then have the dose every 48 hrs for 7-10 days
• Extubation/ airway edema	- 0.25 mg/kg/dose q12 hrs - Begin 12 hrs before planned extubation and continue for 2-4 doses afterwards
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Monitor blood pressure - Assess hemoglobin and serum potassium, and evaluate for hyperglycemia, glycosuria, and occult blood loss
Adverse effects	With long-term use; increased susceptibility to infection, osteoporosis, growth retardation, hyperglycemia, fluid and electrolyte disturbances, cataract, myopathy, GI perforation, hypertension, and acute adrenal insufficiency

N.B.: Dexamethasone given for treatment or prevention of BPD has been associated with a higher risk of cerebral palsy and neurodevelopmental abnormalities. Its use should be avoided except under exceptional clinical circumstances (maximal ventilatory support or high risk of mortality).

Diazepam

Classification	Anticonvulsant
Indications	Status epilepticus, convulsions refractory to other combined anticonvulsant agents, and hyperglycinemia
Dosage	
• Status epilepticus	- 0.l-0.3 mg/kg/dose IV q15-30 minutes for 2-3 doses to a maximum dose of 2-5 mg
• Continuous refractory seizures	- 0.1-0.3 mg/kg/dose IV bolus, then - 0.3 mg/kg/hr as a continuous IV infusion (diluted in NS to 0.1 mg/ml)
Cautions/Monitoring	Prepare for possible respiratory depression
Adverse effects	May cause drowsiness, ataxia, rash, vasodilation, respiratory arrest, and hypotension

Digoxin

Classification	Inotropic agent
Indications	Heart failure, paroxysmal atrioventricular nodal tachycardia, atrial fibrillation, flutter
Dosage: IV (infuse over 10 minutes) - PO	
• Loading*: IV - divided into 3 doses over 24 hrs	PMA ≤ 29 weeks: 0.15 mg/kg divided q8 hrs
	PMA 30-36 weeks: 0.2 mg/kg divided q8 hrs
	PMA >36 weeks: 0.3 mg/kg divided q8 hrs
• Maintenance: IV	PMA <29 weeks: 0.04 mg/kg/dose q24 hrs
	PMA 30-36 weeks: 0.05 mg/kg/dose q24 hrs
	PMA >36 weeks: 0.04 mg/kg/dose q12 hrs
• PO - loading and maintenance	25% greater than IV doses
Compatible solutions	- D5W, D10W, NS, and sterile water for injection - Dilute injectable into fourfolds or more volume of a compatible solution and use immediately
Cautions/Monitoring	- Contraindicated in 2nd- and 3rd-degree block, idiopathic hypertrophic subaortic stenosis, and ventricular arrhythmias - Reduce dose for renal impairment - Monitor heart rate/rhythm, serum potassium, calcium, magnesium, and signs of toxicity (especially in infants receiving diuretics and amphotericin B) - Toxicity is markedly enhanced by hypokalemia - Do not administer IM
Adverse effects	- Vomiting is the most common sign with bradycardia in preterm and term infants - Other adverse effects are feeding intolerance, diarrhea, arrhythmias (paroxysmal ventricular contractions, blocks, and tachycardia), and lethargy

*Digoxin loading dose is generally used when treating arrhythmia and acute congestive heart failure.

N.B.: Treatment of life threatening toxicity with Fab fraction of specific digoxin antibody. Give potassium if hypokalemic.

Dobutamine Hydrochloride

Classification	Sympathomimetic, adrenergic agonist agent
Indications	- Treatment of hypoperfusion and hypotension, especially if related to myocardial dysfunction
Dosage	- 2.5-25 µg/kg/minute - administer by continuous IV infusion - Begin at a low dose and titrate by monitoring effects
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Contraindicated in idiopathic subaortic stenosis, and atrial fibrillation - Correct hypovolemia before use - Do not administer via UAC - Monitor heart rate and blood pressure
Adverse effects	- Hypotension if hypovolemic, ectopic heart beats, and increased heart rate and blood pressure

Dopamine Hydrochloride

Classification	Sympathomimetic, adrenergic agonist agent
Indications	- Treatment of hypotension - Adjunctive therapy for shock refractory to adequate volume replacement - Severe congestive heart failure refractory to digoxin and diuretics
Dosage: continuous IV infusion	
• Low dose	2-5 µg/kg/minute (renal dose)
• Medium dose	5-15 µg/kg/minute (cardiotonic dose)
• High dose	>20 µg/kg/minute (pressor dose)
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Use with extreme caution in patient receiving phenytoin IV, as it may result in severe hypotension and bradycardia - Correct hypovolemia before use - Do not administer via UAC - Continuous monitoring of heart rate, and arterial blood pressure. Assess urine output and peripheral perfusion
Adverse effects	- Arrhythmias, ectopic beats, tachycardia, hypertension, and excessive diuresis and azotemia. - It may increase pulmonary artery pressure - Extravasation may cause tissue necrosis and sloughing of surrounding tissues (if occurs, inject phentolamine, 0.1-0.2 mg/kg diluted to 1 ml of saline, throughout the affected area)

N.B.: Dopamine (or dobutamine) must always be given in a separate IV line, suggested administration:

$$\frac{\textbf{6 x neonate's weight} \times \textbf{desired dose (µg/kg/min)}}{\textbf{Desired fluid rate (ml/hr)}} = \textbf{\# mg Dopamine per 100 ml solution}$$

Epinephrine Hydrochloride

Classification	Adrenergic agent
Indications	Cardiac arrest, refractory hypotension, and bronchospasm
Dosage	
• Cardiac arrest or severe bradycardia	IV push: 0.1-0.3 ml/kg/dose (1:10,000 concentration) may repeat q3-5 minutes for a total of 3 doses, if heart rate remains <60 beats/minute
	Endotracheal tube: 0.3-1.0 ml/kg/dose (1:10,000 concentration)
• Continuous IV infusion	Start at 0.1 μg/kg/minute, adjust dose to desired response to a maximum of 1 μg/kg/minute Maximum IV concentration = 1 mg/50 ml
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	Monitor heart rate and blood pressure continuously
Adverse effects	Hypertension, tachycardia, nausea, pallor, arrhythmias, increased myocardial oxygen consumption, and decreased renal and splanchnic blood flow

Erythromycin

Classification	- Macrolide antibiotic - Motilin receptor agonist
Indication	- Treatment of infections caused by *Chlamydia*, *mycoplasma*, and *ureaplasma* - Treatment and prophylaxis of *Bordetella pertussis*, and ophthalmia neonatorum - Prokinetic agent
Dosage: IV (infuse over > 60 minutes) – PO	
• Systemic infections 10 mg/kg/dose	PNA ≤7 days: q12 hrs
	PNA >7 days, <1200 gm: q12 hrs
	PNA >7 days, ≥1200 gm: q8 hrs
• Feeding intolerance	10 mg/kg/dose PO q6 hrs for 2 days followed by 4 mg/kg/ dose PO q6 hrs for 5 days, 30 minutes before meals
• Ophthalmic(prophylaxis)	Instill 0.5-1 cm in each eye once
• Acute eye infection	Instill 0.5-1 cm in each eye q6 hrs
Cautions/Monitoring	- Parenteral forms are painful and irritative - Monitor liver functions, and CBC
Adverse effects	- Anaphylaxis, rash - Stomatitis and oral or perianal candidiasis - Intrahepatic cholestasis, hepatotoxicity - Erythromycin treatment may be associated with increased risk for development of infantile hypertrophic pyloric stenosis

Ferrous Sulfate

Classification	Oral mineral supplement
Indications	Prophylaxis and treatment of iron deficiency anemia in preterm newborns
Dosage: PO (preferably diluted in formula)	
• Iron deficiency anemia	6 mg/kg/day in divided 4 divided doses
• Prophylaxis	- Growing premature infants: 2 mg/kg/day - Infants <1,000 gm may need 4 mg/kg/day - Start iron therapy no later than 2 months of age
• Supplementation iron with erythropoietin	6 mg/kg/day
Cautions/Monitoring	- Iron supplementation may increase hemolysis without adequate vitamin E therapy - Monitor hemoglobin, reticulocytic count - Monitor for constipation
Adverse effects	Gastrointestinal irritation (vomiting, diarrhea, constipation, and darkened stool color)

Fluconazole

Classification	Systemic antifungal agent	
Indications	Systemic fungal infections, meningitis and superficial mycosis Prophylaxis in VLBW infants cared for in NICUs with high rates of invasive fungal disease	
Dosage: PO, IV infusion (by syringe pump over 60 minutes)		
• Systemic infections, including meningitis	Loading dose: 12 mg/kg	
	Maintenance: 6 mg/kg/dose	PMA ≤36 weeks, PNA 0-14days: q48 hrs
		PMA ≤36weeks, PNA >14days: q24 hrs
		PMA >36weeks, PNA 0-7days: q48 hrs
		PMA >36weeks, PNA >7days: q24 hrs
• Thrush	- Loading dose: 6 mg/kg on day 1 - Then: 3 mg/kg/dose q24 hrs PO	
• Prophylaxis	- Loading: 3 mg/kg/dose, once daily 3 times weekly for first 2 weeks - Then every other day for total of 4-6 weeks (longer duration for infants < 1,000 gm)	
Compatible solutions	D5W and D10W	
Cautions/Monitoring	- Adjust dosage for impaired renal function - Monitor renal and liver function tests	
Adverse actions	- Usually well tolerated - Vomiting, diarrhea, rash, and reversible elevations of liver transaminases	

Furosemide

Classification	Loop diuretic
Indications	Fluid overload, pulmonary edema, congestive heart failure, and hypertension
Dosage: PO, IM, and IV slow push	
• Initial dose	- 1 mg/kg/dose - May increase to a maximum of 2 mg/kg/dose IV or 6 mg/kg/dose PO
• Initial intervals	- Premature infant: q24 hrs - Full-term infant: q12 hrs - Full term infant older than 1 month: q6-8 hrs - Consider alternate-day therapy for long-term use
Compatible solutions	NS and sterile water for injection
Cautions/Monitoring	- Monitor daily weight change, urine output, serum phosphate, and serum electrolytes - Monitor serum potassium in neonates receiving digoxin
Adverse actions	- Hypokalemia, hypocalcemia, and hyponatremia - Hypercalciuria and development of renal calculi - With prolonged use, nephrocalcinosis and hypochloremic metabolic alkalosis

Gentamicin Sulfate

Classification	Aminoglycoside
Indication	Treatment of gram-negative aerobic infections Some activity against coagulase-positive staphylococci
Dosage: IM - IV (infuse over 30 minutes)	
• PMA ≤ 29 weeks (or significant asphyxia, PDA, treatment with indomethacin or impaired renal function)	PNA 0-7 days: 5 mg/kg/dose q48 hrs
	PNA 8-28 days: 4 mg/kg/dose q36 hrs
	PNA ≥29 days: 4 mg/kg/dose q24 hrs
• PMA 30-34 weeks	PNA 0-7 days: 4.5 mg/kg/dose q36 hrs
	PNA ≥8 days: 4 mg/kg/dose q24 hrs
• PMA >35 weeks	4 mg/kg/dose q24 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Measure serum concentration when treating for >48 hrs (desirable levels: trough 0.5-1 μg/ml and peak 6-15 μg/ml). - Modify dosage for impaired renal function - The addition of nephrotoxic and/or ototoxic drugs (e.g., furosemide and vancomycin) may increase adverse effects - Monitor renal function, serum levels pre- and post- 3rd dose
Adverse effects	- Vestibular and auditory ototoxicity, and renal toxicity (in proximal tubules, usually reversible) - Neuromuscular weakness and respiratory failure may occur in infants with hypermagnesemia

Heparin Sodium

Classification	Anticoagulant
Indications	Maintain patency of arterial or venous catheters
Dosage	
• Thrombosis	- Loading dose: 75 units/kg as IV bolus - Maintenance dose: 28 units/kg/hr as continuous infusion - 4 hrs after initiating therapy, measure APTT, then adjust dose to achieve APTT of 60-85 seconds - Treatment should be limited to 10-14 days
• To maintain patency of peripheral and central vascular catheter	0.5-1 unit/ml of IV fluid
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Risk of hemorrhage: intramuscular injections, venous and arterial blood sampling, and peptic ulcer disease - Monitor platelet count every 2-3 days, signs of bleeding and thrombosis
Antidote	Protamine sulfate, 1 mg for each 100 units of heparin given in the preceding 3-4 hrs up to a maximum dose of 50 mg
Adverse actions	Thrombocytopenia, hemorrhage , fever, urticaria, vomiting, increased liver function tests, osteoporosis, and alopecia

Hydrocortisone

Classification	Adrenal corticosteroid
Indications	Acute adrenal insufficiency, congenital adrenal hyperplasia, refractory hypoglycemia and vasopressor resistant hypovolemic shock
Dosage	
• Acute adrenal insufficiency	50-100 mg/m^2 (~25 mg) given IV bolus immediately, followed by 100 mg/m^2/24 hrs by continuous drip or divided every 6 hrs
• Congenital adrenal hyperplasia	- Acute crisis: as acute adrenal insufficiency - Maintenance: once the clinical condition improves, taper the dose by 1/3 per day to reach 10-15 mg/m^2/day PO in 3 doses
• Refractory neonatal hypoglycemia	5 mg/kg/dose IV q12 hrs
• Refractory hypotension in critically ill preterm infants	1 mg/kg IV q8-12 hrs for 2-3 days
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	Acute adrenal insufficiency may occur with abrupt withdrawal following long term therapy or during periods of stress
Adverse effects	With long-term use; increased susceptibility to infection, osteoporosis, growth retardation, myopathy hyperglycemia, cataracts, GI perforation, hypertension, and Cushing syndrome

Ibuprofen

Classification	Non-selective cyclo-oxygenase enzyme inhibitor, inhibitor of prostaglandin synthesis, and nonsteroidal anti-inflammatory agent
Indication	Pharmacologic closure of ductus arteriosus
Dosage	- Initial :10 mg/kg IV one dose - Then: 5 mg/kg IV at 24 and 48 hrs after initial dose
Cautions/Monitoring	- Avoid use with steroids to decrease incidence of GI bleeding - Contraindicated in preterm infants with infection, active bleeding, thrombocytopenia or coagulation defects, NEC and significant renal dysfunction - Use caution in patients with decreased hepatic or renal functions, dehydration, hypertension, history of GI bleeding, or those receiving anticoagulants - Monitor BUN, serum creatinine, CBC, and urine output - Assess ductal closure (echocardiogram – murmurs) and signs of bleeding
Adverse actions	Edema, GI bleeding, GI perforation, neutropenia, anemia, agranulocytosis, inhibition of platelet aggregation, and acute renal failure

Imipenem/Cilastatin

Classification	Broad-spectrum Carbapenem antibiotic
Indication	Treatment of non-CNS infections caused by bacteria, primarily Enterobacteriaceae and anaerobes **resistant to other antibiotics**
Dosage: 20 mg/kg/dose IV infusion over 30 minutes	
• < 1,200 gm	PNA: 0-28 days: q18-24 hrs
	PNA: >29 days: q12 hrs
• 1,200-2,000 gm	q12 hrs
• >2,000 gm	PNA: 0-7 days q12 hrs
	PNA: >7 days q8 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Maximum concentration is 5mg/ml - Periodically monitor CBC and hepatic transaminases - Assess IV site for signs of phlebitis
Adverse effects	- Seizures occur frequently in patients with meningitis, preexisting CNS pathology, and severe renal dysfunction - Local reactions at the injection site and increased platelet counts - Others: eosinophilia, elevated hepatic transaminases, and diarrhea

Immune Globulin, Intravenous (IVIG)

Indications	Adjunct treatment of fulminant neonatal sepsis, hemolytic jaundice and neonatal alloimmune thrombocytopenia
Dosage	- 500-750 mg/kg/dose q24 hrs IV infusion over 2-6 hrs for 1-2 doses - Neonatal alloimmune thrombocytopenia, doses have ranged from 400 mg/kg to 1 gm/kg
Cautions/Monitoring	- Delay immunizations with live virus vaccines until 3-11 months after administration - Monitor heart rate, and blood pressure
Adverse effects	- Transient hypoglycemia, tachycardia, and hypotension - Tenderness, erythema, and indurations at the site of injection - Allergic manifestations and rarely, hypersensitivity reactions with rapid administration

Indomethacin

Classification	Inhibitor of prostaglandin synthesis	
Indications	Pharmacological alternative to a surgical closure of the ductus arteriosus	
Dosage: IV infusion over >30 minutes, all doses given in 12-24 hrs intervals Three doses/course, maximum 2 courses		
	1st dose	2nd and 3rd doses
• PNA ≤48 hrs	0.2 mg/kg/dose	0.1 mg/kg/dose
• PNA 2-7 days	0.2 mg/kg/dose	0.2 mg/kg/dose
• PNA >7 days	0.2 mg/kg/dose	0.25 mg/kg/dose
Cautions/Monitoring	- Contraindicated in active bleeding, significant thrombocytopenia or coagulation defects, NEC and significant renal dysfunction - Use with caution in neonates with cardiac dysfunction, and hypertension - GI perforations occur frequently if concomitantly used with steroids - Monitor urine output, serum electrolytes, BUN, serum creatinine, platelet counts, and PDA size for evidence of success or failure of therapy - Assess stools and gastric aspirate for GI bleeding, prolonged bleeding in puncture sites - Consider withholding enteral feedings during therapy	
Adverse effects	- Decreased platelet aggregation, peptic ulcer, GI intolerance, hemolytic anemia, bone marrow suppression, agranulo-cytosis, and thrombocytopenia - Hypoglycemia (common) - Transient oliguria, electrolyte imbalance, hypertension, indirect hyperbilirubinemia and hepatitis	

Magnesium Sulfate

Indications	Treatment and prevention of hypomagnesemia and refractory hypocalcemia
Dosage: IM - IV infusion over 30 minutes Magnesium sulfate (50% solution) contains 500 mg, or 4 mEq/ml	
• Acute hypomagnesemia	- 0.2-0.4 mEq/kg (0.05-0.1 ml/kg) - Repeated doses may be required q6-12 hrs until the serum magnesium level is normal or symptoms resolve - Concomitant oral magnesium sulfate (50% solution) can be started if oral feeds are tolerated at a dose of 0.2 ml/kg/day. In specific magnesium malabsorption, daily oral doses of 1 ml/kg/day may be required
• Maintenance	- 0.25-0.5 mEq/kg/24 hrs IV (added to parenteral fluids)
Cautions/Monitoring	- Contraindicated in renal failure - Monitor blood pressure, serum magnesium, calcium, and phosphate levels
Adverse effects	Hypotension, flushing, depression of reflexes, depressed cardiac function, and CNS and respiratory depression

N.B.: Ampoule masses and their mEq/ml
100 mg = 0.8 mEq/ml
125 mg = 1.0 mEq/ml
250 mg = 2.0 mEq/ml
500 mg = 4.0 mEq/ml

Meropenem

Classification	A broad spectrum carbapenem antibiotic
Indications	Treatment of pneumococcal meningitis and other serious infections caused by susceptible gram-negative organisms resistant to other antibiotics, especially extended-spectrum beta-lactamase producing *Klebsiella pneumoniae*
Dosage: IV infusion over 30 minutes	
• Sepsis	20 mg/kg/dose q12 hrs
• Meningitis and infections caused by *Pseudomonas* species	40 mg/kg /dose q8 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Maximum concentration is 50 mg/ml - Periodically monitor CBC and hepatic transaminases - Assess IV site for signs of inflammation
Adverse effects	- Diarrhea, nausea/vomiting, and rash - Inflammation at injection site - Increased risks of *pseudomembranous colitis*, and fungal infections

Methicillin Sodium

Classification	Penicillinase-resistant penicillin	
Indication	- Active chiefly against penicillinase-positive and penicillinase-negative staphylococci - Less effective than penicillin G against other gram-positive cocci. No activity against enterococci	
Dosage: IM - IV (infuse over 20 minutes)		
• Meningitis: 50 mg/kg/dose	<2,000 gm, PNA 0-7 days	q12 hrs
	<2,000 gm, PNA >7 days	q8 hrs
	≥2,000 gm, PNA 0-7 days	q8 hrs
	≥2,000 gm, PNA >7 days	q6 hrs
• Other indications: 25 mg/kg/dose	<2,000 gm, PNA 0-7 days	q12 hrs
	<2,000 gm, PNA >7 days	q8 hrs
	>2,000 gm, PNA 0-7 days	q8 hrs
	>2,000 gm, PNA >7 days	q6 hrs
Cautions/Monitoring	- Dosage adjustment is necessary in renal impairment - Monitor CBC, BUN and creatinine	
Adverse effects	- Nephrotoxicity (interstitial nephritis) - Hypersensitivity reactions, anemia, leukopenia, thrombo-cytopenia, phlebitis at the infusion site, and hemorrhagic cystitis (in poorly hydrated patients)	

Metronidazole

Classification	Bactericidal antmicrobial	
Indications	- Treatment of anaerobic infection - Treatment of meningitis, ventriculitis, and endocarditis caused by *(Bacteroids fragilis* and other anaerobes) - Serious intra-abdominal infections - *C. difficile* colitis	
Dosage: PO - IV (infuse over 60 minutes)		
• PNA <7 days	< 1,200 gm	7.5 mg/kg/dose q48 hrs
	1,200-2,000 gm	7.5 mg/kg/dose q24 hrs
	≥ 2,000 gm	7.5mg/kg/dose q12 hrs
• PNA ≥7 days	< 1,200 gm	7.5 mg/kg/dose q24 hrs
	1,200-2,000 gm	7.5mg/kg/dose q12 hrs
	≥ 2,000 gm	15 mg/kg/24 hr q12 hrs
Compatible solutions	D5W and NS	
Cautions/Monitoring	Drug metabolites may cause brownish discoloration of the urine	
Adverse effects	- Occasional vomiting, diarrhea, insomnia, weakness, rash, phlebitis at the injection site - Rarely, leukopenia - Mutagenicity and carcinogenicity may occur (not established in humans)	

Midazolam Hydrochloride

Classification	Benzodiazepine, sedative, hypnotic, anticonvulsant
Indications	- Refractory seizures - May be used for infants on assisted ventilation who are agitated and need sedative before procedures
Dosage	
• Intermittent IV (over at least 5 minutes) may be given IM.	0.05-0.15 mg/kg/dose q2-4 hrs, as needed
• Continuous infusion	0.01-0.06 mg/kg/hr
Compatible solutions	D5W, and NS
Cautions/Monitoring	- Use with caution, particularly if fentanyl is being used concurrently - Monitor respiratory rate, heart rate and blood pressure
Adverse effects	- Respiratory depression and arrest with excessive doses or rapid IV infusions - May cause hypotension

Naloxone Hydrochloride

Classification	Narcotic antagonist
Indications	Treatment of narcotic-induced respiratory depression
Dosage	- 0.1mg/kg/dose, IV push over 30 seconds - Can be administered in SC/IM/endotracheally - Can be repeated q3-5 minutes
Cautions/Monitoring	Monitor for reappearance of respiratory depression and the need for repeated doses
Adverse effects	May precipitate withdrawal symptoms (vomiting, seizures, tachycardia and hypertension) in neonates of narcotic-addicted mothers

Oxacillin Sodium

Classification	Semisynthetic penicillinase-resistant penicillin
Indication	- Mechanism of action is identical to that of other β-lactam antibiotics - Spectrum of activity is identical to methicillin sodium
Dosage: IV (infuse over >10 minutes)	
• Bacteremia: 25mg/kg/dose • Meningitis and sever systemic infection: 50 mg/kg/dose	PNA ≤ 7 days, < 2,000 gm: q12 hrs
	PNA ≤ 7 days, > 2,000 gm: q8 hrs
	PNA >7 days, < 2,000 gm: q8 hrs
	PNA >7 days, > 2,000 gm: q6 hrs
Compatible solutions	- D5W, D10W, and NS - Reconstitute with sterile water for injection to a concentration of 50 mg/ml
Cautions/Monitoring	- Maximal concentration for IV infusion is 100 mg/ml - Avoid IM injection - Monitor CBC, BUN, creatinine, and urine for hematuria and/or proteinuria
Adverse effects	Hypersensitivity reactions (rash), thrombophlebitis, mild leukopenia, and elevation of AST

Penicillin G Preparations

Classification	β -lactam antibiotic	
Indications	Treatment of neonatal meningitis and bacteremia, group B streptococcal infection, and congenital syphilis	
Dosage: IM - IV (infuse over >30 minutes)		
• Bacteremia: 25,000-50,000 units/kg/dose • Meningitis: 75,000-100,000 units /kg/dose	PMA ≤36 weeks, PNA 0-14 days	q12 hrs
	PMA ≤36 weeks, PNA >14 days	q8 hrs
	PMA >36 weeks, PNA 0-7 days	q12 hrs
	PMA >36 weeks, PNA >7 days	q12 hrs
Compatible solutions	D5W, D10W, and NS	
Cautions/Monitoring	- Final concentration for IV infusion is 50,000 units/ml - Monitor serum potassium, and sodium, when using high dose and in infant with renal failure - Assess weekly CBC, BUN, and serum creatinine	
Adverse effects	- Bone marrow suppression, granulocytopenia, anaphylaxis, and hemolytic anemia - Allergic reactions, rash, fever, and change in bowel flora (*Candida* superinfection and diarrhea) - Very large doses may cause seizures - Rapid IV push of potassium penicillin G may cause cardiac arrhythmias and arrest because of the potassium component	

N.B.: Penicillin G (also known as benzylpenicillin) should not be confused with benzathine penicillin used for only IM injections.

Phenobarbital

Classification		Anticonvulsant, sedative, hypnotic
Indications		Tonic-clonic and partial seizures, neonatal withdrawal syndrome, and neonatal jaundice
Dosage		
• Seizures	Loading	20 mg/kg/dose, IV infusion over >15 minutes (infusion rate <1 mg/kg/minute) - Additional doses of 5 mg/kg q5 minutes, until cessation of seizures or a total dose of 40 mg/kg
	Maintenance	- 3-5 mg/kg/day, divided q12 hrs, IV (preferred for seriously ill neonate), IM, or PO - Begin therapy 24 hrs after the loading dose
• Hyperbilirubinemia (cholestasis)		4-5 mg/kg/day, IV/IM/PO for 4-5 days
• Neonatal withdrawal syndrome		5-10 mg/kg/day in 4 divided doses
Compatible solutions		D5W, D10W, and NS
Cautions/Monitoring		- Contraindicated in porphyria - Therapeutic trough serum concentration: 15-40 µg/ml - Abrupt discontinuation in patient with seizure may precipitate status seizures - Monitor respiration during administration - Assess IV site for phlebitis and extravasations
Adverse effects		Respiratory depression, hypotension, collapse, paradoxical excitement, sedation, hepatitis, and exfoliative dermatitis

Phenytoin

Classification		Anticonvulsant
Indications		Treatment of status epilepticus, Seizures unresponsive to Phenobarbital, Digitalis-induced arrhythmia, and supra-ventricular and ventricular arrhythmias
Dosage: IV (infuse over 30-60 minutes) - PO		
• Status epilepticus	Loading	15-20 mg/kg/day IV over at least 30 minutes. dilute to 5 mg/ml with normal saline, start infusion immediately after preparation
	Maintenance	5-8 mg/kg/day IV slow push or PO divided q8-12 hrs
• Anti-arrhythmia (digitalis induced)	Loading	1.25 mg/kg IV q5 minutes up to a total of 15 mg/kg
	Maintenance	5-8 mg/kg/ day, divided q8-12 hrs
Compatible solutions		NS; it is highly unstable in any IV solution
Incompatible solutions:		D5W, and D10W
Cautions/Monitoring		- IV infusion rate should **not** >0.5 mg/kg/minute - Check for multiple drug interactions - Obtain trough level 48 hrs after IV loading dose, therapeutic serum concentration is 18-15 µg/ml - Monitor for bradycardia, arrhythmia and hypotension during infusion - Avoid using in central lines because of the risk of precipitation. If must use a central line, then flush catheter with 1-3 ml normal saline before and after administration because of heparin incompatibility
Adverse effects		- Hypersensitivity reactions, arrhythmias, hyperglycemia, liver damage and blood dyscriasis - Extravasation may cause tissue necrosis - Rapid IV administration results in hypotension, cardio-vascular collapse, and CNS depression

Piperarcillin/Tazobactam

Classification	Combines the extended spectrum antibiotic piperarcillin with the β-lactamase inhibitor tazobactam
Indication	Treatment of non-CNS infections caused by susceptible β-lactamase producing bacteria e.g. *E. coli* and *Pseudomonas*
Dosage: 50-100 mg/kg/dose - IV (infuse over 30 minutes)	
• PMA ≤29 weeks	PNA 0-28 days: q12 hrs
	PNA >28 days: q8 hrs
• PMA 30-36 weeks	PNA 0-14 days: q12 hrs
	PNA >14 days: q8 hrs
• PMA ≥37 weeks	PNA 0-7 days: q12 hrs
	PNA >7 days: q8 hrs
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	Observe IV sites for signs of extravasation
Adverse effects	Esinophilia, hyperbilirubinemia, elevation of ALT, AST, BUN, and serum creatinine

Propranolol

Classification	Non-selective β-adrenergic-receptor blocking agent
Indications	Hypertension, supraventricular tachycardia, premature ventricular contractions, tachycardia, and tetralogy spells
Dosage	
• Starting oral dose	0.25-2 mg/kg/dose q6 hrs, increase as needed to maximum 3.5 mg/kg/dose q6 hrs
• Starting IV dose	0.01 mg/kg q6 hrs over 10 minutes, increase as needed to maximum 0.15 mg/kg/dose q6 hrs
Compatible solutions	D5W, and NS
Cautions/Monitoring	- Use with caution in renal or hepatic failure - Contraindicated in obstructive pulmonary disease, asthma, heart failure, shock, second- or third-degree heart block, and hypoglycemia
Adverse effects	Generally dose-related hypotension, nausea, vomiting, bronchospasm, heart block, depression, hypoglycemia, and depressed myocardial contractility

Prostaglandin E_1

Classification	Prostaglandin
Indication	Temporary maintenance of PDA, in neonates with duct dependant congenital heart disease, such as pulmonary atresia, pulmonary stenosis, tricuspid atresia, transposition of the great arteries, aortic arch interruption, coarctation of the aorta, and severe Tetralogy of Fallot
Dosage	
• Initial	- 0.05-0.1 μg/kg/minute, continuous IV infusion - Titrate to infant's response-oxygenation versus adverse effects
• Maintenance	- May be as low as 0.01 μg/kg/minute
Compatible solutions	D5W and NS
Cautions/Monitoring	- Dilute before administration to a concentration <20 μg/ml - Prepare fresh infusion solution every 24 hrs - Use cautiously in infants with bleeding tendencies - Monitor for **apnea**, bradycardia and severe hypotension; be ready for intubation and resuscitation - Contraindicated in infants with RDS, persistent pulmonary hypertension - Extravasation may cause tissue sloughing and necrosis
Adverse effects	- Apnea (consider aminophylline administration) - Cutaneous vasodilation, seizure-like activity, jitteriness, pyrexia, hypocalcemia, inhibition of platelet aggregation, hypotension, and bradycardia

Pyridoxine (Vitamin B6)

Classification	Water-soluble vitamin supplement
Indications	Prevention and treatment of pyridoxine deficiency, and treatment of pyridoxine dependent seizures
Dosage	
• Pyridoxine dependent seizures	50-100 mg IV or IM over 1 minute. Follow with a 30 minutes observation period. If a response is seen, continue with the maintenance dose
• Maintenance dose	50-100 mg q24 hrs PO
Cautions/Monitoring	Risk of sedation and respiratory depression; mechanical ventilation may be needed
Adverse effects	Sedation, increased AST, decreased serum folic acid level, and allergic reactions

Ranitidine

Classification	Histamine-2 antagonist
Indications	Duodenal and gastric ulcers, gastro-esophageal reflux, and hypersecretory conditions (e.g., Zollinger-Ellison syndrome)
Dosage	
• PO	2 mg/kg/dose q 8hrs
• IV	0.5mg/kg/dose q6 hrs, infuse over 15 minutes (Maximum concentration: 2.5 mg/ml)
• Continuous IV infusion	0.0625 mg/kg/hr
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Use with caution in infants with liver and renal impairment - Gastric pH may be measured to assess efficacy
Adverse effects	- GI disturbance, sedation, elevations in liver enzymes, thrombocytopenia, and bradycardia or tachycardia - In VLBW infants, its use may be associated with a higher risk of NEC

Sodium Bicarbonate (8.4% concentration)

Classification	Alkalinizing agent
Indications	- Treatment for cardiac arrest, metabolic acidosis and renal tubular acidosis - Adjunctive therapy of hyperkalemia
Dosage	
• Cardiac arrest	- 1-2 mEq/kg/minute - IV slow push over 2 minutes - May be repeated with 0.5 mEq/kg every 10 minutes, or as indicated by the acid-base status
• Metabolic acidosis	**HCO_3 dose (mEq) = 0.3 × Base deficit (mEq/L) × Body weight (kg)** - Infuse IV over >30 minutes on syringe pump - Administer half of calculated dose, and then assess the need for remainder.
• Renal tubular acidosis	- Distal: 2-3 mEq/kg/day - PO or IV - Proximal: 5-10 mEq/kg/day - PO or IV
Compatible solution	D5W, D10W, and NS
Cautions/Monitoring	- Maximum concentration used is 0.5 mEq/ml (dilute with sterile water 1:1) - Do not infuse with calcium or phosphate containing solutions- precipitation will occur - Monitor acid base, ventilation status, and serum electrolytes including calcium
Adverse effects	- Rapid correction of metabolic acidosis with sodium bi-carbonate can lead to intraventricular hemorrhage, hyper-osmolality, metabolic alkalosis, hypernatremia, and hypokalemia - Local tissue necrosis

Surfactants

Classification	Natural, animal-derived exogenous surfactant agent
Indications	- Prophylaxis: infants with high risk for RDS (birth weight <1,250 gm, and larger infants with evidence of pulmonary immaturity) - as soon as possible after birth - Rescue therapy: infants with moderate to severe RDS (requirement of mechanical ventilation and FiO_2 >40%) - immediately following the diagnosis of RDS - Treatment of full-term infants with respiratory failure due to meconium aspiration, pneumonia, PPHN
Dosage: administer intratracheally by instillation into 5Fr end-hole catheter inserted into the infant's endotracheal tube (ETT) with the tip of the catheter protruding just beyond the end of ETT and above the carina	
• Beractant	4 ml/kg/dose divided into 4 aliquots, with up to 3 additional doses (4 total) q6 hrs, as needed
• Calfactant	3 ml/kg/dose divided into 4 aliquots, with up to 2 additional doses q 12 hrs, as needed
• Poractant alfa	2.5 ml/kg/dose divided into 2 aliquots followed by up to 2 additional doses of 1.25 ml/kg/dose q12 hrs, as needed
Cautions/Monitoring	- Assess endotracheal tube patency, correct anatomic location, and suction endotracheal tube before administration - Monitor oxygen saturation, heart rate during administration - Delay suctioning post administration as long as possible (minimum of 1 hour) - Monitor arterial blood gases to detect and correct post dose abnormalities of ventilation and oxygenation - Used vials with residual drugs should be discarded
Adverse effects	Transient bradycardia, hypoxemia, pallor, vasoconstriction, hypotension, endotracheal tube blockage, hypercapnia, apnea, and hypertension may occur during the administration process

Vancomycin Hydrochloride

Classification	Bactericidal antibiotic
Indication	- Active against most gram-positive cocci and bacilli - The drug of choice against *methicillin-resistant staphylococci* and *C. difficile*
Dosage: meningitis 15 mg/kg/dose, bacteremia 10 mg/kg/dose IV (infuse over 60 minute)	
• PMA ≤29 wks	PNA 0-14 days: q18 hrs
	PNA >14bdays: q12 hrs
• PMA 30-36wks	PNA 0-14 days: q12 hrs
	PNA >14days: q8 hrs
• PMA >36wks	PNA 0-7 days: q12 hrs
	PNA >7 days: q8 hrs
• Oral	To treat *pseudomembranous colitis* resulting from *C. difficile* or *staphylococcal enterocolitis*; 20-40 mg/kg/day divided q6 hrs for 5-7 days
Compatible solutions	D5W, D10W, and NS
Cautions/Monitoring	- Final concentration for infusion is 5mg/ml - Give with caution in infants with renal impairment or those receiving other nephrotoxic or ototoxic drugs - Monitor trough serum concentration; therapeutic range is 5-15 μg/ml - Monitor serum creatinine
Adverse effects	- Allergy (rash and fever) - Ototoxicity (enhanced by aminoglycoside therapy) - Nephrotoxicity - Thrombophlebitis at the site of injection - Too-rapid infusion may cause rash, chills, and fever (red-man syndrome) mimicking anaphylactic reaction

Vitamin K1

Classification	Fat-soluble vitamin
Indications	Prevention and treatment of hemorrhagic disease of the newborn and vitamin K deficiency
Dosage	
Hemorrhagic disease of the newborn	
• Prophylaxis	<1,500 gm: 0.5 mg IM, SC
	≥1,500 gm: 1mg IM, SC
• Treatment	1-2 mg as a single dose slow IV push
Deficiency states	1 mg/dose PO, IM or slow IV push
Cautions/Monitoring	- Monitor PT/APTT - Allow a minimum of 2-4 hrs to detect a measurable improvement - IV administration is restricted to emergency use, given very slowly, not exceeding 1 mg/minute, and should occur with a physician attendance
Adverse effects	- Severe anaphylactoid reactions have been reported with IV administration - No association between exposure to IM vitamin K at birth and an increased risk of any childhood cancer

Appendices

The Apgar Scoring System

The Apgar score is a tool that can be used objectively to define the state of an infant at given times after birth, traditionally at 1 minute and 5 minutes.

Table (A1-1): The Apgar score in newborn

Sign	0	1	2
Heart rate	Absent	<100 beats/minute	>100 beats/minute
Respiratory effort	Absent	Slow (irregular)	Good crying
Muscle tone	Limp	Some flexion of extremities	Active motion
Reflex irritability	No response	Grimace	Cough or sneeze
Color	Blue	Pale pink body Blue extremities	All pink

From: Apgar V. A proposal for a new method of evaluation of the newborn infant. Aneth Analg 1953; 32: 260.

After one minute: to evaluate the presence of intrapartum asphyxia.

After five minutes: to assess the adequacy of resuscitation.

After ten minutes: to assess prognosis concerning neurological sequelae.

When the 5-minute score is less than 7, additional scores should be assigned every 5 minutes for up to 20 minutes.

Growth Parameters in Neonates

Extrauterine Growth Chart

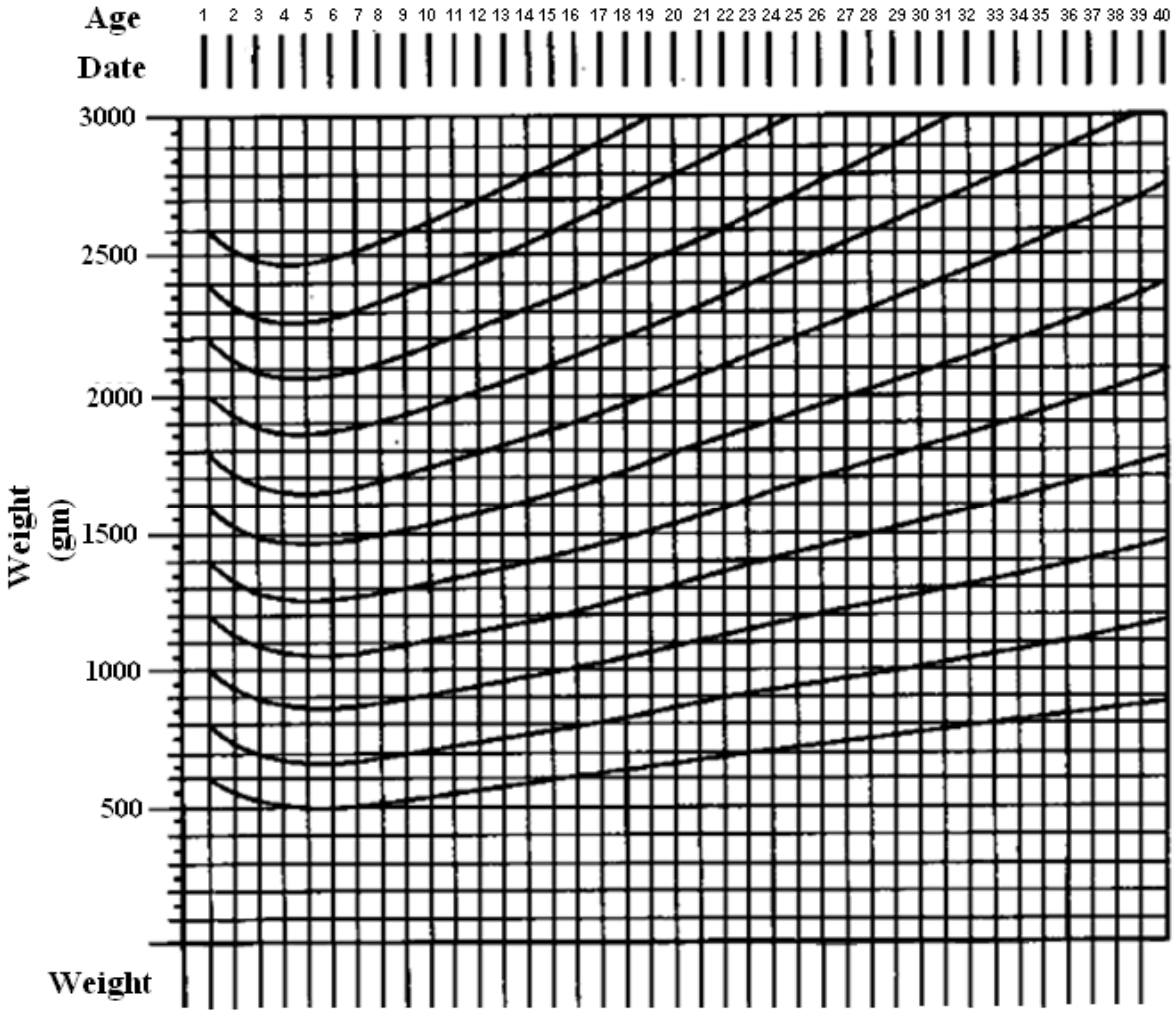


Figure (A2-1): Extrauterine growth chart

From Shaffer SG, Quimiro CL, Anderson JV, et al. Postnatal weight changes in low birth weight infants. Pediatrics 198; 79 (5): 702. Reproduced with permission from Pediatrics

Fetal-Infant Growth Chart for Preterm Infants

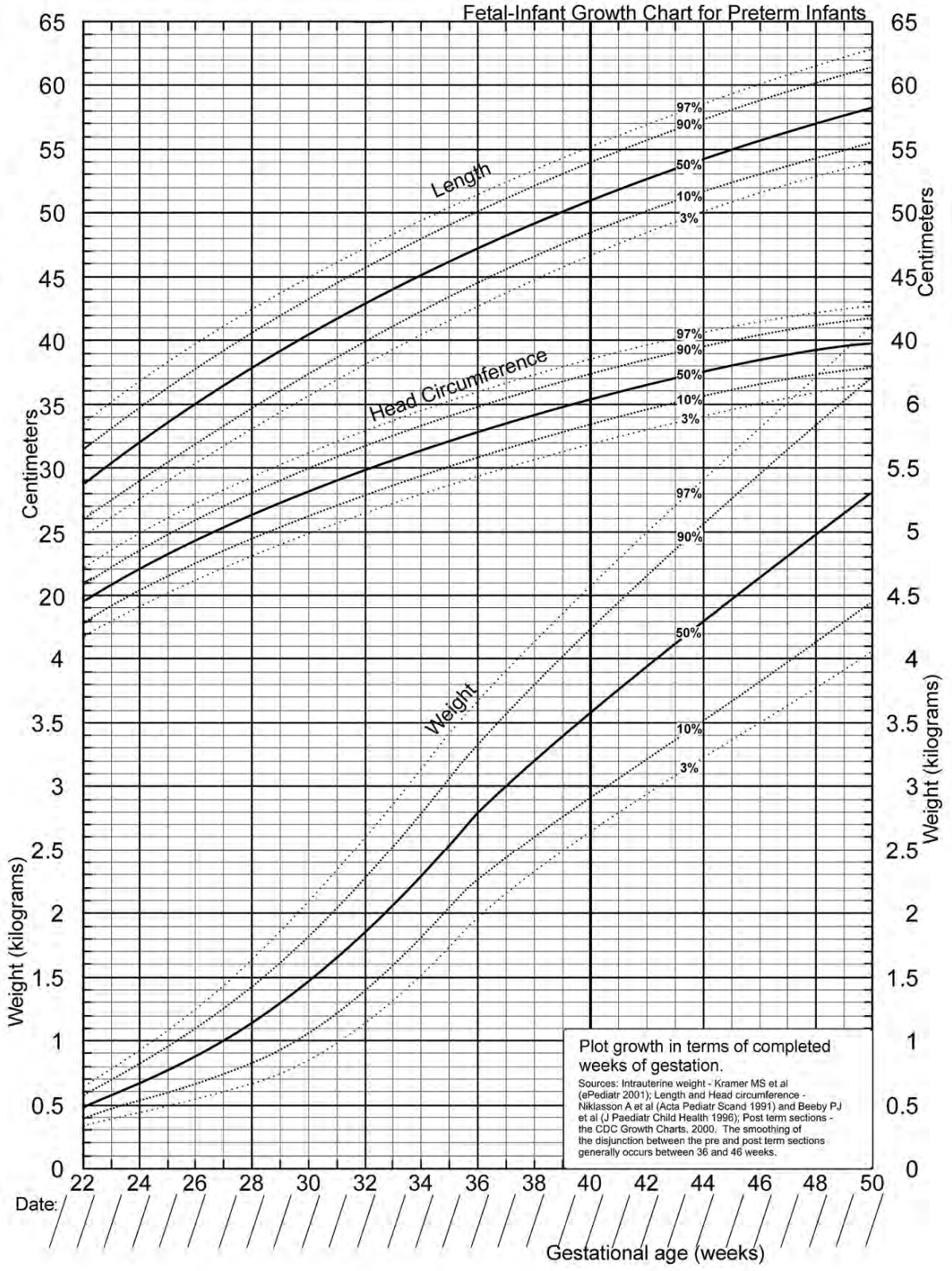


Figure (A2-2): A new fetal-infant growth chart for preterm infants developed through a meta-analysis of published reference studies

Fenton BMC Pediatrics 2003 3:13 doi: 10.1186/1471-2431-3-13. Chart may be downloaded from: http://members.show.ca/growthchart.

Blood Pressure Values in Neonates

Blood Pressure by Gestational Age

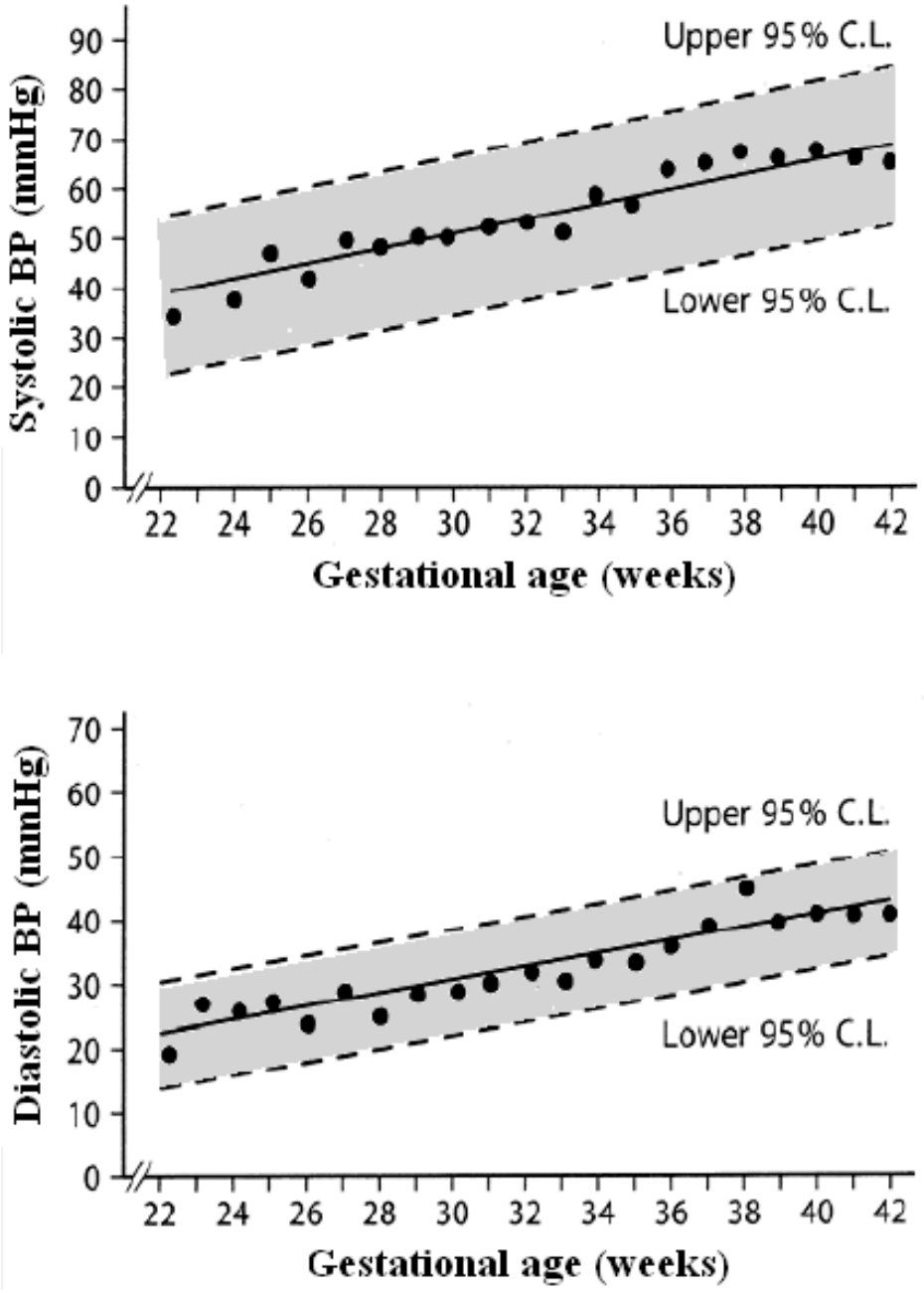


Figure (A3-1): Linear regression between gestational age and mean systolic

(A) and diastolic (B) blood pressure, along with the upper and lower 95% confidence limits, which approximate mean ± 2 standard deviations

From Zubrow AB, Hulman S, Kushner H, Falkner B. Determinants of blood pressure in infants admitted to neonatal intensive care units: A prospective multicenter study. J Perinatol 1995;15:470–479

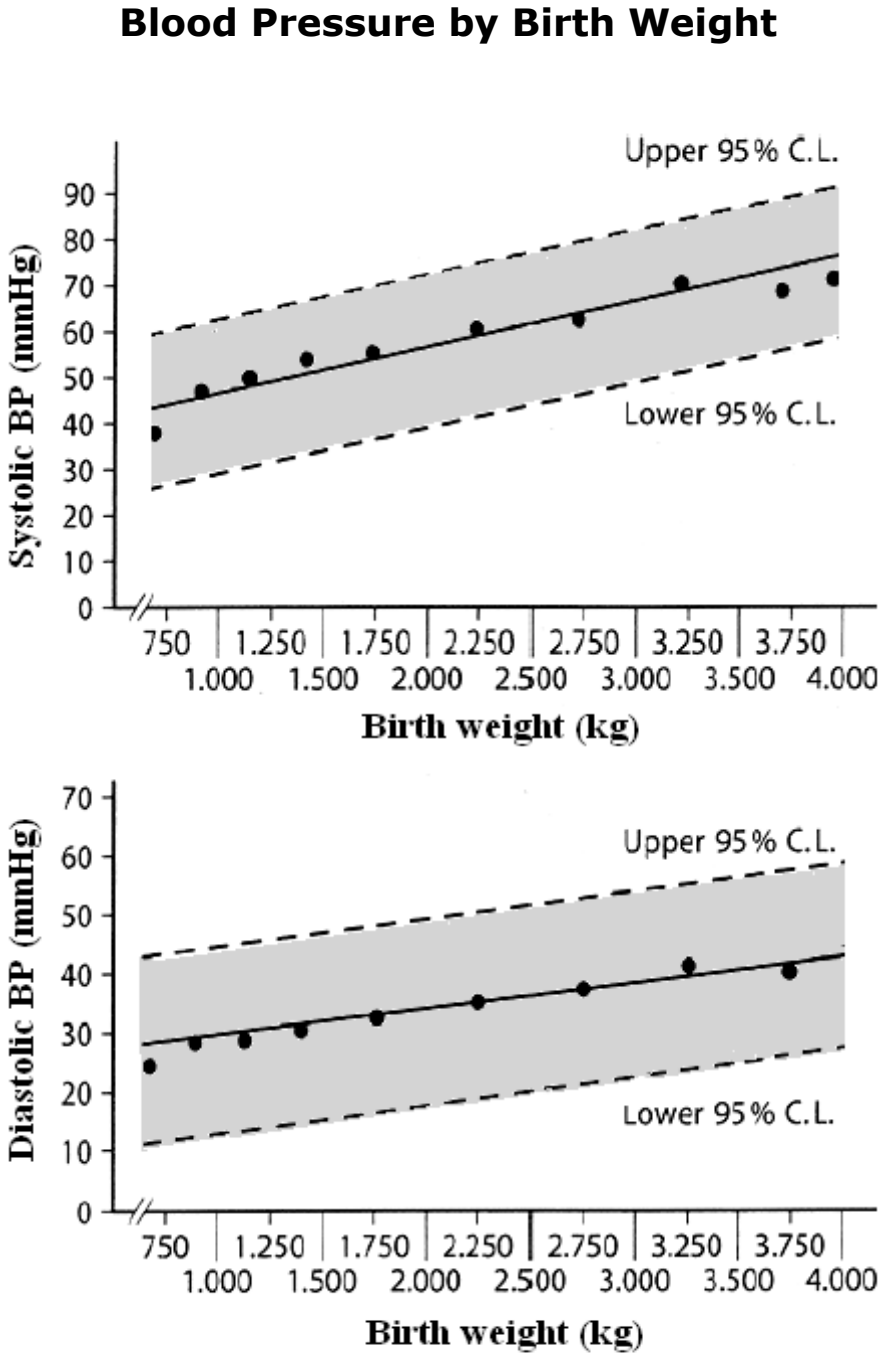


Figure (A3-2): Linear regression between birth weight and mean systolic

(A) and diastolic (B) blood pressure, along with the upper and lower 95% confidence limits, which approximate mean ± 2 standard deviations

From Zubrow AB, Hulman S, Kushner H, Falkner B. Determinants of blood pressure in infants admitted to neonatal intensive care units: A prospective multicenter study. J Perinatol 1995;15:470–479

Blood Pressure by Post-Conceptional Age

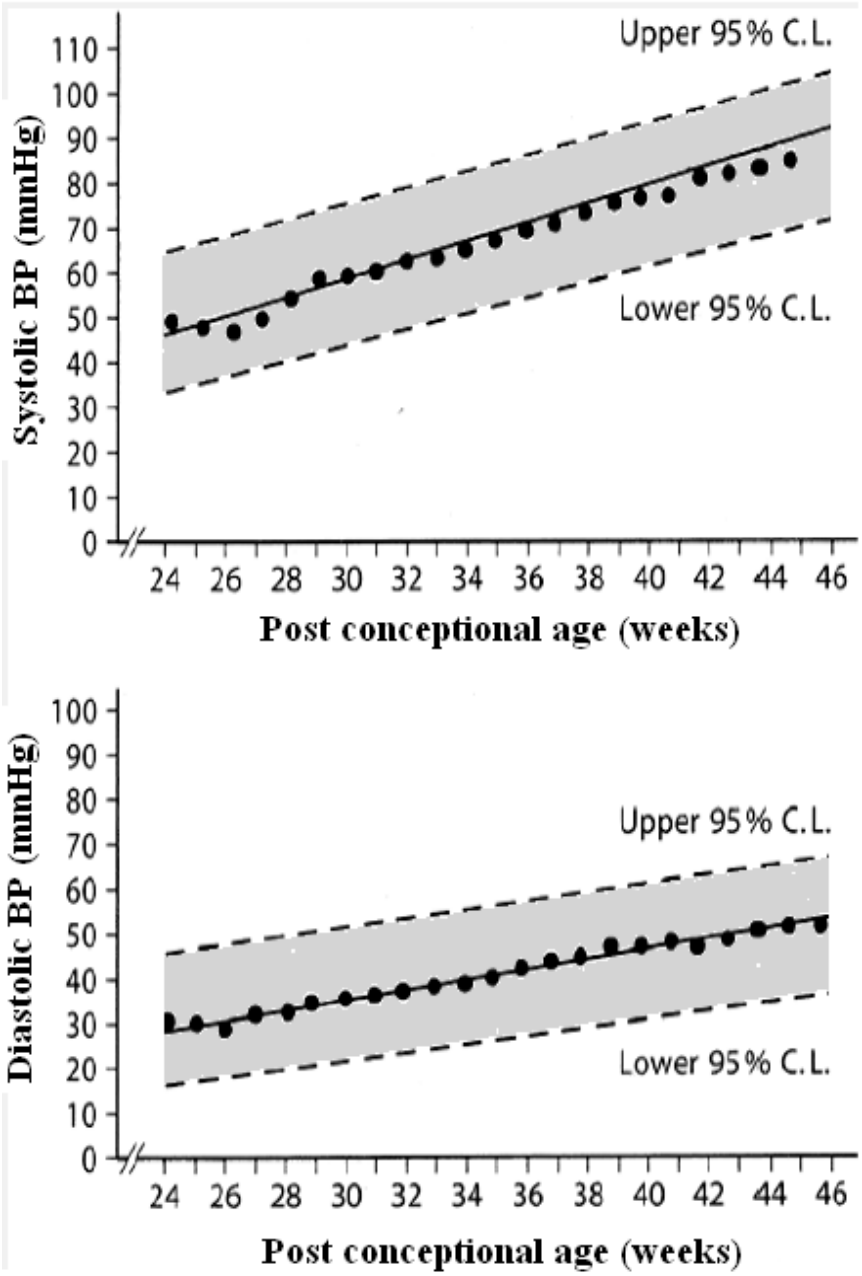


Figure (A3-3): Linear regression between post-conceptional age and mean systolic

(A) and diastolic (B) blood pressure, along with the upper and lower 95% confidence limits, which approximate mean ±2 standard deviations

From Zubrow AB, Hulman S, Kushner H, Falkner B. Determinants of blood pressure in infants admitted to neonatal intensive care units: A prospective multicenter study. J Perinatol 1995;15:470–479

Normal Chemistry Values in Neonates

Table (A4-1): Serum electrolytes and other measured variables in term infants

	Cord Blood		2- to 4-Hour Blood	
	Mean ± SD	**Range**	**Mean ± SD**	**Range**
Na^+ (mEq/L)	138±3	129–144	137±3	130–142
K^+ (mEq/L)	5.3±1.3	3.4–9.9	5.2±0.5	4.4–6.4
Glucose (mg/dl)	75±19	29–120	63±12	29–92
BUN (mg/dl)	6.0±1.7	3.0–10.0	7.1±2.0	4–12
SD: Standard deviation - BUN, blood urea nitrogen				

Adapted from Dollberg S et al. : A reappraisal of neonatal blood chemistry reference ranges using the Nova M electrodes. Am J Perinatol 18:433, 2001

Table (A4-2): Serum electrolyte values in preterm infants

Constituent	Age 1 week		Age 3 weeks		Age 5 weeks		Age 7 weeks	
	Mean ±SD	**Range**	**Mean ±SD**	**Range**	**Mean ±SD**	**Range**	**Mean ±SD**	**Range**
Na (mEq/L)	139.6 ±3.2	133–146	136.3 ±2.9	129–142	136.8 ±2.5	133–148	137.2 ±1.8	133–142
K (mEq/L)	5.6 ±0.5	4.6–6.7	5.8 ±0.6	4.5–7.1	5.5 ±0.6	4.5–6.6	5.7±0.5	4.6–7.1
Ca (mg/dl)	9.2 ±1.1	6.1–11.6	9.6 ±0.5	8.1–11.0	9.4±0.5	8.6–10.5	9.5±0.7	8.6–10.8
BUN (mg/dl)	9.3±5.2	3.1–25.5	13.3 ±7.8	2.1–31.4	13.3±7.1	2.0–26.5	13.4±6.7	2.5–30.5

Adapted from Thomas JL et al: Premature infants: Analysis of serum during the first seven weeks. Clin Chem 14:272, 1968.

Table (A4-3): Normal plasma creatinine values in term and preterm infants (mean± SD)

Age (day)	< 28 weeks	28-32 weeks	32-37 weeks	>37 weeks
3	1.05 ± 0.27	0.88 ± 0.25	0.78 ± 0.22	0.75 ± 0.2
7	0.95 ± 0.36	0.94 ± 0.37	0.77 ± 0.48	0.56 ± 0.4
14	0.81 ± 0.26	0.78 ± 0.36	0.62 ± 0.4	0.43 ± 0.25
28	0.66 ± 0.28	0.59 ± 0.38	0.40 ± 0.28	0.34 ± 0.2

From Rudd PT, Hughes EA, Placzek MM, et al. Reference ranges for plasma creatinine during the first month of life. Arch Dis Child 1983; 58: 212-215.

Hemoglobin Changes in Neonates

Table (A5-1): Hemoglobin changes in babies in the first year of life

Hemoglobin level (gm/dl)			
Week	**Term babies**	**Premature babies (1,200-2,500 gm)**	**Small premature babies (<1,200 gm)**
0	17 (14-20)	16.4 (13.5-19)	16 (13-18)
1	18.8	16	14.8
3	15.9	13.5	13.4
6	12.7	10.7	9.7
10	11.4	9.8	8.5
20	12	10.4	9
50	12	11.5	11
Lowest Hb: mean (range)	10.3 (9.5-11)	9 (8-10)	7.1 (6.5-9)
Time of nadir	6-12 weeks	5-10 weeks	4-8 weeks

From Mentzer WC, Glader B. Erythrocyte disorders in infancy. IN: Taeusch HW, Ballard RA, Gleason CA, eds. Avery's Diseases of the newborn, 8th ed., Philadelphia,Elsevier Saunders, 2005.

Different Glucose Concentrations

Table (A6-1): Preparation of different glucose concentrations

Desired glucose concentration	Preparation of 100 ml
Glucose 5%	Ready made
Glucose 7.5%	50 ml Glucose 5% 50 ml Glucose 10% +
Glucose 10%	Ready made
Glucose 12.5%	62.5 ml Glucose 5% 37.5 ml Glucose 25% +
Glucose 15%	50 ml Glucose 5% 50 ml Glucose 25% +
Glucose 17.5%	50 ml Glucose 10% 50 ml Glucose 25% +
Glucose 20%	75 ml Glucose 25% + 25 ml Glucose 5%
Glucose 25%	Ready made
Glucose 30%	50 ml Glucose 10% 50 ml Glucose 50% +
Glucose 50%	Ready made

Important Maternal Infections and Breastfeeding

Table (A7-1): Maternal infections and lactation

Infectious agents	Breastfeeding		Comments
	Allowed	Not allowed	
Cytomegalovirus (CMV)	✓		- Protective antibodies appear in milk; breast-feeding is an important mean for passive immunity to CMV. - For preterm infants; freeze milk (to decrease viral titer) for the first few weeks before feeding (until antibodies in milk increase).
Flu	✓		- Breastfeeding may help to limit the severity of respiratory symptoms in infected infants. - The mother should wash her hands and wear a mask over her nose and mouth before breastfeeding.
Hepatitis B virus	✓		- All infants born to HBV-infected mothers should receive hepatitis B immune globulin, and the first of the three doses of hepatitis B vaccine within 12 hrs of birth. Mothers should take good care of their nipples to avoid cracking and bleeding.
Hepatitis C virus*	✓	✓	- No evidence that breastfeeding confers risk of HCV infection (HCV infection rate is 4% in both breast and bottle fed infants). - Centers for Disease Control and Prevention (CDC) guidelines do not consider maternal HCV infection a contraindication to breast-feeding, although they suggest that cracked or bleeding nipples may increase risk for transmission. Therefore, if the HCV-positive mother's nipples and/or surrounding areola are cracked and bleeding, the CDC recommends that this mother should stop nursing temporarily and consider expressing and discarding her breast milk until her nipples are healed (HCV is transmitted by infected blood and not by breast milk).
Herpes simplex virus	✓	✓	- Breastfeeding is permitted **if no breast lesions.** Strict hand washing and covering of any lesions (oral or genital lesions) must be practiced.
Human immunodeficiency virus (HIV)	✓	✓	- Avoid breastfeeding if replacement feeding is **A**cceptable, **F**easible, **A**ffordable, **S**ustainable and ***S***afe (AFASS). Otherwise, exclusive breastfeeding for the first six months is recommended. Mixed feeding should be avoided ***(WHO, 2009).***

Table (A7-1): Maternal infections and lactation (Continued)

Infectious agents	Breastfeeding		Comments
	Allowed	Not allowed	
M. Tuberculosis	✓	✓	- Active (open) TB must be separated from the infant; breast milk may be pumped and offered to the baby. If a breastfeeding mother becomes acutely ill with TB, breastfeeding may have to be interrupted. - Mothers with TB who have been treated appropriately for 2 or more weeks (and who are otherwise considered to be non-contagious) are allowed to breastfeed.
Rubella virus	✓		- Neither postpartum immunization with rubella vaccine nor rubella should prevent breast-feeding.
Toxoplama gondii	✓		- Antibodies are present in milk; breastfeeding is allowed.
Varicella (Chickenpox)	✓	✓	- If the mother has varicella within 6 days of labor, isolate the mother and do not allow her to breastfeed until she is no longer contagious. - The infant can receive the mother's expressed breast milk (given by another individual), except when there are lesions of varicella-zoster on the breast.

*The infant should be checked periodically for HCV antibodies during the first 12 to 18 months of life whether or not the infant is breastfed

Maternal Medications and Lactation

Most drugs likely to be prescribed to the nursing mother should have no effect on milk supply or on infant well-being. This is important not only to protect nursing infants from untoward effects of maternal medication but also to allow effective pharmacologic treatment of breast-feeding mothers.

The following should be considered before prescribing drugs to lactating women:

- Is drug therapy really necessary? If drugs are required, consultation between the neonatologist and the mother's physician can be most useful in determining what options to choose.
- The safest drug should be chosen.
- If there is a possibility that a drug may present a risk to the infant, consideration should be given to measurement of blood concentrations in the nursing infant.
- Drug exposure to the nursing infant may be minimized by having the mother take the medication just after she has breastfed the infant or just before the infant is ready to have a lengthy sleep period.

L1	**SAFEST** Drug which has been taken by a large number of breastfeeding mothers without any observed increase in adverse effects in the infant. Controlled studies in breastfeeding women fail to demonstrate a risk to the infant and the possibility of harm to the breastfeeding infant is remote; or the product is not orally bioavailable in an infant.
L2	**SAFER** Drug which has been studied in a limited number of breastfeeding women without an increase in adverse effects in the infant; and/or, the evidence of a demonstrated risk which is likely to follow use of this medication in a breastfeeding woman is remote.
L3	**MODERATELY SAFE** There are no controlled studies in breastfeeding women, however the risk of untoward effects to a breastfed infant is possible; or, controlled studies show only minimal non-threatening adverse effects. Drugs should be given only if the potential benefit justifies the potential risk to the infant.
L4	**POSSIBLY HAZARDOUS** There is positive evidence of risk to a breastfed infant or to breast milk production, but the benefits of use in breastfeeding mothers may be acceptable despite the risk to the infant (e.g. if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
L5	**CONTRAINDICATED** Studies in breastfeeding mothers have demonstrated that there is significant and documented risk to the infant based on human experience, or it is a medication that has a high risk of causing significant damage to an infant. The risk of using the drug in breastfeeding women clearly outweighs any possible benefit from breastfeeding. The drug is contraindicated in women who are breastfeeding an infant.

Table (A8-1): Maternal medications and lactation risk category

Drugs	Lactation Risk Category
Analgesics	
• Acetaminophen	L1
• Aspirin	L3
• Ibuprofen	L1
• Indomethacin	L3
• Ketorolac	L2
• Morphine	L3
• Naproxen	L3 L4 (chronic use)
Antimicrobials	
• Acyclovir	L2
• Amikacin	L2
• Amoxicillin	L1
• Amoxicillin/Clavulanic acid	L1
• Ampicillin/Unasyn	L1
• Azithromycin	L2
• Cefadroxil	L1
• Cefazolin	L1
• Cefotaxime	L2
• Cefoxitin	L1
• Cefprozil	L1
• Ceftazidime	L1
• Ceftriaxone	L2
• Ciprofloxacin	L3
• Clarithromycin	L2

Table (A8-1): Maternal medications and lactation risk category (Continued)

Drugs	Lactation Risk Category
• Clindamycin	L3
• Doxycycline	L3 L4 (chronic use)
• Erythromycin	L3 (early postnatal <3 months) L1
• Ethambutol	L2
• Floxacillin	L1
• Fluconazole	L2
• Gentamicin	L2
• Griseofulvin	L2
• Imipenem/Cilastatin	L2
• Isoniazide	L3
• Itraconazole	L2
• Ketokonazole	L2
• Metronidazole	L2 with high doses (e.g., 2 gm-dose as a single therapy for tichomoniasis), the AAP recommends discontinuing breast feeding for 12-24 hrs after dose, to allow excretion of the drug
• Nitrofurantoin	L2
• Norfloxacin	L3
• Ofloxacin	L2
• Penicillin G	L1
• Piperacillin	L2
• Rifampicin	L2
• Streptomycin	L3
• Sulfamethoxazole*	L3
• Tetracycline	L2 Brief use is compatible (<3 weeks); chronic use is not recommended

Table (A8-1): Maternal medications and lactation risk category (Continued)

Drugs	Lactation Risk Category
• Ticarcillin	L1
• Vancomycin	L1
Anticoagulants*	
• Warfarin	L2
Allergy, asthma, and respiratory medications	
• Albuterol	L1
• Beclomethasone	L2
• Budesonide	L2
• Codeine	L3
• Cetrizine	L2
• Clemastine	L4
• Cromolyn sodium	L1
• Dexamethasone	L3
• Dextromethorphan	L1
• Loratidine	L1
• Motelukast	L3
• Prednisone	L2
• Theophylline	L3
Decongestants	
• Pseudoephedrine	L3 (acute use) L4 (chronic use)
Diabetes medications	
• Insulin	L1
• Tolbutamide	L3

Table (A8-1): Maternal medications and lactation risk category (Continued)

Drugs	Lactation Risk Category
Cardiovascular medications	
• Amiodarone	L5
• Atenolol	L3
• Captopril	L2
• Clonodine	L3
• Digoxin	L2
• Diltiazem	L3
• Enalapril	L2
• Hydralazine	L2
• Labetalol	L2
• Magnesium sulfate	L1
• Methyldopa	L2
• Nifedipine	L2
• Procainamide	L3
• Propranolol	L2
• Quinidine	L2
Anticonvulsants, anti-anxiety, and psychotherapeutic agents	
• Alprazolam	L3
• Caffeine	L2
• Carbamazepine	L2
• Clonazepam	L3
• Clozapine	L3
• Diazepam	L3 L4 (chronic use)

Table (A8-1): Maternal medications and lactation risk category (Continued)

Drugs	Lactation Risk Category
• Ethosuximide	L4
• Fluoxetine	L3 (Neonatal) L4 (older infant)
• Gabapentin	L3
• Haloperidol	L2
• Lithium	L4
• Lorazepam	L3
• Midazolam	L3
• Phenobarbital	L3
• Phenytoin	L2
• Sertraline	L2
• Valproic acid	L2
Gastrointestinal medications	
• Domperidone	L1
• Loperamide	L2
• Metoclopramide	L2
• Omeprazole	L2
• Ranitidine	L2
Contraceptive	
• Contraceptive pill with estrogen/progesterone	L3 (may interfere with milk production)
• Levonorgestrel	L2
• Medroxyprogesterone	L1 L4 (if used first 3 days postpartum)
Diuretics	
• Hydrochlorothiazide	L2
• Furosemide	L3

Table (A8-1): Maternal medications and lactation risk category (Continued)

Drugs	Lactation Risk Category
• Spironolactone	L2
Laxatives	
• Cascara	L3
• Senna	L3
Thyroid medications	
• Carbimazole	L3
• Methimazole	L3
• Propylthiouracil	L2
• L-thyroxin	L1
Anticholinergic agents	
• Atropine	L3

*Avoid suphaemethoxazole in infants with hyperbilirubinaemia and G6PD deficiency

** Heparins (unfractionated and low molecular weight) are not excreted into breast milk because of their high molecular weights and are considered to be safe in during lactation.

From: Hale TW. Medications and Mother's milk, 13th Ed. Amarillo Texas: Hale Publishing, 2008

Drugs generally contraindicated in breastfeeding mothers

- Amiodarone
- Antineoplastic agents
- Bromocriptine
- Chloramphenicol
- Diethylstilbestrol
- Ergot alkaloids
- Iodides
- Lithium
- Methotrexate and immunosuppressants
- Methimazole
- Phenocyclidine
- Pseudoephedrine
- Radiopharmaceuticals

Important X-ray Findings in NICU

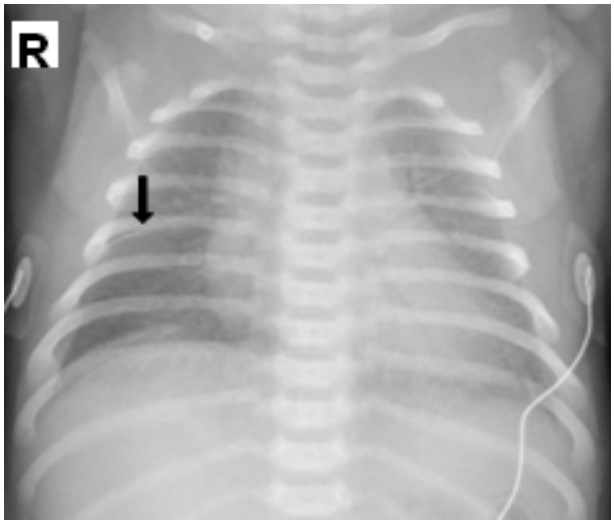


Figure (A9-1): Transient tachypnea of the newborn (From www.adhb.com)

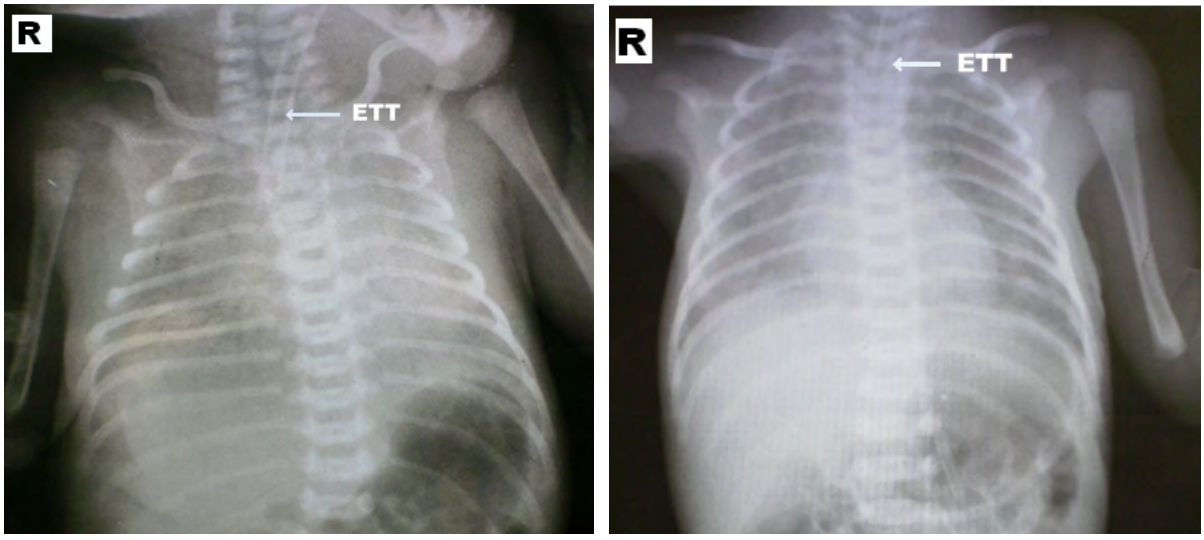


Figure (A9-2): Hyaline membrane disease (Two neonates with RDS)

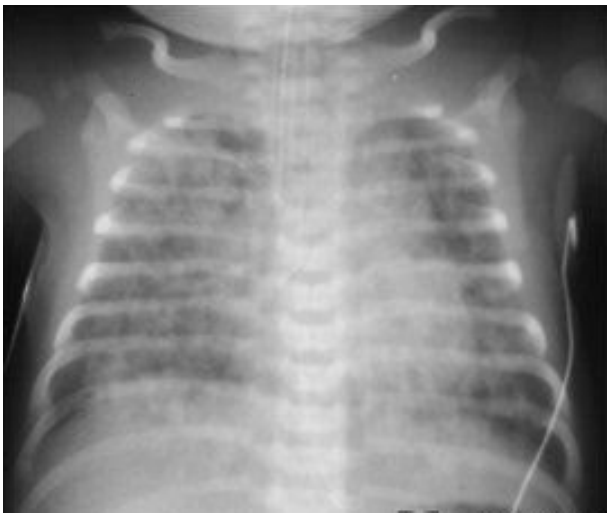


Figure (A9-3): Meconium aspiration (Published with permission from LearningRadiology.com)

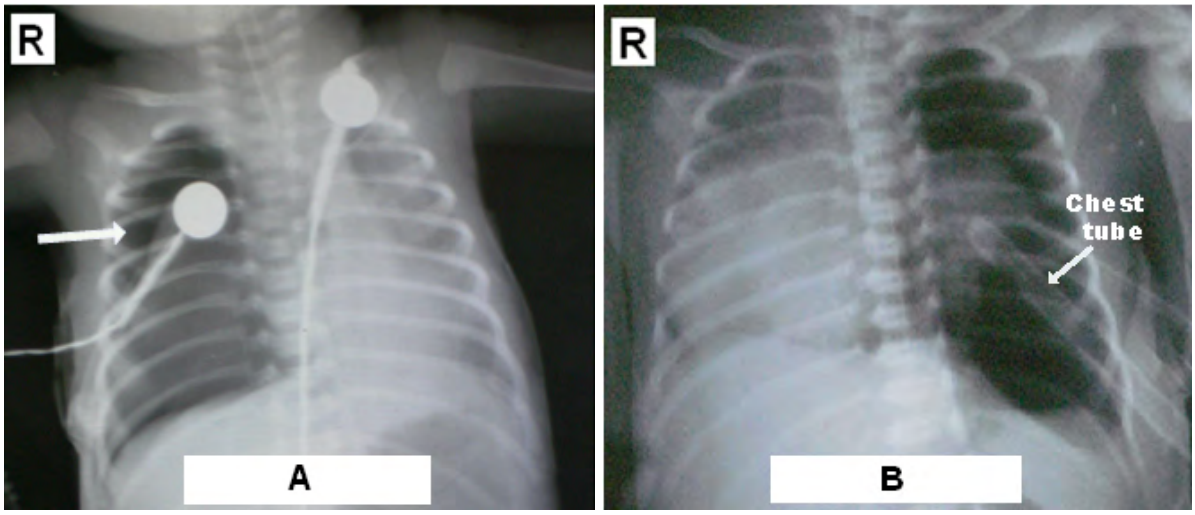


Figure (A9-4): Pneumothorax A) Right side, B) Left side (note the placed chest tube)

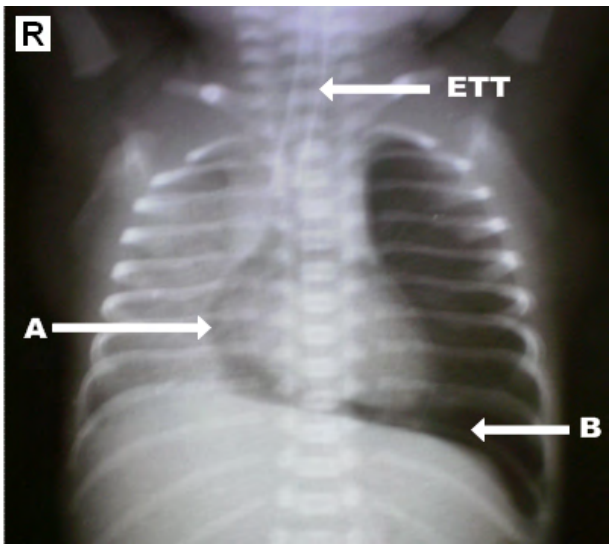


Figure (A9-5): Air leaks (A) Pneumo-pericardium B) Pneumothorax (left side)

(Note ETT shift to the right side)

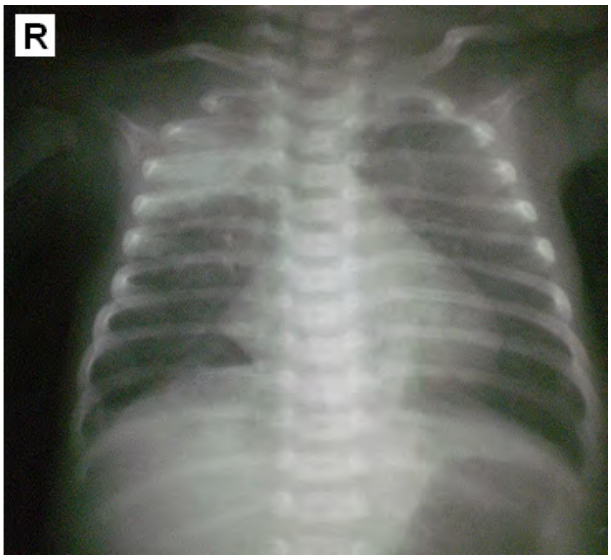


Figure (A9-6): Collapse of upper and middle lobes of the right lung

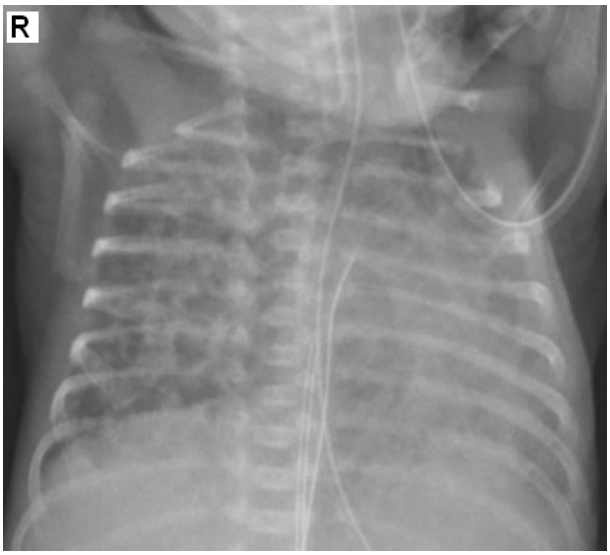


Figure (A9-7): Bronchopulmonary dysplasia (From www.adhb.com)

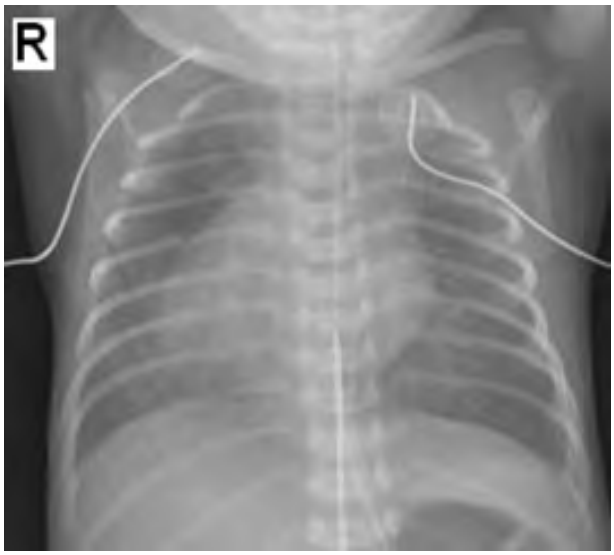


Figure (A9-8): Dextrocardia

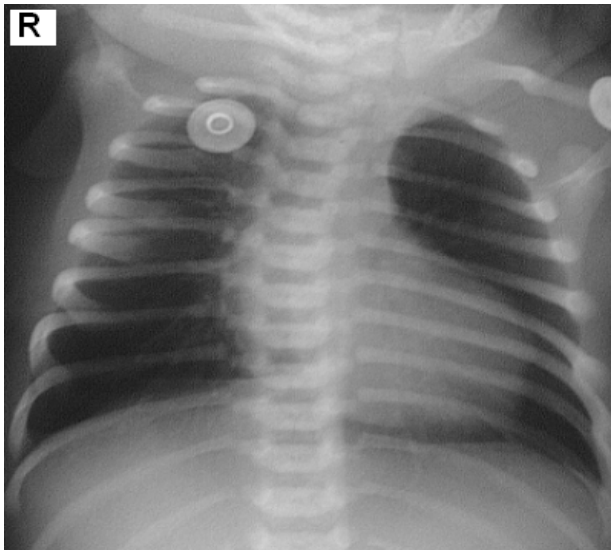


Figure (A9-9): Coeur en sabot in tetralogy of Fallot

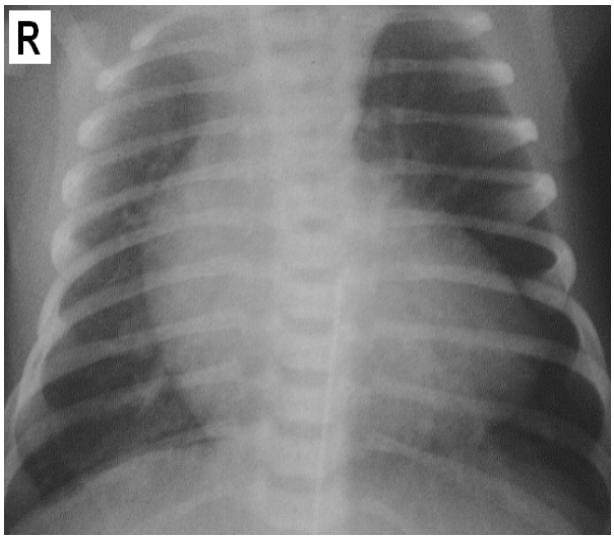


Figure (A9-10): Egg-shaped heart in TGA

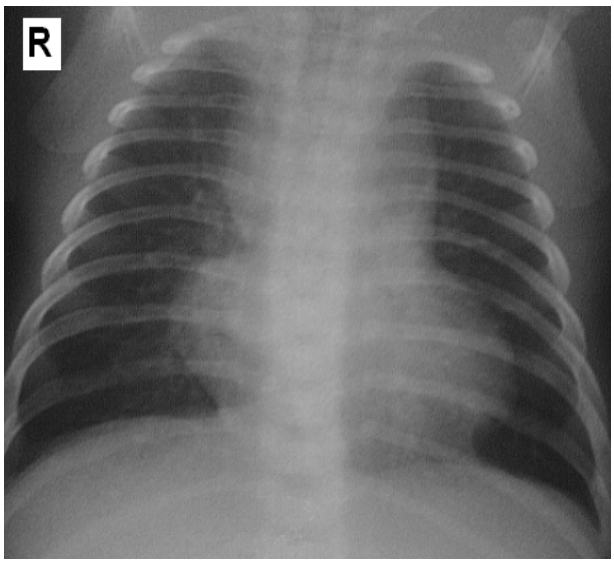


Figure (A9-11): Total anomalous pulmonary venous drainage (figure of 8)

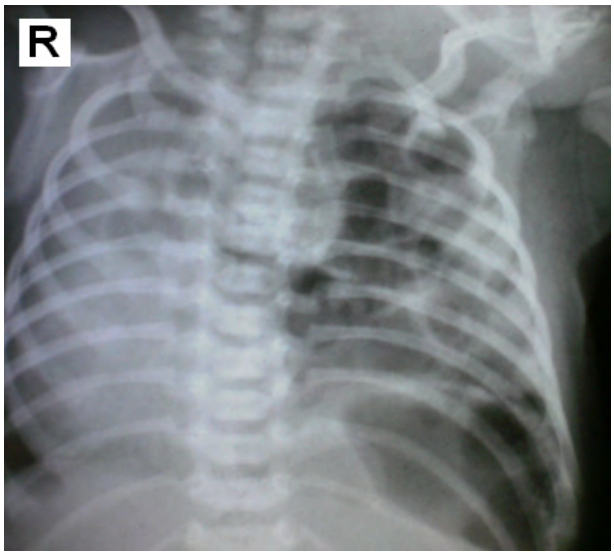


Figure (A9-12): Congenital diaphragmatic hernia (left side)

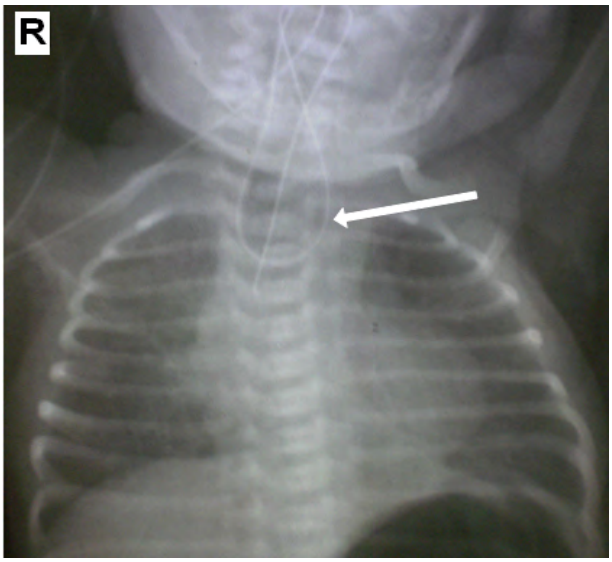


Figure (A9-13): Tracheoesophageal fistula (note the coiled Ryle's tube in the esophageal pouch)

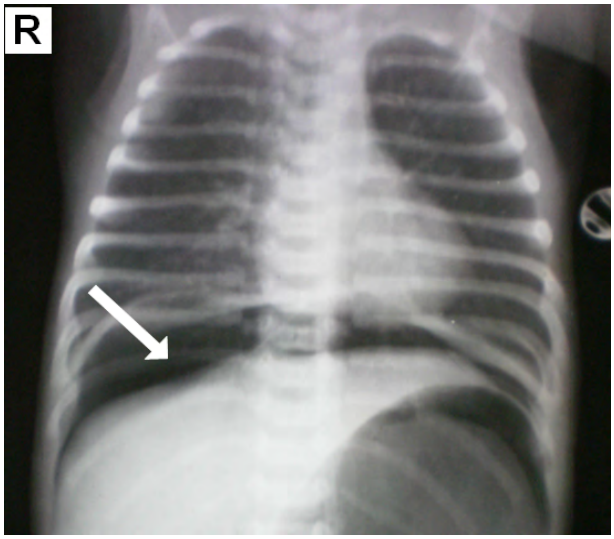


Figure (A9-14): Pneumoperitoneum (note air under diaphragm)

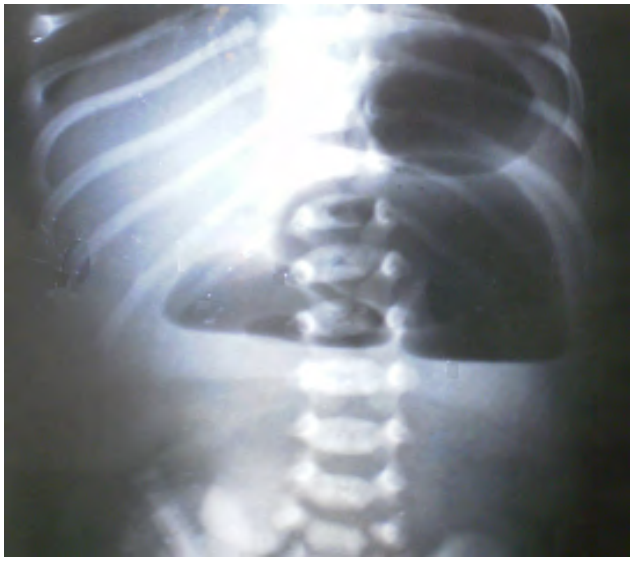


Figure (A9-15): Intestinal obstruction (note the multiple fluid levels)

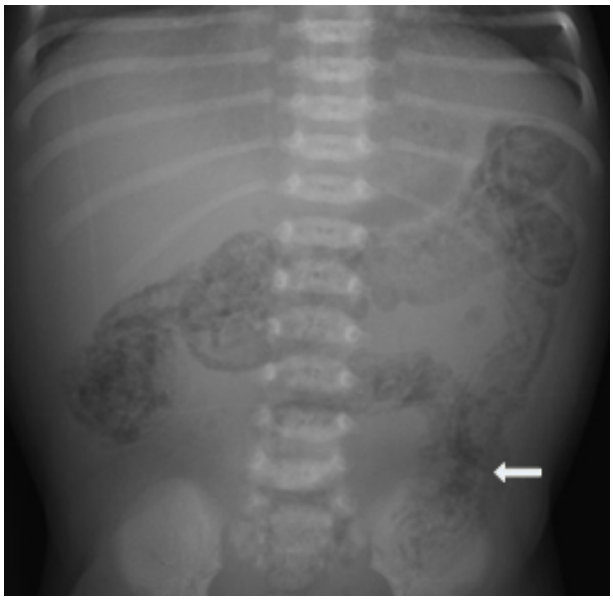


Figure (A9-16): Necrotizing enterocolitis (note pneumatosis intestinalis)
(From Potts AL et al. Necrotizing enterocolitis associated with in utero and breast milk exposure to the selective serotonin reuptake inhibitor, escitalopram. J Perinatol 2007. Reprinted with permission from Macmillan Publishers Ltd.)

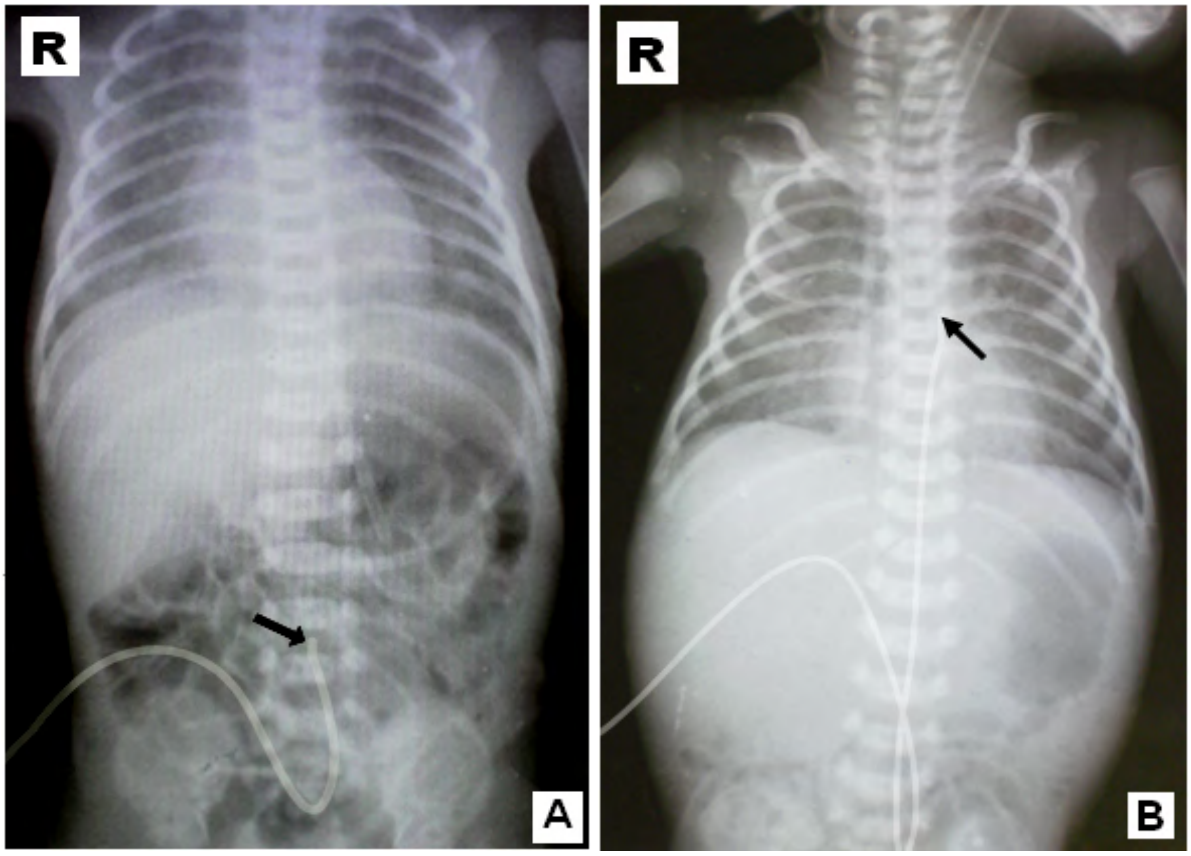


Figure (A9-17): Correct placement of an umbilical artery catheter (A) Low placement, (B) High placement (Note dipping of the UAC down and then up as it enters the umbilical cord into the aorta. This is the hallmark of UAC)

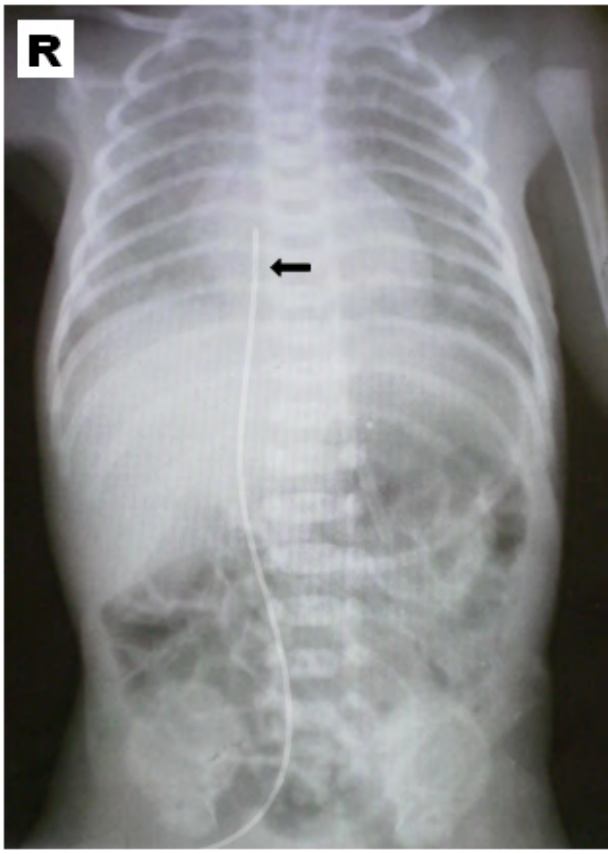


Figure (A9-18): Correct placement of an umbilical venous catheter

(note that the UVC goes straight up)

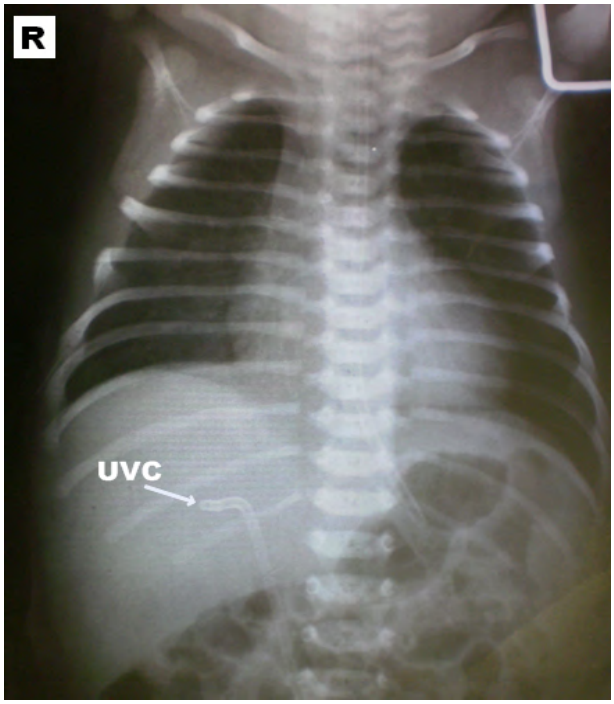


Figure (A9-19): Incorrect placement of an umbilical venous catheter

(intrahepatic position)

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