Medical Education Systems, Inc.

Course 603

NEONATAL

Medical Education Systems, Inc.

TOLL FREE: 877-295-4719
LOCAL: 619-295-0284
FAX: 619-295-0252
EMAILInfo@mededsys.com
WEBSITE: www.mededsys.com
P.O Box 81831 San Diego, CA. 92138-3939.

Neonatal Care

Table of Contents

Introduction

The healthcare goals in neonatal intensive care are primarily to provide the opportunity for survival until the neonate's body systems can more fully develop, enabling their natural defenses to mature. In the past 20 years, neonatal care has developed into an important healthcare specialty, complete with highly specialized critical care equipment, protocols, and facilities. Because of their size and stage of development, the health needs of neonates are quite different from those of adults.

In this continuing education unit, you will explore some of those needs, review developmental stages and the various diseases that afflict newborn infants (including numerous congenital defects). You will also learn about the various scoring and diagnostic tests utilized in neonatal care.

Learning Objectives

Upon completion of this course, you will be able to:

- Identify and discuss the stages of fetal lung development, summarizing its functions in utero and transitions at birth.
- Describe the development of fetal circulation.
- Explain the role surfactant plays in the development of neonates.
- Identify and discuss the stages of labor and delivery, complications that can occur, and preventive steps that can be taken.
- Explain how to interpret neonatal radiographs, and how to treat the most common respiratory diseases that affect infants and children.
- Describe the markers for a high-risk pregnancy, and high-risk infants.
- Identify the clinical signs and appropriate treatments for common neonatal disorders and diseases.

Fetal Anatomy and Physiology

We will begin with a review of pre and postnatal anatomical and physiological development. As you will see below, Table 1 summarizes the various stages of development experienced by the embryo.

Fetal Circulation

In utero, the prenatal circulation depends heavily on the mother's circulatory system for survival and development. During development, fetal nutrition, oxygenated blood, excretion, respiration, and protection are provided by the placenta. Development begins when the blastocyst attaches itself somewhere near the upper portion of the uterine cavity. Diffusion of substances between maternal and fetal blood occurs in the intervillous space created there.

While the ductus venosus and foramen ovale rarely cause problems at birth, if the ductus arteriosus does remain patent or reopens in response to hypoxia, this can lead to problems. If fetal circulation is maintained it can lead to a massive shunt causing hypoxia and pulmonary hypertension. The normal newborn shunt of 20 to 25% is much higher in the presence of a patent ductus arteriosus.

Pulmonary Circulation and Lung Development

The difference between fetal circulatory and nonfetal circulatory systems is that, since the fetus does not use the lungs for gas exchange, very little blood actually perfuses the pulmonary circulation. In the fetus, the body has mechanisms to bypass the lungs.

By 16 to 20 weeks of gestation, the process of pulmonary arterial branching has been nearly completed. The central pulmonary trunk in the fetus has elastic laminae and its walls have become thick. Prior to birth, blood bypasses the lungs in utero, with only about 10% of the cardiac output carried by the pulmonary circulation. With the majority of cardiac output being shunted past the lungs via the ductus arteriosus, fetal pulmonary vascular resistance (PVR) is very high, making flow through the ductus the path of least resistance.

Branching away from the main pulmonary artery, arterial elastic laminae decrease. Arteries with diameters of 2 mm down to approximately 200 microns undergo a transition to a more muscular type of vessel where there are changes in PVR. These *periacinar* are located adjacent to the terminal bronchioles. As the vessels get smaller, the amount of muscle gradually decreases and eventually disappears entirely in vessels adjacent to the alveoli.

Stages of Lung Development

Fetal lung development occurs in five phases:

1. During the **embryonic phase**, which begins at about 4-6 weeks of gestational age, the lung begins as a bud from the foregut.

2. That bud branches into right and left primary bronchi. The branching continues, forming the proximal airways. Common malformations originating in this phase are the laryngeal cleft and tracheoesophageal fistula. There are few structural pulmonary abnormalities that occur during the embryonic phase because an embryo damaged during this period does not usually survive.

3. During the **pseudoglandular phase**, which lasts from about week seven to week sixteen, the predominant feature involves the formation of conducting airways. At about week 8, the diaphragm is also formed. During the pseudoglandular phase, the mucous glands, cilia, goblet cells, and cartilage also begin to appear in the conducting airways. Respiratory epithelium begins to differentiate during this phase, so injuries then can result in abnormal bronchial positions, connections, or number of bronchi. If the diaphragm does not form sufficiently to separate the thoracic and abdominal cavities, diaphragmatic hernia may result.

4. During the **canalicular phase**, weeks seventeen to twenty-eight, the gas exchanging area of the lung develops. Multivesicular and lamellar bodies associated with surfactant production begin to appear at about 20 weeks, and differentiation of Type I and Type II pneumocytes begins during this phase. Pulmonary capillaries are near alveoli at this point, but not near enough for effective gas exchange. Alveolar wall thickness is approximately 45 microns at 20 weeks gestation, and it decreases to about 20 microns at 32 weeks, then eventually to fifteen microns at term. In comparison, adult thickness is about 1 micron.

   Surfactant produced during the canalicular phase is immature and easily destroyed. Its chemical composition (thus its functional capability) changes dramatically in the latter stages of gestation. The alveolar surface area at the end of this phase is approximately 1 square meter, and it increases to about 4 square meters at birth. Injuries to the fetus during this time can cause damage to the gas-exchanging area of the lung, causing a deficiency in alveoli, which may be severe enough to produce pulmonary hypoplasia. The gas-exchanging portion of the lung matures during the final two phases:

5. During the **saccular phase**, which lasts from weeks twenty-nine to thirty-five, interstitial tissue space decreases and airspace walls narrow. They become more compact, and lateral projections extend from the walls to divide the airspaces into smaller units. At 32 to 36 weeks alveoli are present.

6. The **alveolar phase**, from week thirty-six on, is devoted to final development and maturation of the alveoli. The number of alveoli at birth has been estimated to be anywhere from 10 to 150 million, and increases after birth becoming complete by the time the infant is 2 to 3 years old. At this point, the structure of the lung is usually sufficient to survive injuries, but injuries in this phase may interfere with alveolarization and lung function

Fetal Breathing and Lung Fluid

The prenatal lungs do not function as gas exchange organs, but they do serve important purposes:

1. The lung is a primary source of amniotic fluids.
2. Lungs act as reservoirs of carbohydrates needed for fetal energy.
3. They produce surfactant beginning at about 24 weeks

Fetal breathing movements, which appear to be essential for normal development, begin at around 12 weeks gestation. Factors that can affect fetal breathing movements include:

- maternal cigarette smoke, which stops fetal breathing for many hours.
- maternal consumption of alcohol or drugs
- decreases in 0_2, $C0_2$, or glucose
- stress
- prostaglandins

Arousal of the fetus appears to be more related to fetal breathing movements than central nervous system or chemoreceptor stimulation. When fetal breathing movements are absent, the cause is related to chromosomal and other abnormalities, or death. The fetus has breathing movements approximately 30% of the time during the last 10 weeks of gestation.

In utero, the lungs are filled with fluid, and fetal breathing movements exchange this fluid with amniotic fluid. Diagnostic testing of lung maturation via amniocentesis is made possible as a result of this fluid exchange. When Type II pneumocytes mature, they secrete surfactant into the lung and amniotic fluid.

Normal fetal development requires the presence of adequate amounts of lung and amniotic fluid. A diminished amount of either can result in a hypoplastic lung. Hypoplasia is a decrease in either lung weight or volume at birth. A decrease in alveolar number or an increase in alveolar size also can occur. An absence of fetal breathing movements or a lack of adequate space for lung growth may also cause hypoplasia.

The presence and chemical composition of surfactant can be tested in the amniotic fluid samples. Caution needs to be taken while obtaining these samples via amniocentesis because at 14-17 weeks, amniocentesis may reduce birth weight and lung volume; while at 22-25 weeks, amniocentesis may cause a decrease in the size and number of alveoli

Lung fluid, which contains glucose and other carbohydrates, acts as a storage reservoir that can be utilized after delivery. When the lung fluid is absorbed at birth, the materials are made available for use by the newborn's entire body. After delivery, the flow of fluid from lungs into the interstitium and lymphatics is facilitated by increased alveolar pore size.

During lung development, collagen is the dominant connective tissue in airways, blood vessels, and nonrespiratory components of the lung.

While collagen fibers appear disorderly in actively branching airways, they are orderly in formed airways. Elastin, not collagen, is the dominant connective tissue in lung parenchyma.

Elastin first appears at 20 to 25 weeks gestation. Neither collagen nor elastin is particularly prominent at birth; however, the amount of elastin increases rapidly within 6 months after birth, helping to explain the easy rupture and decreased elastic recoil of the newborn's lungs. As the amount of elastin increases, the lung becomes more elastic.

A hypoplastic lung, one that has defective or incomplete development, is generally smaller than normal. Lung size is assessed via lung weight, volume, or DNA; however, lung weight is considered a poor indicator of development because most problems increase lung weight. When a lung weight-body ratio is used for assessment, a ratio <0.015 in a fetus less than 28 weeks old or a ratio <0.012 in an older fetus, is considered hypoplastic.

A better indicator of lung size is a measurement of inflated lung volume, because lung volume is unaffected by most fetal lung diseases. The correlation between crown-rump length and lung volume over the last half of gestation is excellent. Lung volume can therefore be predicted from crown-rump length, with lungs less than 69% of predicted volume being considered hypoplastic. Using lung DNA to reveal the number of cells present is another technique for assessing lung size. If lung DNA is <100 mg/kg body weight, the lungs are considered hypoplastic.

Table 1: Embryological Development of the Pulmonary System

Reviewing the stages of lung development on a weekly basis, you can see how each detail of a mature lung is filled in:

Gestational Age in Weeks	Anatomical Description
3 weeks (3 mm embryo)	The lung structure arises as a pouch from a primitive foregut.
4 weeks	Cartilaginous rings seen in trachea.
6 weeks	Tracheobronchial tree with 18 segmental bronchi has developed.
6-7 weeks (14 mm embryo)	A series of monopodial and irregular dichotomies branching results in 10 principle branches on the right and 8 on the left.
8 weeks	Diaphragm is formed.
10 weeks	The development of cartilage begins.
12 weeks	Mucous glands, goblet cells, and cilia are formed.
16 weeks	The bronchi formation is nearing completion and cartilage continues to develop.

20 weeks	Differentiation of respiratory epithelium. The airways are patent and the pulmonary vascular system begins to develop.
23-24 weeks	Surfactant production, lung parenchyma, and pulmonary circulation are complete.
24 weeks	The bronchi show outpouching at their terminal ends and these begin to multiply and form clusters.
26 weeks	A-C membrane may sustain extrauterine life.
26-28 weeks	Extrauterine life is now possible, although usually difficult. The pulmonary vascular system is functional and the pulmonary structures are nearing completion.
34-36 weeks	A-C membrane mature, alveolar number increasing.

Surfactant

Surfactant is the active agent in the alveoli that cuts surface tension and reduces the need for high pressures to open the alveoli on inspiration. Surfactant is also important for changing capillary and interstitial pressures, facilitating removal of fluids from the lungs, and lowering pulmonary vascular resistance at birth.

The production of surfactant, a mixture of phospholipids (70-80%) and protein in relatively consistent proportions, sharply decreases after 34 to 35 weeks gestation. Evaluation of the content of the surfactant provides valuable information regarding the surfactant-producing system's maturity. Just prior to term, the lungs' volume stabilizes, and the lipid composition of aspirates changes. After about 20 weeks gestation, phosphatidylcholine in surfactant is produced and saved.

By contrasting amount of lecithin with that of sphingomyelin in the amniotic sample, a ratio of lecithin/sphingomyelin (L/S) can be calculated. A ratio of greater than 2 indicates lung maturity, while ratios less than 1 can be suggestive of pulmonary immaturity and the potential for respiratory distress syndrome (RDS). However, the RCP should be aware of the potential for deceptively high L/S ratios in infants whose mothers are diabetic, or if there is blood or meconium in the amniotic fluid.

The so-called *shake-test* can provide an estimate of the presence of surfactant. Mix the amniotic fluid with ethanol and *shake* the mixture approximately 15 seconds.

Because surfactant produces stable bubbles, a closed ring of bubbles seen at the container's edge after 15 minutes indicates the presence of adequate surfactant. When no bubbles are seen after 15 minutes, an L/S ratio test should be conducted.

Surfactant production can be accelerated in premature (<34 weeks gestation) neonates by administering corticosteroids, which can also reduce the incidence and severity of RDS in

some infants. Since steroids can mask the presence of infections in infants, they should be used with caution.

Fetal lung maturation can also be accelerated by the release of catecholamines during birth. The secretion of surfactant can be accelerated by: beta-adrenergic drugs, methylxanthines, a decrease in $PaC0_2$, alveolar stretch, and cAMP (Cyclic Adenosine Monophosphate). Inhibition of surfactant secretion can be caused by: decreased pulmonary blood flow, cholinergic stimulation, hypoxia, hyperoxia, and decreased pH levels.

The High-Risk Infant

Infants at high-risk are those who are expected to need special medical procedures at delivery. Both maternal and infant conditions can put a newborn at risk, and some of the factors include but are not limited to those on the following list. At the end of the outline, you will find a more in-depth discussion of some risk factors.

Maternal issues that can put an infant at risk for a problem delivery include:

- Health: Obesity or overweight condition, diabetic, emotionally stressed, viral infection early in pregnancy, exposure to radiation
- Lifestyle issues: tobacco, drug or alcohol use
- Obstetrical issues and complications:
    - Previous delivery problems (still borns, preemies)
    - First pregnancy late in life
    - Multiple birth (twins, etc.)
    - Post or prematurity
    - Breech positioning
    - Cesarean section
    - Toxemia of pregnancy
    - Abnormal or insufficient placenta
    - Prolapsed cord
    - Premature rupture of amniotic sac
    - Meconium in amniotic fluid

At the time of delivery, the infant can present with conditions that signal high-risk condition, including:

- Less than 36 weeks of gestation
- Acute Respiratory Distress Syndrome (ARDS)
- Infection, blood diseases, or other anomalies
- The need for medications or special surgeries at delivery

It is crucial to assess fetal risk factors prior to birth. Approximately 29% of all pregnancies are deemed to be at risk for at least one of the complications listed above. In addition, approximately 5-10% of those at-risk pregnancies require the administration of CPR.

Reviewing of **maternal history** is an obvious way to identify potentially high-risk neonates. Complications may occur if you find evidence of a history of heart or lung disease, use of controlled substances, cigarette smoking, or infections. Low socioeconomic status or lack of education can also be indicators of potential problems because they are often related to inadequate prenatal care.

Expectant mothers under 17 years of age and over the age of 38 should be seen as potentially being *at risk*, and the history of both current and all previous pregnancies should be reviewed for risk factors no matter the age of the soon-to-be mother. When reviewing clinical records, remember that the term *gravida* refers to pregnancy. *Para* refers to a pregnancy that terminated with the delivery of a *viable* neonate. *Primipara* refers to the mother's first delivery. *Multiparous* refers to a woman who has had two or more pregnancies which resulted in viable fetuses.

A mother's prior pregnancies involving problems should be considered carefully because history has a strong tendency to repeat itself in matters relating to childbirth. A history of fetal asphyxia, prematurity, RDS, maternal toxemia, ruptured membranes, infections, or bleeding during the current pregnancy are all reasons to consider the current fetus as being *at risk* for complications.

Multiple gestations can lead to problems, including: a breech birth, placental and cord problems, intrauterine growth retardation, and increased chance for premature death. Mortality increases with twins, particularly identical twins. Twin transfusion syndrome, where the circulations are connected, is also possible. This causes one baby to be polycythemic and the other to be anemic. The polycythernic baby manifests congestive heart failure and increased bilirubin levels. The anemic baby manifests hypotensive symptoms.

The presence of **maternal diabetes mellitus (DM)** is another cause for concern because problems commonly associated with DM include:

- prematurity
- congenital anomalies
- a predisposition to toxemia
- birth injury due to large baby
- still birth

Less severe DM is associated with delayed maturation of the lung, while severe DM causes chronic intrauterine stress and can accelerate lung maturation. Infants of diabetic mothers are more susceptible to infection, and more likely to be hypoglycemic, hypocalcemic, or have hyperbilirubinemia.

Toxemia involves the spread of bacterial toxins by the bloodstream and is a condition resulting from metabolic disturbances, such as those that occur during pregnancy. The

resultant maternal hypertension can have serious consequences and lead to eclampsia (convulsions and/or coma). The term pre-eclampsia, which is often used interchangeably with toxemia, means a toxemia of late pregnancy which is characterized by hypertension, edema and proteinuria.

Toxemia during pregnancy causes a decrease in placental blood flow leading to uteroplacental insufficiency (UPI). UPI may occur in post-maturity infants, cyanotic maternal heart disease, or chronic hypoxia from maternal pulmonary disease.

UPI is more likely in the older primigravida, and can result in: intrauterine growth retardation, fetal death, chronic asphyxia, or the passage of meconium. When UPI is suspected, it can be assessed by measuring maternal urinary estriol levels. Urinary estriol normally increases throughout pregnancy, but measurements showing low or falling levels are indicative of UPI.

The placenta normally implants in the upper wall of the uterine cavity, but when an implantation takes place in the lower portion of the uterus, it is called **placenta previa**, or if the placenta separates prematurely from the uteral wall **(abruptio placentae)**, the fetus is placed at risk. There are three types of placenta previa:

- A *low implantation* occupies the lower portion of the uterus, but does not cover the cervical opening.
- A *partial placenta previa,* covers a portion of the cervical opening, but does not cover it completely.
- In *total placenta previa*, the placenta is implanted low and completely covers the cervical opening.

All types of placenta previa can be readily diagnosed by ultrasound, and all cause varying degrees of obstruction to fetal passage and increase the chance of premature labor, early separation of the placenta, and hemorrhage. The most serious of these complications involves the early separation of the placenta from the uterus, referred to as *abruptio placentae*.

Separation of the placenta frequently causes premature labor, complete with its attendant risks, to begin. Fetal mortality approaches 50% due to the acuteness of blood loss, and maternal mortality ranges from 2 to 10% in severe cases ending in fetal death. The most common cause of abruption is maternal hypertension of any origin, including preeclampsia. Treatment of abruptio placentae includes strict management of blood volume, maintaining a hematocrit of 30-vol%. This is accomplished by IV administration of blood or crystalloid solutions.

Premature rupture of membranes (ruptures occurring 24 or more hours prior to delivery) put premature neonates at risk because of the increased potential for infection. Infants are considered postmature after the 42nd week of gestation, at which time the placenta begins to deteriorate. These babies often appear small for their gestational age and show signs of dwindling away. Postmaturity also predisposes to increased morbidity, including intrauterine asphyxia, meconium passage, difficult labor, and even premature death.

The **delivery circumstances** can also be predictive of potential problems. Vaginal delivery literally squeezes much of the fluid out of the neonate's lungs, easing the transition to life outside the mother's womb. On the other hand, cesarean-section deliveries don't allow for the squeezing action, increasing the chances that neonate will need special treatment to clear fluid out of the lungs and airway.

The neonate's **amniotic fluid** should be examined at birth for odor, color, consistency, and the presence of meconium. Normal amniotic fluid is thin, pale, and watery. Thick or foul smelling fluid may be indicative of infection. Yellow fluid can be related to infection or hypoxia. If part of the placenta is not perfused, the amniotic fluid may have a red wine color.

Meconium, a dark greenish stool, passes into the amniotic fluid in about 3-5% of preterm births, 10% in term babies, and about 40% of the time in post-term fetuses of more than 42 weeks gestation. The presence of thick particulate meconium in the amniotic fluid requires that as soon the head is delivered, the mouth, oro- and laryngopharynx be thoroughly suctioned to remove any meconium present. Upon delivery of the distressed neonate, the trachea should immediately intubated, suction applied to the end of the endotracheal tube, and the tube withdrawn.

Suction pressure should be set at 100 mm Hg, and suction applied for no more than 3-5 seconds. If meconium is suctioned out of the trachea, the neonate should be re-intubated with a new endotracheal tube and the procedure repeated until no meconium is suctioned. Blowby oxygen can then be delivered to help alleviate hypoxia with positive pressure ventilation beginning after completion of suctioning.

Each hospital needs to have a protocol covering the problem created when a severely depressed newborn has also aspirated meconium. Which risk is greater: that of blowing meconium further into the lungs with PPV before the trachea is clear, or risking asphyxia by not providing PPV until the trachea is clear? The general consensus on the issue seems to be that in severely depressed newborns, it may not be possible to clear the trachea of all meconium before initiating PPV. Be sure you know your hospital's policy on this clinical dilemma.

The average **fetal heart rate (FHR)** in early gestation is 140 beats per minute, dropping to an average of 120/min near term. FHR should be monitored continuously during labor, with normal ranging from 120 to 160/min. Fetal cardiac status can be measured either by simple auscultation with a stethoscope, or with relatively easy-to-use sophisticated electronics. Either way, routine monitoring of fetal heart rates has so significantly diminished adverse results of delivery that nearly every labor room now has a fetal heart monitor.

There is a normal beat-to-beat variation in the FHR, and an intact neural system responds to stimuli by increasing or decreasing FHR. For example, in a normal fetus, a loud noise causes a transient increase in FHR. If there is no FHR response to stimuli, higher brain-functions may not exist, and a total lack of variation may indicate brain stem activity only.

FHR monitoring can identify fetal distress (see Table 2) that is difficult to diagnose otherwise, and because the FHR monitor shows heart responses to asphyxia, it is an

excellent way to identify infants who are being asphyxiated in utero. Since FHR also should correlate with contractions (normally, there is an increase of 15-20 beats in FHR with each contraction), FHR is usually monitored along with uterine contractions so the correlation between the two can be observed.

Table 2: The FHR and patterns associated with fetal and neonatal distress

PATTERN	PROBLEM
Severe bradycardia (<80/min) and loss of variability	Fetal hemorrhage, asphyxia
Sustained tachycardia, no abnormal patterns	Infection, often with apnea
Late decelerations and loss of variability	Asphyxia
Severe, recurrent variable decelerations and loss of variability	Asphyxia, possible hypovolemia
Sinusoidal	Severe anemia with asphyxia

If fetal distress is suspected following FHR monitoring, the assessment of fetal scalp pH is used as a secondary tool to determine fetal well-being. The acid-base balance of the fetus is determined by the viability of the placenta, and its ability to exchange oxygen and carbon dioxide between maternal and fetal blood. If that exchange is disrupted, either at the placenta or in the cord, the resultant drop in pH can be measured.

There are two reasons for the drop in pH:

1. as blood gas exchange decreases, fetal $PaCO_2$ increases, decreasing the pH;

2. facing hypoxia, the fetus begins to metabolize glycogen without oxygen, resulting in a dramatic increase in lactic acid. This metabolic acid, combined with increased $PaCO_2$, causes the pH to drop.

The fetal scalp blood sample is obtained through the cervix between contractions. Normal fetal blood pH is considered to be above 7.25. A pH of 7.2 to 7.24 shows slight asphyxia, and a pH of less than 7.2 signifies severe asphyxia. Since maternal pH can influence fetal pH, it may also be necessary to determine the acid-base status of the mother concurrently. Fetal scalp pH is useful only in the presence of abnormal FHR tracings, since normal tracing indicates a healthy infant in most instances.

Equipment Preparation for the High-Risk Infant

In the presence of any of the high-risk situations just discussed, practitioners should anticipate respiratory problems and be prepared with whatever equipment will be necessary to:

- create a patent airway
- deliver warm and moist oxygen
- ventilate the patient
- deliver emergency medications
- maintain infant warmth
- provide for any or all of the above

Thermoregulation

The neonate is at highest risk of heat loss shortly after delivery. Thermoregulation is of utmost importance in the care of a newborn. The goal in the delivery room is to maintain an environmental temperature such that the neonate's core temperature remains in the normal range of 36.5 to 37.5°C. For this goal to be achieved, all avenues of heat loss must be minimized or eliminated. The mechanisms of heat loss in the newborn include:

- **Evaporation** can occur shortly after birth, when the infant is wet. As the liquid dries and evaporates it takes valuable heat with it. Immediately after delivery, every newborn should immediately be completely dried with a warmed towel or blanket. The head and face are particularly important. This drying helps reduce the evaporative heat loss. Thereafter, the neonate should be kept dry.

- **Radiant loss** involves the loss of heat from merely being placed near a cold surface, causing the transfer of heat from the warm baby to the nearby cooler object. After being dried, the neonate should be wrapped in a warm blanket and immediately placed beneath a radiant heater for resuscitation or examinations. Since a tremendous amount of heat loss can occur from the infant's head, a cap or other covering should be used.

- Both **convective and conductive loss**es pose threats to the neonate's thermoregulation. Conduction takes place when the infant is placed on a cold surface, which pulls heat away from the baby. Convective heat loss is caused by air turbulence in the room that cools the infant. The neonate should be placed on a warming mattress and kept covered as much as possible to avoid convective heat loss. As quickly as possible, the neonate should be placed in a pre-warmed incubator. The longer the baby is left out in the open, the greater the chance of hypothermia.

The goal regarding neonates' thermoregulation is to achieve and maintain a neutral thermal environment (NTE), an environment that allows the infant to maintain his/her internal temperature without increasing oxygen consumption. Too much or too little heat are both adverse situations that lead to increased 02 consumption and apnea. To maintain that proper temperature:

- a thermistor is placed on the neonate's skin to monitor skin temperature
- the thermistor is connected to a servo control on the heat source
- the servo control then adjusts the heat to maintain the NTE.

Guidelines for setting of NTE are based upon infant age and weight. The following can be used as a general guideline:

WEIGHT
(grams)

AGE	**<12OO**	**1200-1500**	**1500-2500**	**>2500**
				(>36wks)
0-24 hrs	34.0-35.4°C	33.9-34.3°C	32.8-33.8°C	32.0-33.7°C
24-96 hrs	34.0-35.0°C	33.0-34.2°C	31.1-33.2°C	29.8-32.8°C
4-14 days	----------	32.6-34.0°C	31.0-33.2°C	29.0-32.6°C

Having reviewed development of fetal anatomy and physiology, risk factors, monitoring, anticipation, and preparation for problems, it is time to discuss the actual delivery and the first few minutes of extrauterine life.

Labor and Delivery

The labor and delivery processes go through three distinct stages, including:

- **Stage 1**: The mother's contractions begin to dilate cervix and continue until dilation measures approximately 10 cm.
- **Stage 2**: The fetus is forced through the mother's cervical canal as a result of the contractions and abdominal wall *pushing* forces. The newborn's head normally presents first, and then the fetus rotates about 90 so the shoulders can present, permitting it to pass through the canal. As the infant's delivery is completed, the umbilical cord is clamped.
- **Stage 3**: When the placenta is expelled, the delivery is complete.

The Infant

At birth, expansion of the lungs causes PVR to fall dramatically. Ventilation helps to overcome fetal pulmonary vasoconstriction through several mechanisms. The first is a rise in Pa02 associated with filling the alveoli with air. This has a direct vasodilator effect on the capillaries. As more blood passes through the lungs and is exposed to air, vasoconstricting prostaglandins are inactivated. In the fetus, these prostaglandins are necessary to help maintain a high PVR and keep blood flowing through the ductus arteriosus.

A rising Pa02 also increases circulating bradykinin levels. This helps constrict the ductus and force more blood through the pulmonary circulation. Mechanical expansion of the lungs stretches and straightens the capillaries which, in turn, decrease the resistance to flow. In utero, the capillaries are very kinked and the path is tortuous. This keeps the PVR high. Stretching the alveoli and surrounding tissue corrects this.

As the lungs expand with air, P02 rises, the pathway is straightened, and prostaglandins are metabolized. More blood is now able to flow through the pulmonary capillaries and less through the ductus. Catecholamine release, triggered by the delivery process and the cutting of the umbilical cord, causes active constriction of the ductus to begin. Flow through the ductus is furthered impeded by rising aortic pressure.

Following delivery, neonatal pulmonary artery pressure declines incrementally from an average mean pressure of 39mm Hg at ten hours, to about 29 mm Hg at 15 hours. During the same time frame, neonatal aortic pressure rises to between 80-100 mm Hg at 20 hours post delivery.

The normal newborn shunt (20-25%) is considerably different from that of normal adults (5-10%), possibly due to continued leakage through the neonate's ductus and foramen ovale.

Neonate's average blood pressure varies according to gestational age and weight. The average neonatal systemic blood pressure at one hour is:

Weight	**Systole**	**Diastole**	**Mean**
1000-2000 g	49	26	35
2000-3000 g	59	32	43
over 3000 g	70	44	53

Average blood pressure at 12 hours is:

Weight	**Systole**	**Diastole**	**Mean**
1000-2000 g	50	30	38
2000-3000 g	59	35	42
over 3000 g	66	41	50

Infant Scoring Systems

As soon as the delivery is complete, there are numerous assessments to be made in order to determine the infant's health status. These include checking the respiratory and cardiac status, and weight. The Apgar scoring system (see Figure 1), named after Dr. Virginia Apgar, was developed as an objective way to evaluate the general status of the newborn at one minute and five minutes after birth. APGAR is also an acronym for what the practitioner will assess: The practitioner evaluates newborn **A**ppearance, **P**ulse, **G**rimace, **A**ctivity, **R**espiratory rate and effort.

The five areas examined are respiratory effort, heart rate, muscle tone, reflex irritability, and color (see Figure 1). Each area is given a score of 0, 1, or 2 depending on the response noted. A score of "0" indicates maximum distress/dysfunction for that parameter. A score of "2" means the opposite. The first score is assessed at 1 minute after delivery, with a second evaluation performed at 5 minutes. Since the Apgar is an objective assessment of the infant's status, a 5-minute score that is higher than the 1-minute score indicates the effectiveness of the resuscitation.

After assigning numerical scores for the categories, scores are totaled, with normal infants scoring 7 to 10, moderately depressed infants scoring 4 to 6, and severely depressed infants scoring less than 4. Realistically, in the clinical setting the latter infants are not scored immediately because they are obviously in severe distress, and resuscitation measures are instituted before there is time to total scores.

The Apgar evaluations can be done every 5 minutes as needed, up to 20 minutes or when the resuscitation ends. The 5-minute Apgar score is predictive of future impairment, with a low score being associated with a likelihood of long-term damage. For example, an Apgar score of two or less at one minute is associated with a high mortality rate. An Apgar score of 8-10 is considered normal.

Figure 1. The Apgar scoring system.

Scoring Component	How Component is Tested	Score 0	Score 1	Score 2
• Heart rate	Auscultation or count pulses at junction of umbilical cord & abdomen	Absent	Slow below 100	Over 100
• Respiratory Effort	Observation	Apnea	Slow, Irregular	Good, yelling
• Muscle tone	Observation: resistance to straightening of extremities	Limp	Somewhat flexible	Well flexed
• Reflex Effort	Flick soles of feet/insert catheter in nostril	No Response	Grimace withdraws	Vigorous cry
• Color	Observation	Blue or pale hands & feet blue	Body pink;	Completely pink

As you can see, the Apgar is an excellent method for assessing the effectiveness of resuscitation; however it should not be used as the sole basis for making resuscitative decisions. One limitation of the Apgar system is that it was designed to assess normal full term infants, not preemies, so it is less valuable in their assessment. For evaluating premature neonates, umbilical cord pH or the Silverman-Anderson scoring system may be more valuable than Apgar.

In order to assess the degree of respiratory distress in neonates, practitioners often use the Silverman-Anderson scoring system. Like the Apgar system it evaluates five parameters and assigns a numerical score for each parameter. However, unlike the Apgar score, the lower the total score the better the baby's condition in the Silverman-Anderson system. The best score possible in each category is a "0" the worst is a "2". Parameters assessed are: retractions of the upper chest, lower chest, and xiphoid, nasal flaring, and expiratory grunt.

Table 3. Silverman-Anderson Scoring System

Score	0	1	2
• Upper Chest Retractions	synchronized	lag on inspiration	see-saw movement
• Lower Chest Retractions	none	just visible	marked
• Xiphoid Retractions	none	just visible	marked
• Nasal Flaring	none	minimal	marked
• Expiratory Grunting	none	stethoscope only	Observed visually or audibly without stethascope

As you can see from Table 3, neonates with no retractions, flaring or grunting with synchronized respiratory movements are scored with "0s". Infants with visible retractions of the lower chest and xiphoid, with the upper chest lagging compared to the lower on inspiration, receive a "1". Minimal nasal flaring and an expiratory grunt heard only with a stethoscope also receive a "1". Marked retractions with a "see-saw" movement of the upper and lower chests scores a "2". Marked nasal flaring and audible expiratory grunting also receive a "2". Normal babies have a cumulative score close to "0". Severely depressed babies score close to "10".

Cardiac and Pulmonary Diseases in the Infant

RCPs need to be alert to the clinical signs of cardiac and pulmonary diseases in infants, including:

- Tachypnea (respiratory rate above 60)
- Wheezing (can indicate edema in small airways)
- Retractions (can indicate increased work of breathing)
- Rales (indicate fluid in small airways)
- Grunting (can increase the functional residual capacity)
- Nasal flaring (sign of respiratory distress)

Meconium Aspiration

Meconium is present in the amniotic fluid of nearly 10% of all infants at birth, and of those, between 20-25% go on to suffer some form of significant pulmonary disorder. Pneumothorax is frequently a complication of meconium aspiration. Clinical indications include: tachypnea, rasping or faint respirations, patchy infiltrates on x-rays, hyperinflation, and severe cyanosis.

Aggressive suctioning is called for to eliminate airway obstructions, and placement of a nasogastric tube is needed to evacuate swallowed meconium and stomach contents. Treatment for metabolic acidosis is required, and supplemental oxygen with mechanical ventilation may be needed in order to maintain the infant's ABGs. Oxygen consumption and carbon dioxide production can be kept to a minimum through thermoregulation.

Pneumothorax

Tension pneumothorax can present as a complication of meconium aspiration, ventilation with positive pressure, pneumonia, hyaline membrane disease, and diaphragmatic hernia. Any newborn in respiratory distress should be reviewed for the presence of pneumothorax. Since pneumothorax can be seen in nearly 1% of all normal deliveries, even asymptomatic infants require observation of vital signs.

Clinical signs include onset of respiratory agitation or distress, tachypnea, nasal flaring and grunting, cyanosis, and movement of the apical pulse from the site of the pneumothorax. The most effective differential diagnosis can be made from radiographs. Severe distress may require insertion of a closed system chest tube with continuous suction. The rate of absorption can be enhanced with pure oxygen, but retrolental fibroplasia is a risk.

Pneumonia

Enteric organisms such as E. coli and group B streptococcus are the most frequent causative organisms of perinatal infections. Postnatal pneumonia is most often caused by contamination of the neonate's airway by infected humidifier reservoirs, poor hand washing, and other contaminated equipment. Nonbacterial organisms that can cause pneumonia are acquired by contact with an infected birth canal or nosocomial infection.

The diagnosis of neonatal pneumonia is clearly an inexact science. It is generally based on the history, physical examination, chest x-ray results, and lab data. Symptoms of pneumonia in a neonate, which often present within 48 hours of delivery, include tachycardia, signs of respiratory distress, flaccidity, pale skin, cyanosis, and foul smelling amniotic fluid indicating the presence of infection.

Other clinical signs may include an inconsistent WBC (either depressed below 5,000 or elevated above 15,000), elevated temperature, and/or x-rays showing unilateral or bilateral streaky densities in the perihilar region. Signs of a pneumonia acquired postdelivery can include an increasing tachycardia, poor feeding, lethargy, and aspiration of feedings.

Treatment of neonate pneumonia includes aggressive pulmonary suctioning, thermoregulation, fluid and electrolyte control, supplemental oxygen therapy, identification of the pathogen, and treatment with broad-spectrum antibiotics. Clinical symptoms need to be treated as they appear, with blood gas values closely monitored and treated.

Diaphragmatic Hernia

Diaphragmatic hernia, which occurs in about 1 in 2,200 births, is an extreme emergency and must be treated and corrected immediately upon diagnosis. Herniation of abdominal contents into the thorax is caused by an incomplete embryologic formation of the diaphragm. Ninety percent of the time it occurs on the left side, slightly lateral and posterior, through the foramen of Bochdalek.

When the herniation occurs on the left side, the stomach and intestines may enter the thorax and compress the lung, pushing the mediastinum to the right. The degree of distress noted in the neonate depends on the severity of the herniation. As the neonate begins breathing, the presence of the abdominal contents compresses the lungs, making it very difficult to complete inspiration. As air further distends the intestines and stomach, compressing the lungs even more, the neonate's respiratory distress worsens.

Symptoms of diaphragmatic hernia include cyanosis, respiratory distress, a flattened abdomen, excess amniotic fluid, and bowel sounds in the chest. Chest x-rays showing the loops of bowel in the thorax serve to confirm the diagnosis. In left-sided hernias, heart sounds can be heard in the right chest: X-rays in right-sided hernias show a large density created by the liver in the right thorax.

The treatment includes immediate insertion of a nasal gastric tube attached to suction and evacuate abdominal gas. Ventilation, if needed, should be done through an endotracheal tube using rates near or above 100/min, and low PIP and PEEP pressures in order to avoid barotrauma. Surgical repair of the defect should be done through the abdomen or chest, and an umbilical artery catheter should be used to monitor blood gases and pressure.

Postoperative therapies should last for at least 24 hours, and usually includes a chest tube, mechanical ventilation, and therapies necessary for maintaining ABG's and preventing atelectasis. Improvement in patient status can usually be seen by the third postoperative day, allowing for medications to be decreased and the infant to be slowly weaned from the ventilator

Bronchopulmonary Dysplasia (BPD)

Ironically, the increasingly sophisticated protocols and equipment for treating prematurely born infants have not had an impact on bronchopulmonary dysplasia--in fact, its incidence has actually increased in the last two decades. Despite advances in the study of BPD, its exact etiology remains unknown; however, most cases of BPD occur subsequent to the treatment of RDS. Ironically, the treatment for RDS is considered to be the primary cause of BPD, which involves high pressures and high FIO_2s.

The pathophysiology of BPD appears to linked to the following four factors:

- oxygen toxicity
- barotrauma
- presence of a PDA
- fluid overload

Prolonged exposure to high concentrations of oxygen leads to edema and thickening of the alveolar membrane, and ultimately to hemorrhage of the alveolar tissues, which eventually become necrotic. As the lung attempts to heal itself, the new cells are damaged by the same factors, and the disease is perpetuated.

The diagnosis of BPD can be made from a chronic need for oxygen therapy and ventilator support, and confirmed by chest x-rays and laboratory studies. Lab studies include arterial

blood gas analysis, which shows evidence of chronic lung disease (ie., hypoxia, hypercarbia and increased bicarbonate levels). As the patient progresses through the disease, the ECG will show a right axis deviation of the heart and possible hypertrophy of the right ventricle.

Pulmonary function studies will show an increased respiratory rate, decreased tidal volumes, and normal minute ventilation. Airway resistance, especially in the lower airways, is increased and the lung compliance is typically decreased as a result of airway and lung parenchymal damage.

Chest x-rays on neonates with a history of high $FI0_2$ and positive pressure for several days may show density in all areas with a streaking appearance to the density. The chest x-ray (CXR) characteristics in BPD are generally seen as falling into four stages:

- Stage I: In the first 3 days of life, the CXR is typical of RDS, with bilateral frosted or ground glass appearance.
- Stage II: In days 4-10 of life, the lungs become opaque with granular infiltrates that obscure the cardiac markings.
- Stage III: This occurs during the first 10-20 days of life, and begins showing multiple small cyst formations within the lung fields with a visible cardiac silhouette. There may also be some areas of lung hyperexpansion.
- Stage IV: This occurs following day 28 of life with CXRs showing an increased lung density and the formation of larger, irregular cysts.

Treatment of BPD

There are a variety of approaches to treating BPD, but the most important goal in treatment is to avoid or reduce those factors leading to its development and perpetuation. During mechanical ventilation of the neonate, the goal is to use the lowest possible airway pressures to achieve sufficient gas exchange. If possible, it is recommended to use pressures, rates, and FIO_2s that maintain the PaO_2 at 45 to 55 mm Hg. Transcutaneous monitors and pulse oximeters are used to maintain these parameters, and to avoid the need for numerous arterial blood gases. Besides preventive measures, treatment includes:

Mechanical ventilation: Use an endotracheal tube small enough to allow a small leak in order to prevent subglottic stenosis in long-term cases. If treatment is planned for more than 1-2 months, a tracheostomy may be preferable. Adequate humidification of inspired gases is important for avoiding mucus plugging from thickened secretions. Extubate as quickly as tolerated.

Respiratory therapy procedures: Patients generally need chest physical therapy, suctioning, and aerosolized bronchodilators.

Fluid therapy: should be aimed at maintaining adequate hydration and urination. Diuretics such as furosemide are often needed. If patients lose excess water rapidly, they may be subjected to pneumothoraces if ventilator pressures and rates are not decreased. Long-term use of diuretics calls for maintaining calcium and phosphorus levels.

Right-heart failure: Symptomatic right-sided heart failure may be treated with digoxin in addition to diuretics. BPD patients need frequent blood work, which depletes volumes, so transfusions may be needed to maintain a hematocrit above 40%.

Nutrition: BPD patients may require 120 to 150 cal/kg/day to achieve growth and meet needs of lung repair.

Vitamin E: deficiency tends to increase incidence of oxygen toxicity; administration of vitamin E supplements decreases lung injury caused by administration of oxygen.

Respiratory Distress Syndrome (RDS)

This syndrome, also known as hyaline membrane disease, is one of the most predominant lung problems experienced by neonates. It mainly strikes infants under 35 weeks old, affecting the younger newborns more than older infants. Diagnostic improvements and treatment advances including CPAP, PEEP have significantly cut the RDS mortality rates, but it remains a serious problem.

The etiology of RDS is well understood: a significant deficiency in pulmonary surfactant production. This deficiency decreases lung compliance, increases the infant's work of breathing (WOB), tires an already weakened system and causes atelectasis, decreased alveolar ventilation, hypoperfusion, and even asphyxia. Problems during pregnancy, including maternal diabetes and bleeding prior to labor, can be factors contributing to the incidence of RDS.

Although many factors contribute to the deficiency of surfactant, the main contributor is prematurity of the neonatal pulmonary system. Although surfactant is produced near gestational week 22, it can easily be disrupted by hypoxemia, hypothermia, and acidosis, all of which plague the premature neonate. It is not until the mature surfactant is produced near week 35 that these stressors do not disrupt the production, and the fetal lungs are considered mature.

The symptoms of RDS usually worsen gradually for the first 48-72 hours, followed by stabilization, and a slow recovery period. Stabilization of the disease is often associated with diuresis. The highest incidence of mortality from RDS occurs within the first 72 hours. If death occurs following 72 hours, RDS is usually secondary to complications such as barotraumatic air leaks, intracranial hemorrhages, or infections rather than being due to the lung disease.

The ideal treatment for RDS would obviously be to prevent it from occurring. The administration of glucocorticoids to the mother at least two days prior to delivery has been shown to promote fetal lung and surfactant development. The difficulty in treating RDS is in maintaining adequate alveolar ventilation without inflicting damage on the lungs. The goal of treatment is to support the patient's respiratory system adequately while minimizing complications--something that is easy to envision, but difficult to accomplish.

Treatment of RDS involves a variety of issues, including:

- maintenance of a patent airway and respiratory acid-base balance
- remaining alert to other systems being affected by decreased ventilation
- providing crucial support until the infant matures

Treatment of RDS also requires adequate hydration, including electrolyte balance. Diuretics, such as furosemide, are used widely in the management of fluid balance in the neonate. Maintenance of thermoregulation is also of vital importance in treating RDS. The use of a pulse oximeter and transcutaneous monitor, along with supportive blood gases, allows for the titration of ventilatory support to meet the neonate's needs, and should be considered mandatory equipment for treating RDS.

Successful management of neonatal RDS patients requires anticipation of potential complications. That anticipation can prevent some complications and allow for rapid treatment of others. Potential complications include:

- Intracranial hemorrhage occurs in 40% of infants weighing less than 1500 g, and the risk increases as positive pressure is initiated.
- Barotraumatic injury leading to pulmonary air leaks, particularly as higher ventilator pressures are needed to maintain adequate ventilation and oxygenation.
- Disseminated intravascular coagulation (DIC), which leads to profuse bleeding throughout the body, is caused by a disruption of coagulation factors. Neonates with RDS have an increased incidence of DIC.
- Infection is common because of the presence of an endotracheal tube. Sterile techniques when intubating and suctioning can reduce chances of pulmonary infection.
- Patent ductus arteriosus (PDA) is another common complication of RDS.

Congenital Anomalies

Neonates experience a variety of respiratory and cardiac anomalies. The anomalies that can inflict the fetal respiratory tract during development include:

- an atresia of the upper esophagus with an accompanying fistula between the lower esophagus and trachea
- esophageal atresia without a fistula
- a normal esophagus and trachea with a fistula connecting the two ("H" type)
- lower esophageal atresia with the upper esophagus attaching to the trachea
- both upper and lower esophageal attachments to the trachea
- choanal atresia (tissue blockage at the posterior nasal chamber)
- herniation of the diaphragm

- Pierre-Robin (micrognathia) which causes respiratory distress because of airway occlusion by the tongue

Cardiac defects occur in about 1 percent of all newborn deliveries, and the anomalies include:

- The ductus arteriosus sometimes fails to close following delivery (PDA), causing the shunting of blood away from the lungs and making it difficult for the newborn to maintain oxygenation.

- Defects in the atrial septum also cause blood to shunt from the left atrium to the right.

- Ventricular septal defects allow blood to shunt from the left ventricle to the right.

- The Tetralogy of Fallot is a well-known defect that includes ventricular septal defects, an overriding aorta, hypertrophy of the right ventricle, and pulmonary valve obstruction.

- Transposition of the great vessel occurs when the aorta arises from the right ventricle, and the pulmonary artery arises from the left ventricle.

- Coarctation of the aorta involves a constriction of the aorta, severely impeding the flow of blood.

- With tricuspid atresia, blood flow between the right atrium and ventricle is interrupted and shunting through the foramen ovale occurs.

- Anomalous venous return involves the return of pulmonary blood flow to the right atrium instead of the left.

- In truncus arteriosus, one large vessel acts both as the aorta and pulmonary artery.

- Hypoplastic left-heart syndrome involves outflow from the left ventricle being impeded by coarctation of the aorta and stenosis of the aortic valve.

The respiratory care provided neonates with these anomalies depends on whether the defects increase or decrease the flow of blood to the lungs. Defects that reduce pulmonary flow include tricuspid atresia and the Tetralogy of Fallot. Increased blood flow is caused by VSD, coarctation of the aorta, subaortic stenosis, PDA, and anomalous venous return.

Lung compliance is generally increased in neonates with decreased pulmonary blood flow. Using high ventilatory pressures can further compromise blood flow and worsen V/Q ratios. Changing the frequency of ventilation instead of inspiratory pressures can help

maintain low mean airway pressure while still meeting the neonate's ventilatory needs. Judicial use of oxygen is frequently required since high PaO_2 levels will increase the chance of closure of the PDA, which may be the only source of pulmonary blood flow.

Neonates who are experiencing increased pulmonary blood flow have decreased lung compliance and require higher ventilatory pressures and PEEP in order to maintain adequate V/Q ratios. Higher pulmonary blood pressures are less affected by increases in ventilatory pressures for these neonates. In all cases, RCPs caring for these patients need to be prepared to adjust ventilator settings to compensate for any changes in compliance.

Neonatal Chest Disease Index

Neonates can be affected by a wide variety of chest diseases, many of which can be diagnosed through radiography. We will discuss and illustrate some of these in great detail. The rest are simply shown on this Index so you can be aware of their existence. We begin by showing some normal neonatal radiographs, and then move on to illustrate and discuss some of the diseases.

- Normal Neonatal Chest, Inspiratory
- Normal Neonatal Chest, Expiratory
- Normal Neonatal Chest, Prominent Thymus
- Normal Neonatal Chest, Prominent Skin Folds
- Normal Neonatal Chest, Lordotic
- Normal Neonatal Chest, Rotated
- Neonatal Chest with Normally Positioned Tubes and Lines
- Neonatal Chest with Normally Positioned Extracorporeal Membrane Oxygenation (ECMO) Catheters
- Bronchopulmonary Dysplasia (BPD)
- Chylothorax
- Congenital Lobar Emphysema (CLE)
- Cystic Adenomatoid Malformation (CAM)
- Diaphragmatic Hernia (Congenital Diaphragmatic Hernia) (CDH)
- Erythroblastosis Fetalis (Immune Hydrops Fetalis) (Hemolytic Disease of the Newborn)
- Hyaline Membrane Disease (Respiratory Distress Syndrome) (HMD) (RDS)
- Meconium Aspiration Syndrome
- Neuromuscular Paralysis
- Patent Ductus Arteriosus (PDA)
- Persistent Fetal Circulation (PFC)
- Phrenic Nerve Paralysis
- Pneumomediastinum (PMS)
- Pneumonia, Aspiration
- Pneumonia, Chlamydia
- Pneumonia, Neonatal (Group B Streptococcus)
- Pneumopericardium (PPC)
- Pneumothorax (PTX)

- Pneumothorax, Anteromedial (PTX)
- Pneumothorax, Tension (PTX)
- Pulmonary Hypoplasia Due to Fetal Anuria Syndrome
- Pulmonary Hypoplasia Due to Skeletal Dysplasias
- Pulmonary Interstitial Emphysema (PIE)
- Pulmonary Lymphangiectasia
- Wet Lung Disease (Transient Tachypnea of the Newborn) (TTN) (Retained Fetal Lung Liquid)

Normal Neonatal Chest, Inspiratory
Clinical Presentation:
Not applicable.

Etiology/Pathophysiology:
Not applicable.

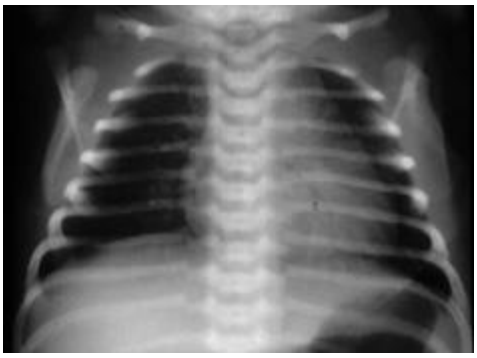
Pathology:
Not applicable

Imaging Findings:
When interpreting a chest x-ray in the neonate, the entire film should be examined, and not just the chest. Use of the "ABC" approach ensures that all areas of the film are systematically examined.

A - Abdomen - check for: bowel gas pattern suggesting ileus or obstruction, free intraperitoneal air, abnormal calcifications, abdominal situs, and diaphragm position.

B - Bone - check for: fractures, lytic or blastic lesions, and metabolic bone diseases.

C - Chest - check for: midline trachea and mediastinum, abnormal mediastinal and cardiac contours, position of the aortic arch, pleural effusions, pulmonary vascularity, pneumomediastinum, pneumothorax, pneumopericardium, infiltrates, and atelectasis. In older infants and children, a good inspiratory chest film is one in which the relationship of the 6th anterior rib ends intersect the domes of the diaphragm. This may be difficult to evaluate in the neonate where proper positioning is difficult.


Supine inspiratory chest radiograph of a neonate.

DDX:
Not applicable

References:
Haller JO, Slovis TL: Introduction to radiology in clinical pediatrics. Yearbook Medical Publishers (Chicago) 1984.

Normal Neonatal Chest, Expiratory
Clinical Presentation:
Not applicable

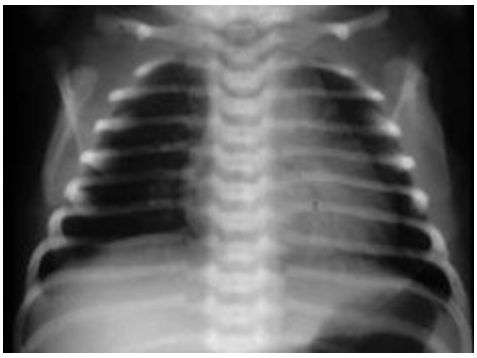
Etiology/Pathophysiology:
Unexpanded alveoli cause decreased thoracic volume.

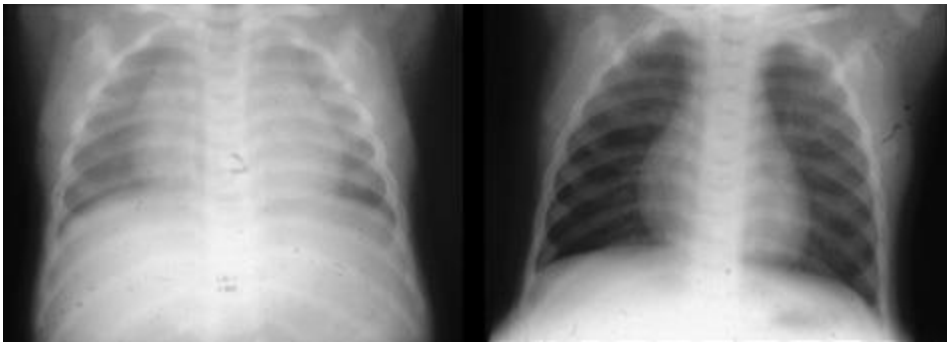
Pathology:
Collapsed alveoli.

Imaging Findings:
In older infants and children, a good inspiratory chest film is one in which the relationship of the 6th anterior rib ends intersect the domes of the diaphragm. This may be difficult to evaluate in the neonate where proper positioning is difficult because the neonate is connected to a number of life support systems. Because the volume of the thorax is decreased in an expiratory film, the following are seen: increased pulmonary opacity, confluent and prominent pulmonary vasculature shadows, and an increase in the size and prominence of the heart and mediastinal contents

DDX:

- Pneumonia
- Cardiomegaly
- Mediastinal mass
- Vascular congestion
- Congestive heart failure
- Pulmonary edema.


Supine inspiratory chest radiograph of a neonate


Supine expiratory chest radiograph (left) and inspiratory chest radiograph (right) in the same neonate.

Normal Neonatal Chest, Prominent Thymus
Clinical Presentation:
Not applicable

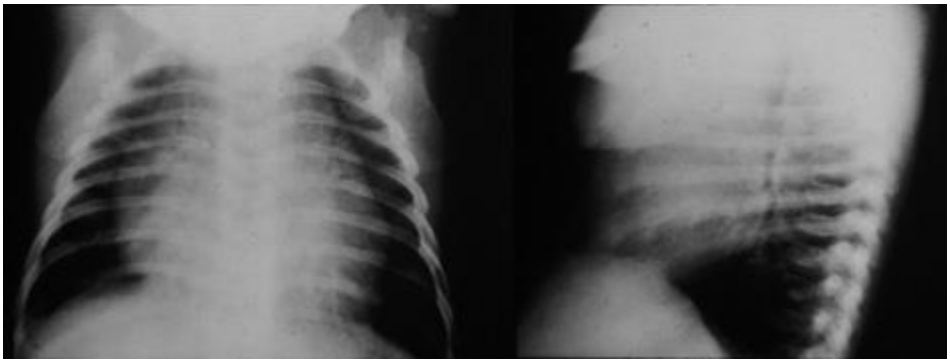
Etiology/Pathophysiology:
Not applicable

Pathology:
Not applicable

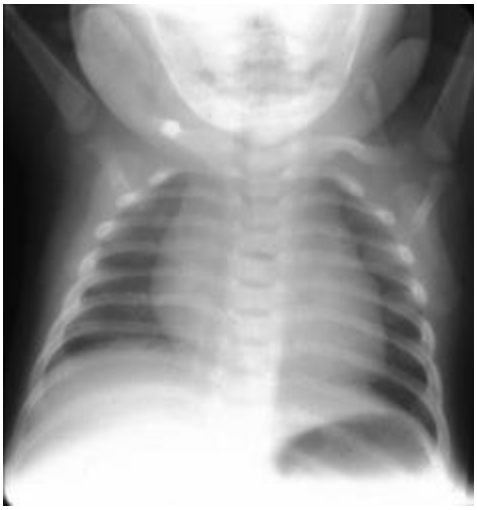
Imaging Findings:
The thymus is a thin, bilobed organ located in the superior mediastinum that has a variable size and shape. The thymus lies anteriorly in relationship to the heart and great vessels. The relative size of the thymus increases with expiration and decreases with inspiration. The thymus decreases in size during periods of stress, such as during sepsis. Occasionally the thymus may extend inferiorly to the level of the diaphragm. Thymic contour is variable. Because the thymus is a soft organ, overlying ribs may indent it, causing a "wave" sign. The right lobe of the thymus can insinuate into the minor fissure, causing a "sail" sign.

DDX:

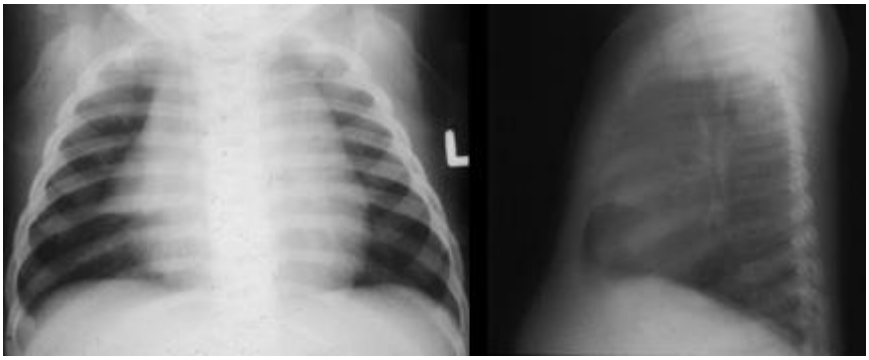
- Abnormal cardiac contour
- Mediastinal mass



AP and lateral chest radiographs show a prominent thymus in a neonate.



AP chest radiograph demonstrates a thymic wave sign with the left border of the thymus being indented by overlying ribs.



AP and lateral chest radiographs reveal a thymic sail sign with the right lobe of the thymus insinuating into the minor fissure.

Normal Neonatal Chest, Prominent Skin Folds
Clinical Presentation:
Not applicable

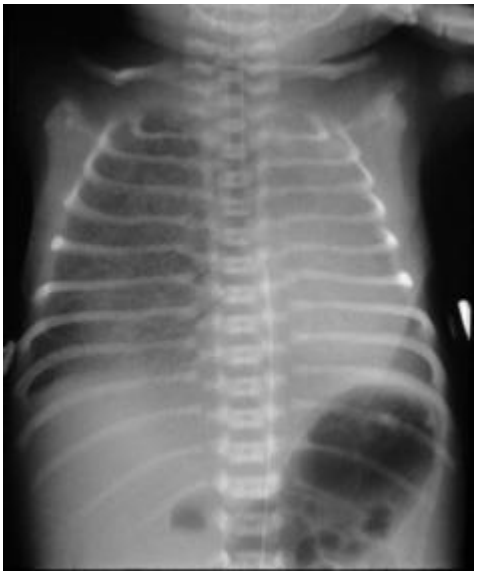
Etiology/Pathophysiology:
Not applicable

Pathology:
Not applicable

Imaging Findings:
Skin folds can be seen as curvilinear densities projecting over the lung bases laterally. They can mimic a pneumothorax, but can be differentiated from pneumothorax because the skin fold margins extend beyond the confines of the lung and pleura.

DDX:

- Pneumothorax



Supine chest radiograph demonstrates a skin fold projecting over the lateral aspect of the left lung base. Notice how it extends beyond the confines of the lung and pleura.

Normal Neonatal Chest, Lordotic
Clinical Presentation:
Not applicable.

Etiology/Pathophysiology:
Not applicable

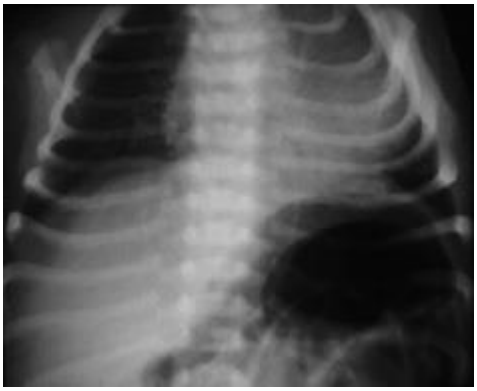
Pathology:
Not applicable

Imaging Findings:
The anterior arc of a rib on a normally aligned film should be directed downward, below

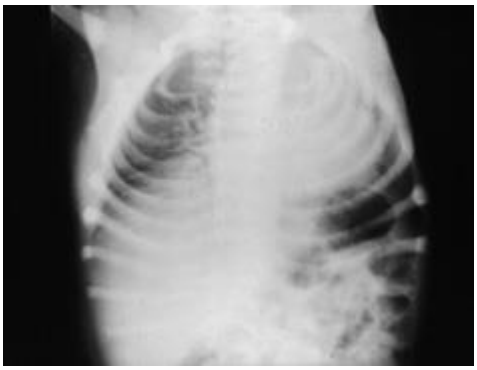
the normally horizontal posterior rib. If the x-ray tube is angled cephalad or if the infant is not lying flat, a lordotic film is obtained. This results in the anterior arc of the rib projecting cephalad above the posterior rib. In severe lordotic distortion the ribs can appear dysplastic, the lung volumes decreased, the cardiac silhouette may have an elevated apex and appear enlarged, and the central portions of the diaphragm may appear elevated, simulating a diaphragmatic hernia. A normal appearing lateral view taken at the same time of the frontal view will confirm the lordotic nature of the frontal film.

DDX:

- Dysplastic ribs
- Cardiomegaly
- Diaphragmatic hernia



Supine lordotic chest radiograph demonstrates falsely appearing dysplastic ribs, low lung volumes, elevated cardiac apex and central diaphragm elevation.



Supine lordotic chest radiograph demonstrates falsely appearing dysplastic ribs, low lung volumes, elevated cardiac apex and central diaphragm elevation.

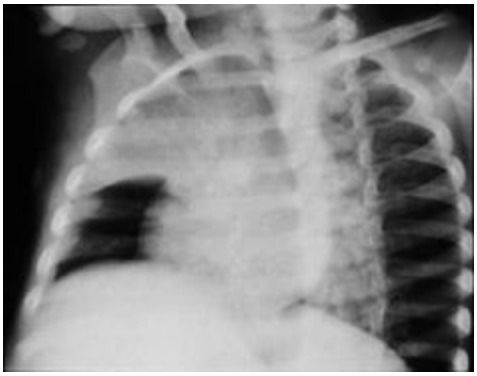
Normal Neonatal Chest, Rotated
Clinical Presentation:
Not applicable

Etiology/Pathophysiology:
Not applicable

Pathology:
Not applicable

Imaging Findings:
In a properly aligned frontal chest radiograph the distance from the spine to the anterior end of the ribs should be equal, bilaterally, at each level. A rotated film can simulate abnormal mediastinal shift. **DDX:**

- Abnormal mediastinal shift


Supine rotated chest radiograph simulates mediastinal shift to the right.

Neonatal Chest with Normally Positioned Tubes and Lines
Clinical Presentation:
Not Applicable

Etiology/Pathophysiology:
Not Applicable

Pathology:
Not Applicable

Imaging Findings:
The position of the tubes and lines on a neonatal chest x-ray should be as follows:

Endotracheal tube (ETT) tip: beneath the thoracic inlet and above the carina

Nasogastric tube (NGT) tip: within the stomach

Feeding tube (FT) tip: within the third portion of the duodenum

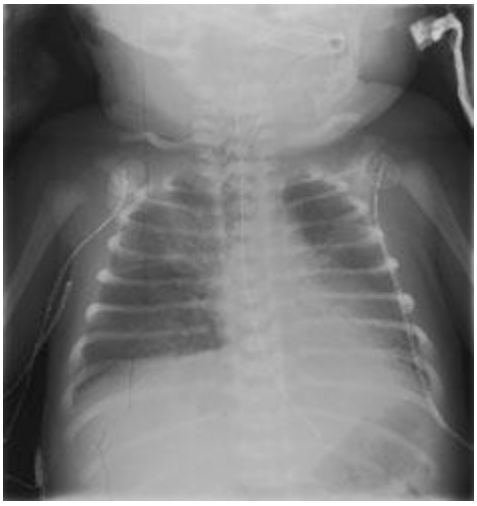
Central venous line tip placed from subclavian/jugular/antecubital approaches should be within the superior vena cava (SVC)

Central venous line tips placed from a femoral approach should be low in the inferior vena cava (IVC) [below L3] or at the junction of the inferior vena cava and right atrium (RA)

Umbilical artery catheter (UAC) tip: can be either high [between T7 and T11] or low [below L3]. On the lateral film the UAC dips into the pelvis from the umbilicus through one of the paired umbilical arteries and then courses through the internal iliac artery and then into the common iliac artery and aorta. The UAC generally projects over the left side of the spine on the AP film.

Umbilical venous catheter (UVC) tip: at the junction of the right atrium (RA) and the superior vena cava (SVC). On the lateral film the UVC extends cephalad from the umbilicus through the umbilical vein and then courses into the portal vein, across the ductus venosus, and into the inferior vena cava. The UVC generally projects over the right side of the spine on the supine x-ray.

DDX:
Not applicable



Supine chest radiograph showing the endotracheal tube tip projecting between the clavicles and the carina, the nasogastric tube tip projecting over the stomach, the umbilical arterial catheter tip projecting at the level of the T8 vertebral body and the umbilical venous catheter tip projecting at the level of the inferior vena cava / right atrium junction.

Neonatal Chest with Normally Positioned Extracorporeal Membrane Oxygenation (ECMO) Catheters
Clinical Presentation:
Patient in respiratory failure.

Etiology/Pathophysiology:
ECMO is a technique for pulmonary bypass, used to support patients with severe

respiratory and or cardiac failure who are not responsive to conventional therapy. The idea is to allow the lungs time to heal with mechanical ventilation being reduced to minimum levels. Through large bore cannulas unoxygenated blood is removed from the body, passed through the ECMO circuit, which oxygenates the blood, and then reintroduced into the body through a large bore cannula. The most common indications for ECMO are meconium aspiration, congenital diaphragmatic hernia and neonatal pneumonia, which are severe enough to result in pulmonary hypertension and right-to-left shunting.

Pathology:
Not Applicable

Imaging Findings:
The Endotracheal tube (ETT), Nasogastric tube (NGT), Feeding tube (FT), Central venous line, Umbilical arterial catheter (UAC), and Umbilical venous catheter (UVC) tips should be in their normal positions. The tips of the ECMO arterial and venous catheters are often non-opaque, and their exact positions are often difficult to ascertain.

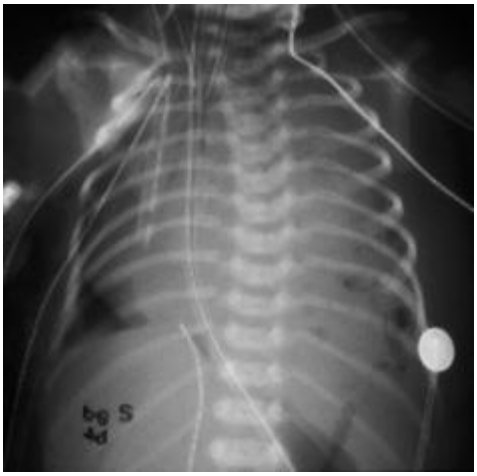
In arterial-venous (AV) ECMO the tip of the arterial catheter should be within the aortic arch and the tip of the venous catheter should be within the right atrium.

In venous-venous (V-V) ECMO the tip of the sole venous catheter should be within the right atrium pointing toward the tricuspid valve

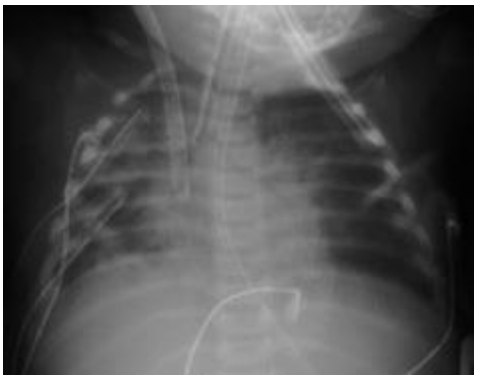
Body wall edema is present because the patient is paralyzed while on the ECMO circuit.

The lungs are opaque due to a combination of fluid in the alveoli, atelectasis, and effusion.

DDX:
Not applicable



Supine chest radiograph demonstrates the tip of the arterial cannula projecting over the aortic arch, the tip of the venous cannula projecting over the right atrium, the tip of the endotracheal tube projecting between the clavicles and the carina and the tip of the nasogastric tube projecting over the stomach.



Supine chest radiograph demonstrates the tip of the venous cannula projecting over the right atrium, the tip of the endotracheal tube projecting at the carina and the tip of the nasogastric tube projecting over the stomach.

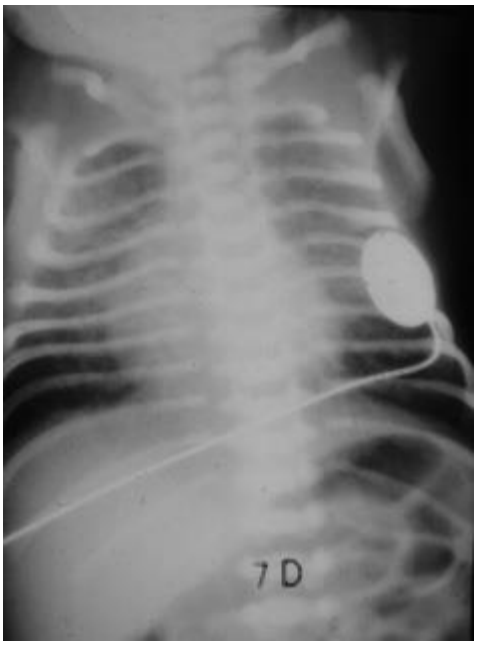
Bronchopulmonary Dysplasia (BPD)
Clinical Presentation:
Premature infant who had severe lung disease (usually hyaline membrane disease) and was treated with ventilatory and oxygen therapy.

Etiology/Pathophysiology:
BPD is an end-stage lung disease due primarily to oxygen toxicity from chronic ventilatory support. Other contributing factors include the effects of intermittent positive pressure ventilation, patent ductus arteriosus, and problems with pulmonary toilet. It is most commonly seen as a sequela to hyaline membrane disease, but can also be seen as a sequela to meconium aspiration, persistent fetal circulation, or congenital heart disease.

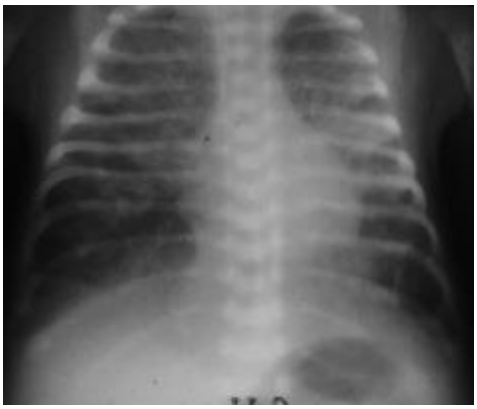
Pathology:
Initially, generalized capillary leakage and mucosal necrosis is seen. At 1-2 weeks exudative alveolar and airway necrosis occurs along with hyaline membrane formation, mucosal squamous metaplasia and interstitial edema. At 2-3 weeks overdistended alveoli and scarred lung are observed. At several months, large lung cysts and progressive interstitial and alveolar septal fibrosis is seen.

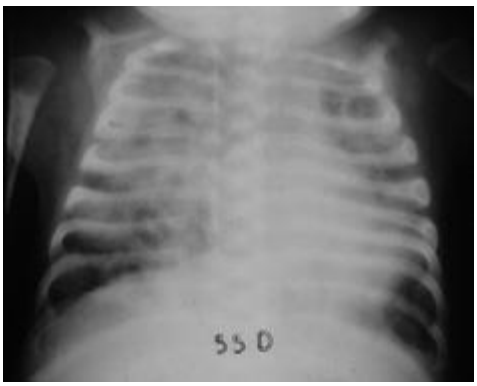
Imaging Findings:
As ventilation techniques change, the classic radiographic stages of BPD are rarely seen. Classically, over time, the imaging findings progress. Initially the typical "ground glass" pattern of hyaline membrane disease is seen. At 1-2 weeks complete opacification of the lungs ("white out") is observed. At 2-3 weeks multiple small cystic lucencies of relatively uniform size and distribution are seen giving the lung a bubbly appearance. By several months of age, lung volume is increased, and the small cystic lucencies have coalesced into larger ones surrounded by fibrotic stranding. In most survivors, clinical and radiologic signs of BPD clear within 2-3 years.

DDX:
Not applicable

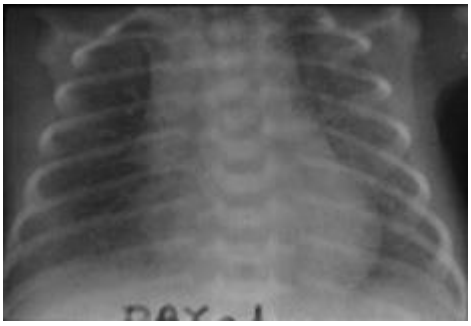


Patient “A”, supine chest radiograph obtained at 1 week of age reveals a ground glass appearance to the lungs.

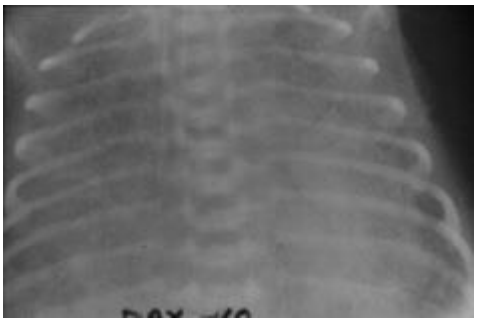

Supine chest radiograph obtained in the same patient at 1 month of age shows the development of small cystic lucencies in the lungs.



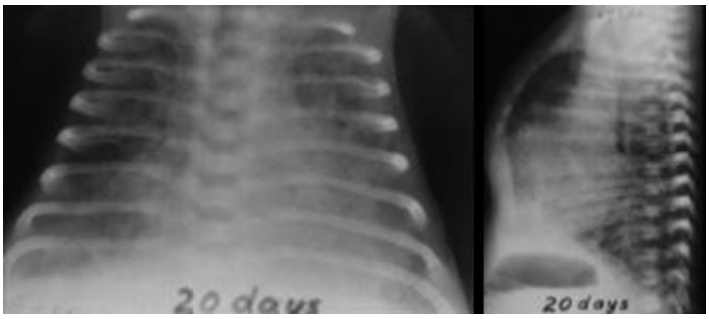
Supine chest radiograph obtained in the same patient at 2 months of age shows continued development of small cystic lucencies in the lungs.



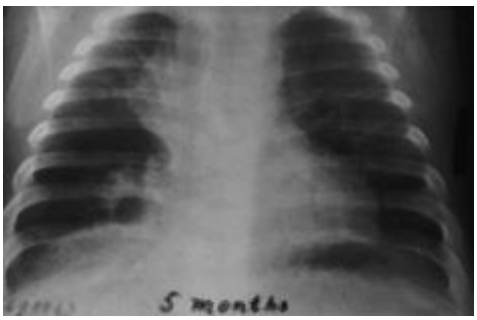
Patient “B”, supine chest radiograph obtained at 1 day of age reveals a ground glass appearance to the lungs.



Supine chest radiograph obtained in the same patient at 10 days of age reveals complete opacification of the lungs.



Supine and lateral chest radiographs obtained in the same patient at 20 days of age show the development of small cystic lucencies in the lungs and increased lung volume



Supine chest radiograph obtained in the same patient at 5 months of age shows the small cystic lucencies to have coalesced into larger lucencies with interspersed fibrotic stranding.

Chylothorax
Clinical Presentation:
Respiratory distress. Fifty percent present in first 24 hours of life, and 70% present within one week of birth.

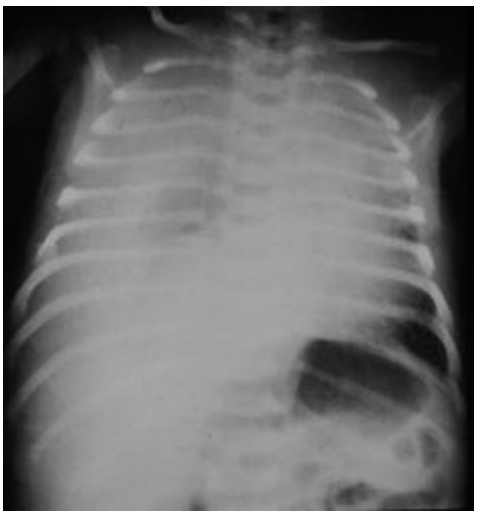
Etiology/Pathophysiology:
Chylothorax is the accumulation of lymphatic fluid in the pleural space. Abruptly elevated venous pressure during delivery can lead to thoracic duct rupture, which leads to intrapleural accumulation of lymph fluid. Initially the fluid is serous, but turns chylous after milk feedings. This is the most frequent cause of a large pleural effusion in newborn. It is rarely bilateral, and is rarely associated with generalized lymphangiomatosis. It is diagnosed and usually managed successfully via thoracenteses.

Pathology:
Not applicable

Imaging Findings:
Usually unilateral and usually on right side (60%). It is difficult to find the exact site of lymph extravasation with contrast studies.

DDX:

- Erythroblastosis fetalis
- Congestive heart failure
- Cystic adenomatoid malformation
- Urine ascites
- Hemothorax from trauma
- Pneumonia


Supine chest radiograph demonstrates a large right-sided pleural fluid collection

Congenital Lobar Emphysema (CLE)
Clinical Presentation:
Usually have symptoms of respiratory distress in the first week of life. Although most

present in the first 6 months of life, they can have a delayed presentation. The symptoms are dependent on the degree of compression of the normal lung.

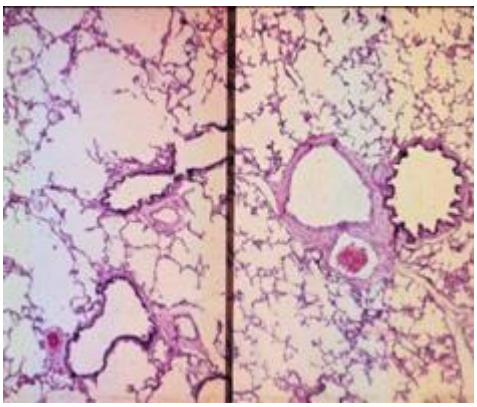
Etiology/Pathophysiology:
Congenital overdistension of the lobe can be due to an intrinsic airway obstruction or alveolar overgrowth. Usually only one lobe is involved. A definite etiology is seen in only 50% of patients.

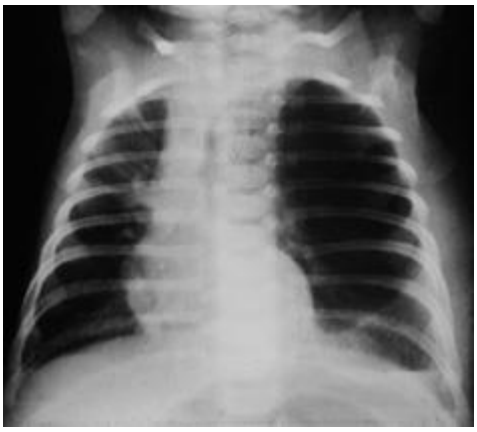
Pathology:
Intrinsic cartilage anomaly or compression by an extrinsic vascular structure.

Imaging Findings:
Progressive overdistension of a lobe that compresses adjacent lobes and causes mediastinal shift to the contralateral side is seen. The overdistended lobe appears oligemic. The most frequently affected lobes are left upper lobe (43%), right middle lobe (32%), and right upper lobe (20%). It is rarely seen in the lower lobes. CLE can begin by having fluid in it, causing it to look like an opaque lung mass, but then the fluid clears via resorption and is replaced by air and it takes on its normal cystic appearance.

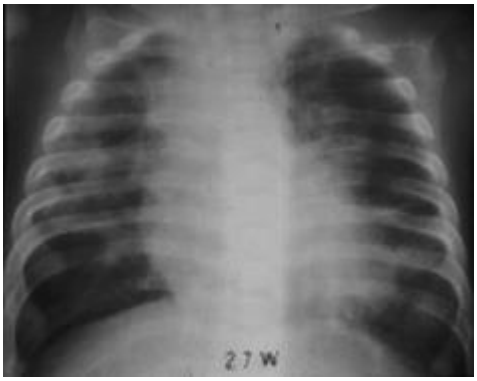
DDX:

- Cystic Adenomatoid Malformation - Usually has multiple cysts, unlike congenital lobar emphysema which has only one cyst.
- Diaphragmatic Hernia - Loops of bowel in thorax usually easily identified, can be confirmed via upper GI.
- Bronchial obstruction due to foreign body or mucous plug - Seen in older children
- Extrinsic obstruction from vascular structures
- Congenital lung cyst

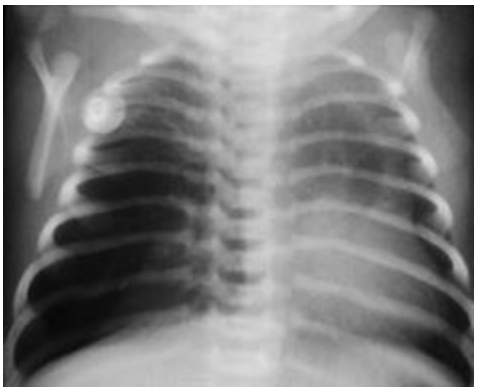

Photomicrograph demonstrates lung affected by congenital lobar emphysema



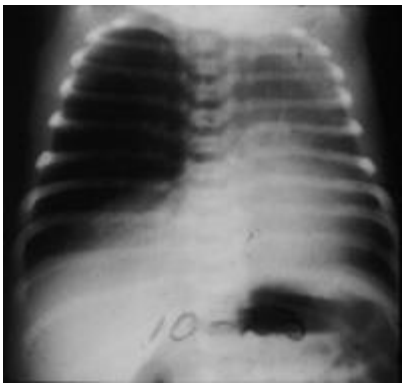
Supine chest radiograph showing a large cystic lucency in the left upper lobe



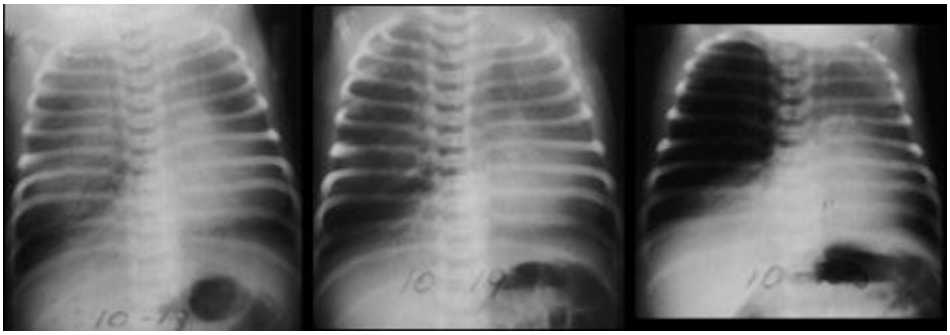
Supine chest radiograph obtained in the same patient at 7 months of age shows the small cystic lucencies to have coalesced into larger lucencies with interspersed fibrotic stranding. Increased lung volumes are also present.



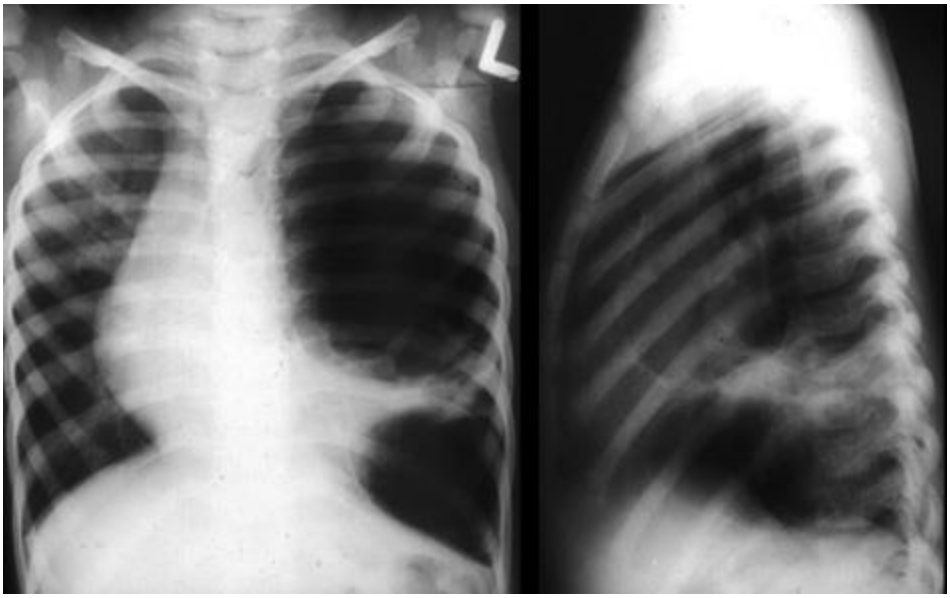
Supine chest radiograph showing a large cystic lucency in the right middle lobe



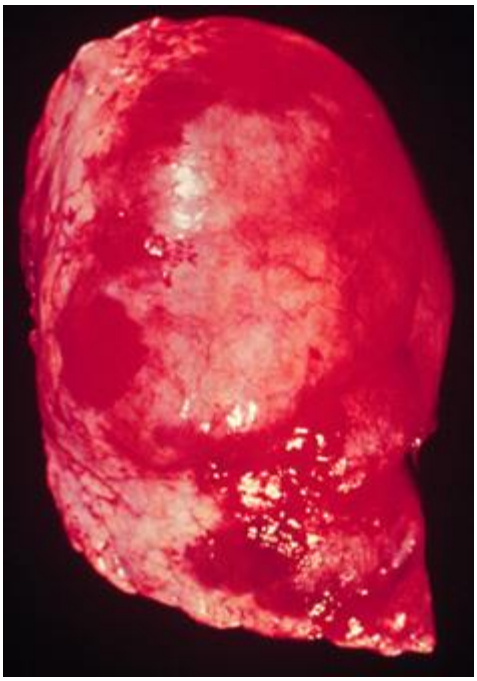
Supine chest radiograph showing a large cystic lucency in the right upper lobe.



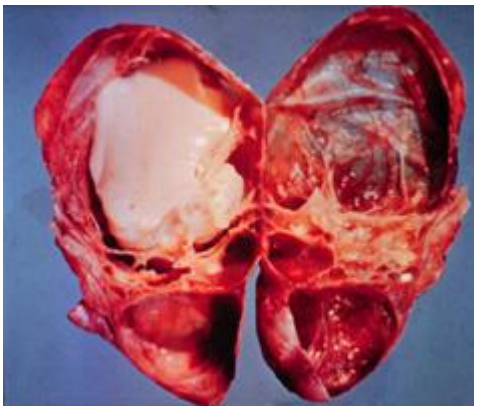
Series of three chest radiographs showing a congenital lobar emphysema presenting initially as a fluid-filled mass in the right upper lobe (left) that slowly clears of fluid (middle) and finally is overdistended with air (right).



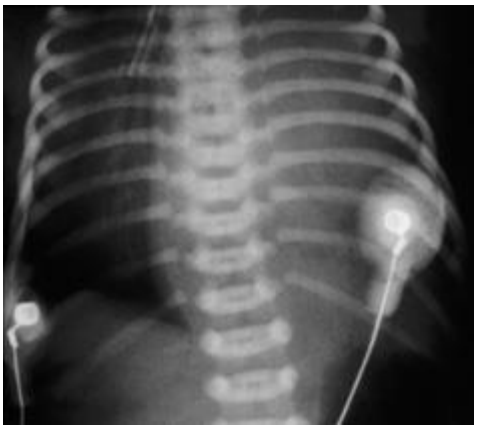
AP and lateral chest radiographs show a cystic mass in the left upper lobe.



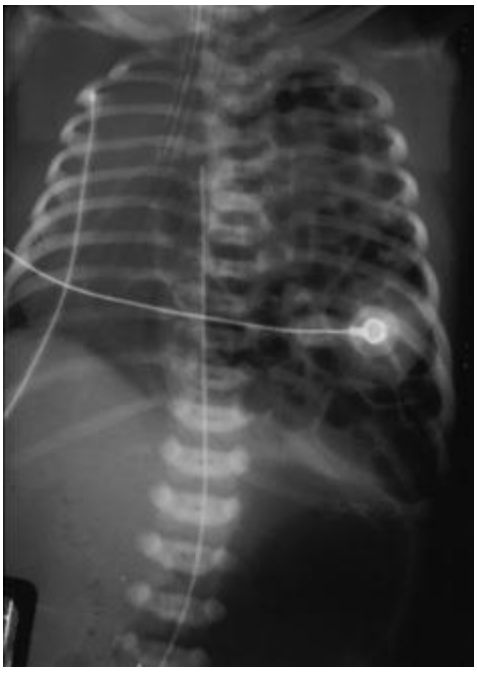
Gross photograph of the resected distended left upper lobe in the same patient.



Gross photograph of the sectioned left upper lobe in the same patient shows several large cysts.



Supine chest radiograph at one hour of life shows a solid mass in the left hemithorax causing mediastinal shift to the right, evidenced by the position of the endotracheal tube.



Supine chest radiograph at three hours of life in the same patient shows a multiseptated cystic mass in the left hemithorax causing mediastinal shift to the right.

Cystic Adenomatoid Malformation (CAM)
Clinical Presentation:
The most common presentation is acute respiratory distress in the newborn in the first few hours of life. Alternatively, it can present at several months or several years of age as recurrent pneumonias.

Etiology/Pathophysiology:
Congenital hamartomatous lesion of the lung.

Pathology:
There are 3 subtypes, all of which lack normal bronchial communications:

Type I - multiple large air or fluid filled cysts, usually greater than 2.0 cm in diameter

Type II - variably sized less bulky lesion with smaller cysts

Type III - bulky mass composed of multiple tiny, microscopic cysts resembling bronchi that involves the entire lobe. Adenomatous hyperplasia with an increase in terminal bronchiolar structures, as well as a polypoid arrangement of mucosal epithelium is seen.

Imaging Findings:
Seen with equal frequency in any lobe. Can rarely be bilateral.

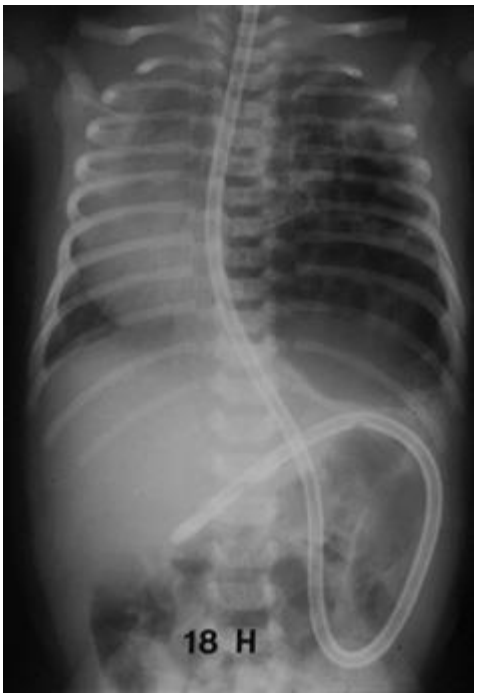
Type I - multiple large air or fluid filled cysts that produce a mediastinal shift and compression of adjacent lung. The most common type is Type I. It may have air fluid levels in its cysts. If infected, it may appear homogeneously opacified.

Type II - variable sized less bulky lesion with smaller cysts with less mediastinal shift and respiratory distress.

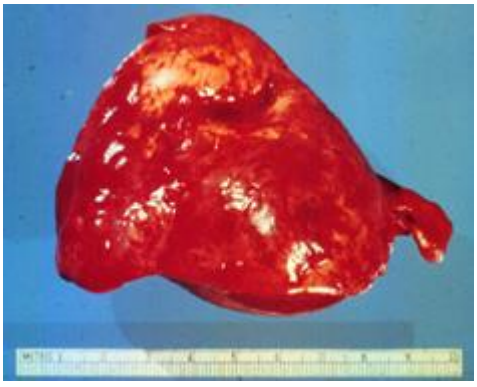
Type III - bulky radiographically solid mass composed of multiple tiny cysts that involve the entire lobe.

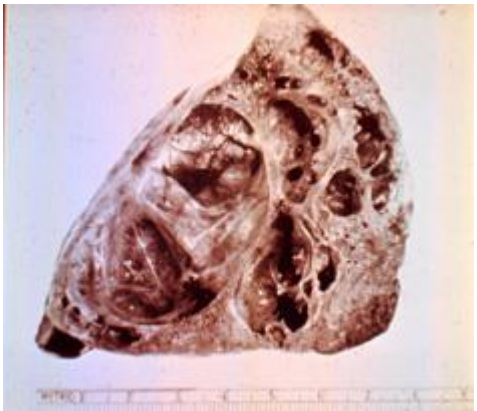
DDX:

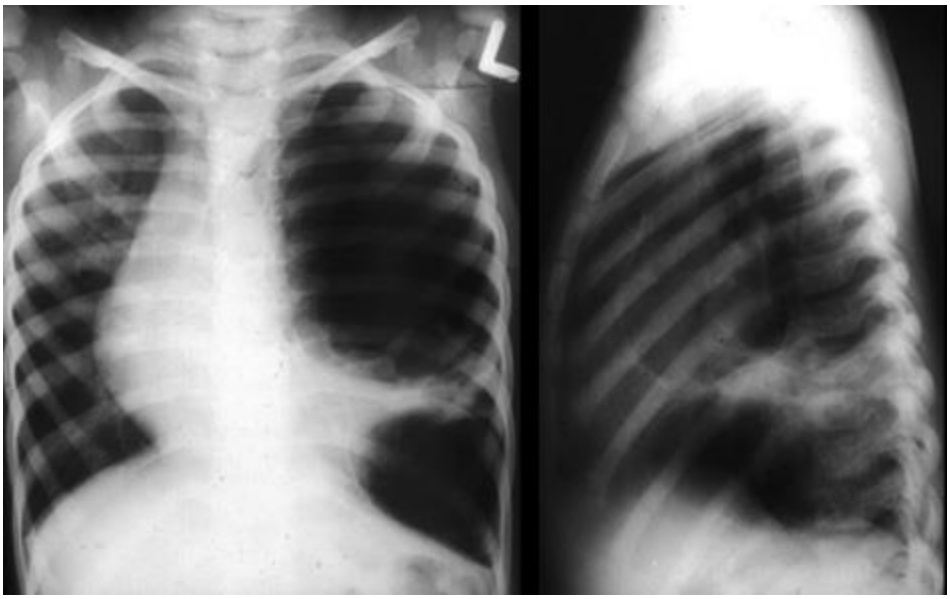
- Diaphragmatic hernia – the abdominal organs are in the chest cavity.
- CAM – abdominal organs are in a normal position
- Congenital lobar emphysema
- Sequestration
- Post infectious pneumatocele
- Foreign body, trachea - in an older child.



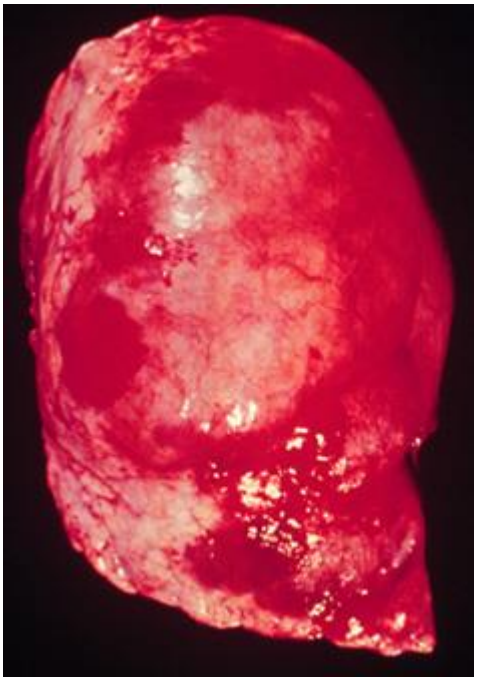
Supine chest radiograph showing a complex cystic mass in the left upper lobe.

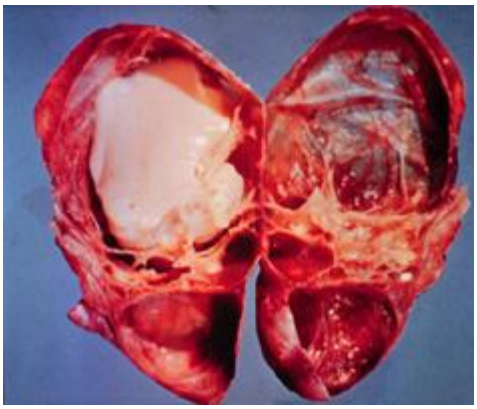

Gross photograph of the resected distended left upper lobe in the same patient.


Gross photograph of the sectioned left upper lobe in the same patient shows multiple large cysts.

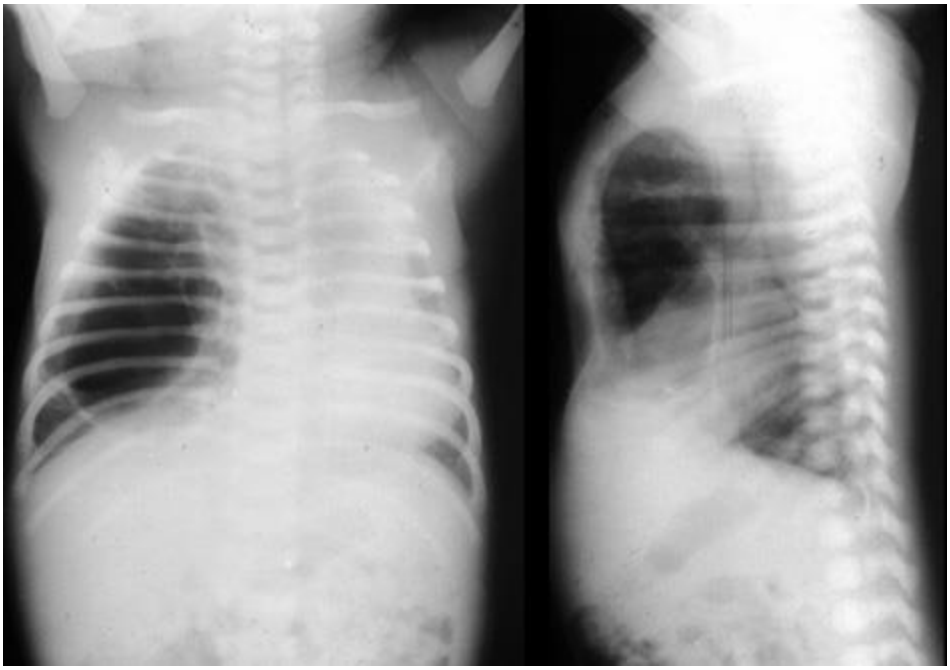


AP and lateral chest radiographs show a cystic mass in the left upper lobe.

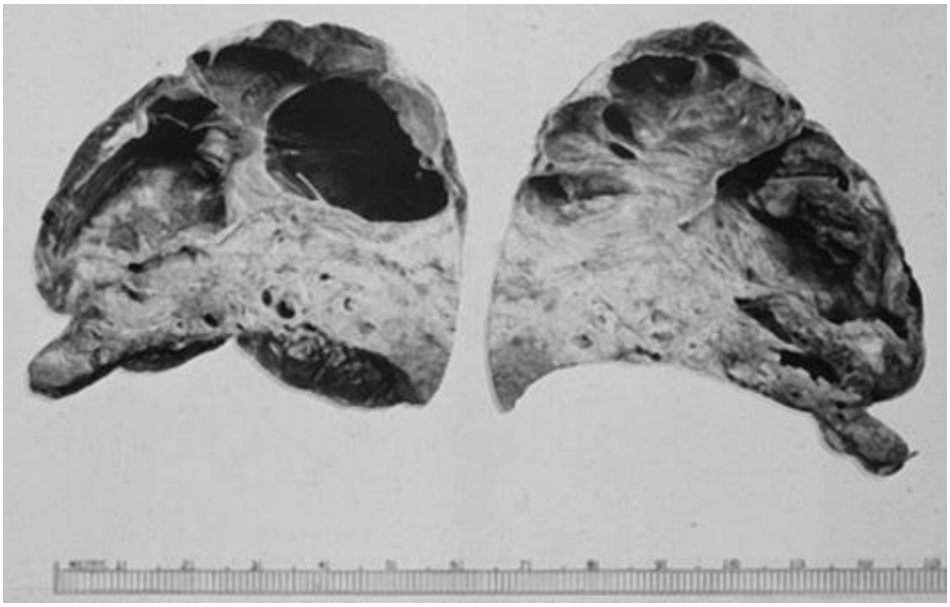

Gross photograph of the resected distended left upper lobe in the same patient.



Gross photograph of the sectioned left upper lobe in the same patient shows several large cysts.

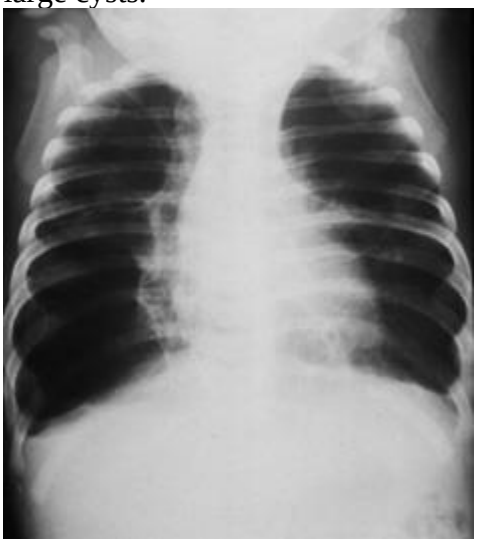


AP and lateral chest radiographs show a cystic mass in the right upper lobe.

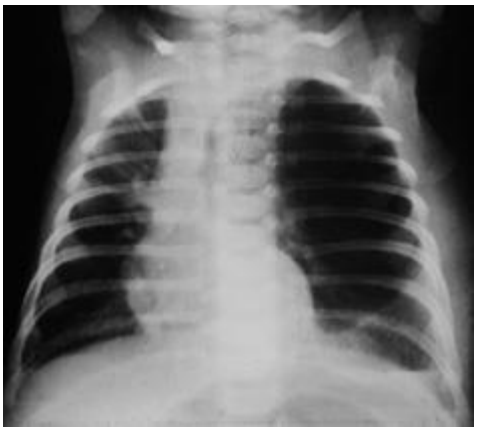


Gross photograph of the sectioned right lung in the same patient shows several large cysts

Autopsy gross photograph showing the abnormally enlarged left lung containing multiple large cysts.



AP chest radiograph shows cystic masses in the left and right lungs.


Supine chest radiograph showing a large cystic lucency in the left upper lobe.

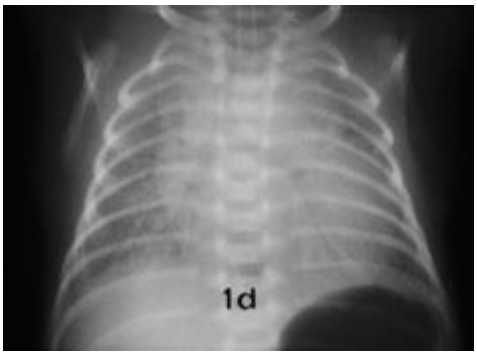
Patent Ductus Arteriosus (PDA)
Clinical Presentation:
Neonate who suddenly develops increased oxygen and ventilatory requirements.

Etiology/Pathophysiology:
The ductus arteriosus (DA) usually closes within 24 hours of birth and is obliterated anatomically in 1 - 8 weeks. The DA can reopen in a neonate with hypoxemia or severe pulmonary disease. Initially, postnatal pulmonary hypertension may prevent a left to right shunt from developing, but by a week after birth the physiologic decrease in the patient's pulmonary hypertension may allow a left to right shunt to develop through the PDA.

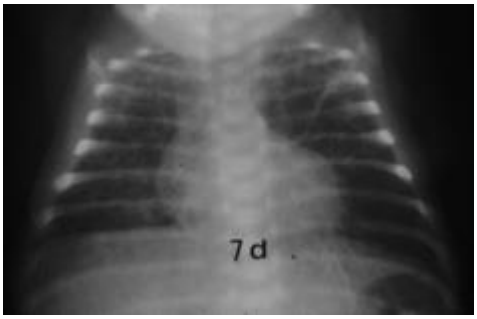
Pathology:
Not applicable

Imaging Findings:
Initially the CXR shows the underlying pulmonary disease. As the PDA opens, the CXR shows a slight increase in heart size and prominence of central pulmonary vessels which can progress. Pulmonary interstitial edema leading to some obscuring of vascular sharpness is usually seen secondary to left heart failure. An aortogram shows opacification of pulmonary arteries, veins and right atrium as well as the aorta. The definitive diagnosis is via echocardiogram.

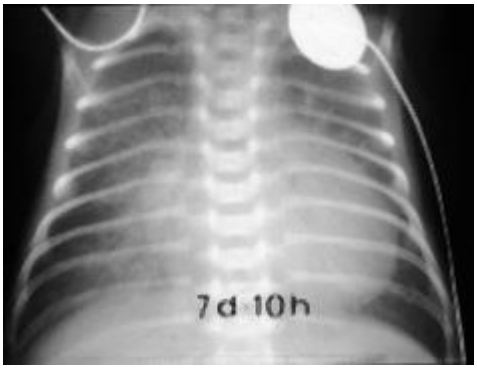
DDX:
Not applicable



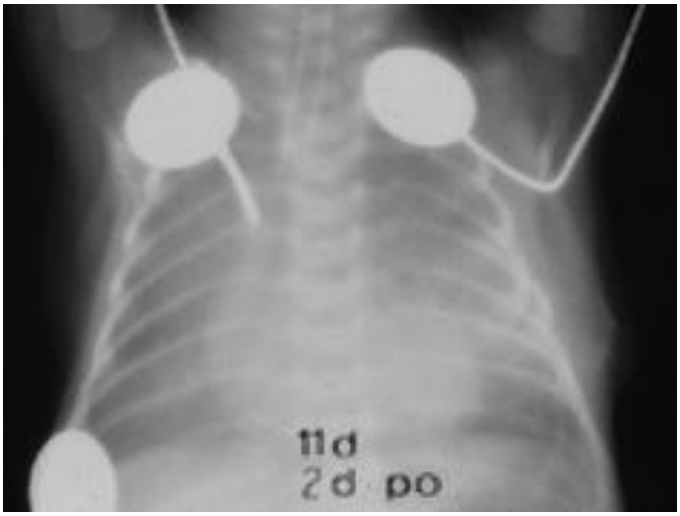
Supine radiograph on day one of life of a newborn with Hyaline Membrane Disease.



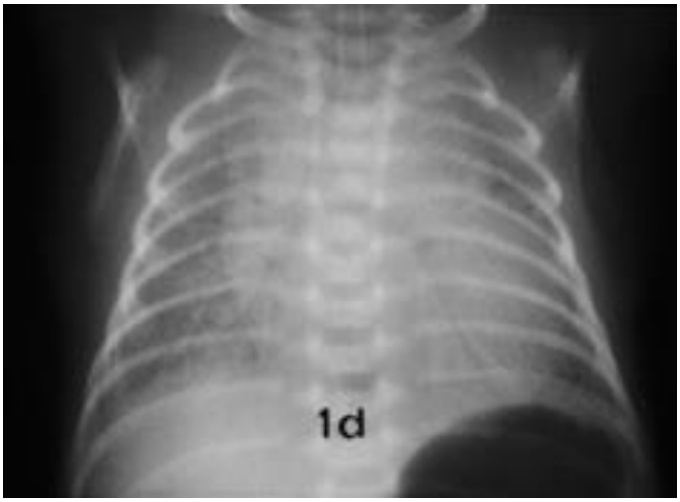
Supine radiograph on day seven of life in the same patient. The lungs are clearing of parenchymal disease.



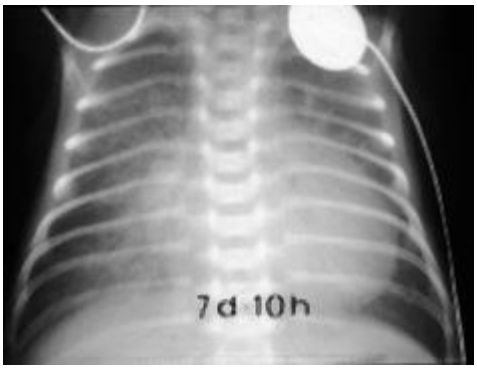
Supine radiograph on day eight of life in the same patient shows the heart enlarging and the pulmonary vasculature becoming very prominent as the ductus opens.



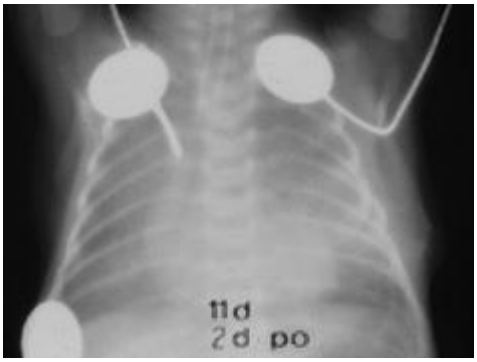
Supine radiograph on day eleven of life in the same patient with the ductus still open showing pulmonary edema.



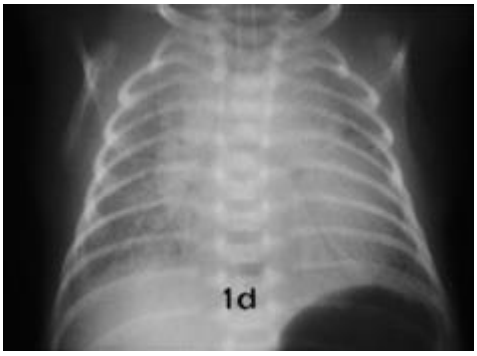
Supine radiograph on day one of life of a newborn with Hyaline Membrane Disease.



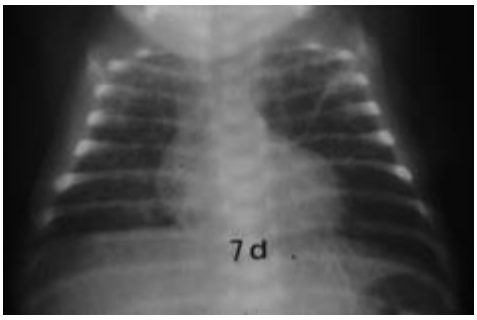
Supine radiograph on day eight of life in the same patient shows the heart enlarging and the pulmonary vasculature becoming very prominent as the ductus opens.



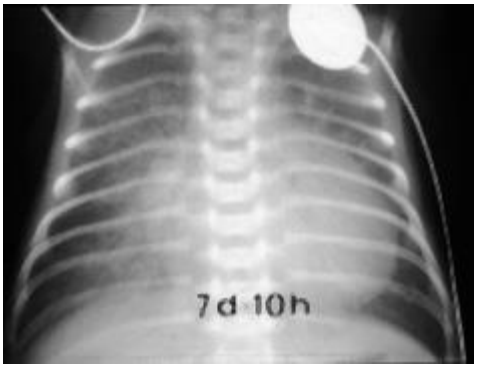
Supine radiograph on day eleven of life in the same patient with the ductus still open showing pulmonary edema.



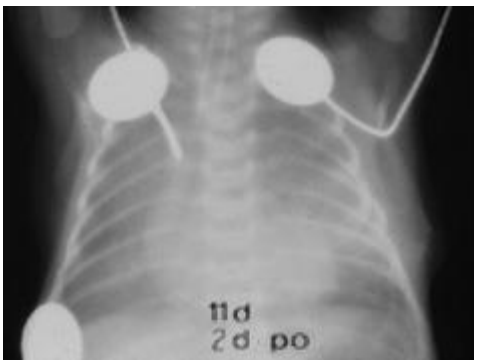
Supine radiograph on day one of life of a newborn with Hyaline Membrane Disease.



Supine radiograph on day seven of life in the same patient. The lungs are clearing of parenchymal disease.



Supine radiograph on day eight of life in the same patient shows the heart enlarging and the pulmonary vasculature becoming very prominent as the ductus opens.



Supine radiograph on day eleven of life in the same patient with the ductus still open showing pulmonary edema.

Resuscitation of Newborns

Since every baby born is potentially a case for resuscitation, the skills and knowledge required for proper resuscitation are likely the most important ones possessed by caregivers who work with newborns. As a result, it is strongly recommended that each practitioner complete the Neonatal Resuscitation program offered jointly by the American Academy of Pediatrics and the American Heart Association. The information on resuscitation offered in this CEU is intended as a review, not a comprehensive course on resuscitation.

The purpose of the neonatal resuscitation is to reverse asphyxia before irreparable damage occurs. A successful resuscitation can be divided into three steps, also known as the ABCs of Resuscitation:

A-- Establish an open airway

Position the infant

Suction the mouth, nose, and in some instances the trachea

If necessary, insert an ET tube to ensure an open airway

B-- Initiate breathing

Use tactile stimulation to initiate respirations

Use PPV when necessary, using either: bag and mask, or bag and ET tube

C-- Maintain circulation

Stimulate and maintain the circulation with chest compressions and/or medications

The resuscitation procedure begins immediately at the time of birth. The procedure should follow the AHA's most current standards, and as soon as the fetus's head is presented, When the head of the fetus is presented, suctioning of the nose and mouth should begin. Apgar scores are then recorded at both one and five-minute intervals (see Table 3).

Table 3. Resuscitation and Apgar scores.

Apgar Score	Resuscitation Efforts
8 to 10	Requires simple suctioning of airways, drying and warming.
5 to 7	Requires gentle stimulation. If there is a failure to respond in approximately 60 seconds, assisted ventilation is required with oxygen enriched mixture.
3 to 4	Generally, these infants will respond to bag-mask ventilation alone.
0 to 2	Requires cardiopulmonary resuscitation.

Medications that are used for resuscitation and that should be readily available in the delivery room include: sodium bicarbonate, isoproterenol, dextrose, epinephrine, calcium, Narcan, dopamine, atropine, and volume expanders. If endotracheal intubation is necessary, it should be performed gently but gently.

It is necessary to have endotracheal tubes available ranging in size from 2.5 to 4.0 mm. The following table provides guidelines for choosing the proper size uncuffed tube:

Tube Size (ID MM)	Neonate Weight	Gestational Age
2.5	<1000 g	<28 weeks
3.0	1000-2000 g	28-34 weeks
3.5	2000-3000 g	34-38 weeks
4.0	>3000 g	>38 weeks

Effective resuscitation of newborns greatly depends on how well the delivery room and its trained personnel are prepared for handling emergencies.

Common Respiratory Diseases of Infants and Children

Croup (Laryngotracheal bronchitis--LTB)

Croup is the name given to a group of inflammatory diseases that primarily affect infants and children. The most common manifestation of croup is laryngotracheitis, which is the result of a viral organism, with approximately 75% of all cases involving parainfluenza virus. The remaining 25% are caused by RSV, influenzae, and mycoplasma pneumonia.

The onset of laryngotracheitis is much like that of a common cold, complete with rhinorrhea, fever, cough, and upper airway congestion. The symptoms available for diagnosis of croup present much more slowly (usually 3-4 days) than is seen in epiglotitis. The patient awakens in the night with a tight, barky cough, and has upper airway stridor on inspiration and expiration. There is also a degree of distress relative to the amount of airway obstruction. A-P x-rays show the narrowing of the airway at the laryngeal level, and the trachea on the x-rays of these patients has been described as being shaped like an hourglass, a pencil, and a steeple.

Laryngotracheobronchitis is the name given to a bacterial superinfection of laryngotracheitis, and it involves the upper airway structures and then progresses to the bronchial airways and structures. Spasmodic croup is an apparent allergic response that results in the sudden onset of a barky cough, shortness of breath, and stridor. The patient with spasmodic croup is typically healthy, with no signs of upper respiratory infection. The distinguishing feature can be seen in some familial history of spasmodic croup.

The treatment of croup varies according to its severity, with mild cases being successfully monitored and treated at home with room humidifiers, hydration, and close observation. More serious signs such as retractions, increased respiratory rate or nasal flaring are indicators of the need for medical intervention. Since croup has a viral origin, nebulized racemic epinephrine (0.2 to 0.5 ml mixed with 2.5 ml saline) is used because it causes local vasoconstriction of the swollen subglottic tissues and reduces the edema.

If this treatment fails to eliminate the stridor, the patient needs to be hospitalized, with medication nebulizer treatments continued as needed every 1-2 hours to relieve the airway occlusion. Weaning treatments would be applied every 4-6 hours after symptoms subside. While croup is not usually considered life-threatening, any disease that causes swelling of the airway requires close monitoring for signs of worsening condition. Croup patients, therefore, should be monitored for breath sounds, respiratory rate, and the presence of retractions at four-hour intervals until airway swelling subsides.

Epiglottitis

This is an acute inflammatory disease of infants and children that affects not only the epiglottis, but also the surrounding aryepiglottic folds and arytenoid cartilages. While there are several viruses that can cause epiglottitis, it is generally considered to be bacterial in nature with most cases being caused by type b Haemophilus influenzae. Unlike LTB, epiglottitis **is** a life-threatening disease requiring prompt diagnosis and treatment.

There is a rapid onset with moderate to severe respiratory distress, sore throat, possibly high-pitched stridor with drooling, and difficulty in swallowing. Mortality from epiglottitis is due to blockage of the trachea by edematous, inflamed tissues leading to asphyxiation. The rapid onset of tracheal blockage makes intubation extremely difficult, and the probability of anoxic brain damage becomes more pronounced.

Because of its fulminant nature, the treatment of epiglottitis needs to be handled as an emergency. First priority should be given to the establishment of an airway, either by intubation or tracheostomy, until the swelling has subsided.

Following the establishment of an airway, treatment of the infection involves administration of antibiotics such as chloramphenicol and ampicillin. The epiglottic inflammation usually can be eliminated within 24-36 hours, at which time the patient may be extubated. If paralyzation is necessary, mechanical ventilation may be employed since the otherwise healthy lung requires very low pressures, rates, and FIO_2s to maintain ventilation.

Bronchiolitis

Acute bronchiolitis is a viral infection that leads to swelling, inflammation, and constriction in the bronchioles. While its consequences are gravest among infants less than six months, it presents potentially serious problems in children up to three years of age. The respiratory syncytial virus (RSV) is the primary causative agent, causing about 75% of all cases. RSV is highly contagious, and requires extreme care in hand washing and other precautions in order to prevent nosocomial outbreaks.

Clinically, the child with bronchiolitis begins with a typical upper airway infection complete with rhinorrhea, cough, and fever that lasts 2-3 days. With the onset of bronchiolar involvement, the cough worsens, and patients under 3 years of age begin showing signs of small airway obstruction and congestion. These signs include: expiratory wheeze, tachypnea, cyanosis in severe cases, low-grade fever, possible intercostal retractions, bilateral crepitant rales, and hyperinflation. Infants older than 3 years are rarely affected to this degree.

The treatment depends on the age of the infant and severity of symptoms. Infants less than 4 months of age may require hospitalization to control intake of fluids and potential apnea. The level of distress and blood gas values determine the next step of treatment for those infants hospitalized. Older infants or those with less severe distress, apnea, and worsening blood gas values are treated with Ribavirin because of its specific antiviral activity against RSV.

While Ribavirin is not needed by all bronchiolitis patients, infants considered at high-risk benefit greatly from its administration. The medication is delivered via a special small-particle aerosol generator (SPAG), with 12-18 hours a day of treatment for at least 3 and no more than 7 days. RCPs should take extreme care to avoid unintentionally inhaling any of the ribavirin being administered. Other treatments include aerosolized bronchodilators, Alpha-2A-interferon, immunoglobulin A, and RSV immune globulin.

Asthma

Asthma is briefly mentioned here because it is an airway disorder in which a patient's hyperactive airways spasm and constrict, swell, and pour secretions into the lumen in response to a variety of stimuli. It is the most common pediatric lung disease, ant the most frequent cause of hospitalization in the United States. About 1 in every 12 school-age children in the U.S. have asthma, and between 3-5% of the adult population has asthma, with 50% of them acquiring it prior to age 10.

While asthma's exact etiology is not known for sure, there are several factors that precipitate acute attacks, including:

- Allergens (molds, pollens)
- Indoor irritants (dusts, second hand smoke, animal danders)
- Outdoor irritants (air pollution, smoke)
- Viral infections
- Foods
- Aspirin and related medications
- Exercise
- Emotional reactions

Asthma can be classified on the basis of the types of agents which are causative:

- **Extrinsic** asthma is caused by external agents such as allergies to pollens, dust and various medications.

- **Intrinsic** asthma is caused by internal allergens such as emotional reactions, exercise, and respiratory tract infections.

Asthmatic episodes are usually characterized by the presence of coughs, wheezing, and dyspnea. They also are associated with decreased alveolar ventilation with severe bronchospasm, and prolonged expiration along with sibilant or sonorous rales.

Asthma attacks generally vary widely in severity from person to person, and episode to episode. Status asthmaticus involves prolonged periods of bronchospasm which are generally not responsive to treatment, and can even become life-threatening.

Asthma treatments require discovering what precipitates the patient's attacks, finding ways for avoiding those factors, and treating the effects of the attacks when they occur. Oxygen is nearly always indicated to treat for hypoxemia, keeping PaO_2 above 55 mm Hg. Bronchospasm requires administration of aerosolized medications, usually with bronchodilators. Corticosteroids are effective prophylactics for hyperreactivity. Mechanical ventilation and psychological counseling are often also necessary.

Despite advances in treatment protocols, asthma continues to be a significant cause of respiratory distress among pediatric populations. Drug treatment is mainly focused on preventing the release of inflammatory mediators, reversing bronchospasms, and reducing

inflammation in the airways. There continue to be promising research findings focusing on new longer acting medications which are designed to prevent or slow the onset of asthma.

Miscellaneous Neonate/Pediatric Care Issues

There are a variety of other pulmonary-related problems affecting the neonatal/pediatric populations, and requiring the attention of health care professionals, including:

Aspiration Syndromes: Since infants are seemingly obsessed with putting objects of all sorts into their little mouths, they are at high-risk of having their narrow airways accidentally obstructed. Aspiration of gastric contents is commonly the result of reflux in neonates, and the pathologic result of aspiration is airtrapping and tissue damage secondary to hydrocarbon aspiration. The trapping of air behind the object placed in the infant's mouth causes hyperexpansion of the lung, reduced ventilation, and possible pneumothoraces. The aspiration of hydrocarbons can cause toxic damage to the epithelial lining of the lung.

Treatment of an aspirated foreign object primarily involves actions aimed at removing the object. Chest physiotherapy often helps dislodge the object, while more severe cases may require the use of a bronchoscope to retrieve it.

Smoke Inhalation: Household fires give off many acids and aldehydes in their smoke, and inhalation of these noxious fumes can cause serious toxicities in the blood and tissues. Neonates, whose pulmonary systems are delicate even under normal conditions, are at high-risk for serious injury. Treatment of patients for smoke inhalation and carbon monoxide poisoning involves the immediate application of 100% oxygen, preferably under pressure.

The victims of smoke inhalation are also at risk for development of RDS, making it necessary for the caregivers to closely monitor their status. Antibiotics are given to combat lung infections, nebulized bronchodilators are helpful in maintaining the patency of the airways, and mechanical ventilation is required for comatose patients in order to establish an airway and administer oxygen.

Sudden Infant Death Syndrome (SIDS): While SIDS accounts for the highest number of deaths among infants under a year old, little is known regarding its etiology. The common event in all SIDS deaths is a quiet cessation of breathing during sleep. In fact, the diagnosis of SIDS is not made until an autopsy has been performed. In 1992, the American Academy of Pediatrics recommended that infants not be placed in the prone position to sleep because of association with SIDS.

While no exact relationship between the prone position and SIDS has been established, the reduction in the number of infants sleeping prone has recently been cited as a factor in the decline in SIDS-related deaths. Other factors that have been identified as elevating the risk for SIDS among infants include:

- the use of natural fiber mattresses

- swaddling
- recent illness
- the use of heating in the bedroom
- low birth weight
- prematurity
- a five minute Apgar score under 7
- low maternal age and education level
- multiple births
- maternal smoking ·
- male gender
- black race

Even with a knowledge of the various risk factors, it remains impossible to identify those infants who will die of SIDS, and the incidence remains at about 2 out of every 1,000 births.

Cystic Fibrosis (Mucoviscidosis)

CF is a chronic pulmonary disease that is characterized by tenacious mucus production which causes obstruction, leading to hyperinflation, an increased chest diameter (barrel chest), atelectasis, and infection.

A majority of patients with CF are diagnosed in childhood, but a few are not diagnosed until their mid to late teens. The most reliable diagnostic indicator of CF is the determination of abnormally high sweat chloride levels. Other symptoms associated with CF include: a chronic paroxysmal cough, cyanosis, digital clubbing, atelectasis, hemoptysis, hypoxemia, hypercapnia, and pneumothorax.

Until a cure is found for CF, treatment is primarily aimed at improving long-term survival and improving the quality of life. Protocols call for treating the pulmonary, dietary and psychological aspects of the disease. Therapies available for effectively treating CF patients include administration of mists, aerosols, positive-pressure, physiotherapy, antibiotics, and oxygen.

One of the issues associated with neonatal care is that of ***access.*** Not all neonates have equal access to the specialized care units we have discussed. Therefore, we offering for your review:

Access to Neonatal Intensive Care

Taken from: The Future of Children Vol. 5 No. 1 Spring 1995

Abstract

The birth of a high-risk infant is still a relatively rare, not totally predictable event; and the management of high-risk newborns requires highly skilled personnel and sophisticated technology. In the early days of neonatal intensive care, scarce resources led to regionalized systems of neonatal and, later, perinatal services, generally based on voluntary agreements but sometimes reinforced by planning legislation. At present, a vastly increased pool of skilled professionals and technical resources is available in the context of a rapidly changing medical care system characterized by intense competition, coalescence of services under large managed care plans, and substantial cost pressures. The evidence suggests that, in many areas, these forces have led to the dismantling of regional networks; however, the full potential for these changes to hinder or facilitate access to neonatal intensive care remains to be assessed.

The issue of access to special neonatal hospital care emerged only in the twentieth century. Prior to the turn of the century, most births occurred in the home setting, and the limited care repertoire for ill newborns could likewise be provided in that setting. Indeed, it was only in the late 1800s that care of infants less than two years of age was wrested from obstetricians and placed in the domain of pediatricians.1

In an era when at least 10% of all infants died before their first birthday, the fate of an infant born smaller than average was considered particularly grim and beyond the scope of most medical care. Attempts to improve the outcomes of small babies by providing nutrition and warmth were slow in evolving. Not all such efforts were restricted to medical settings, and popularization of the special care for small newborns was accomplished through exhibits at world's fairs and other such currently unlikely settings.2

In the first half of this century, the place of delivery shifted from home to hospital with the growing realization that hospital deliveries could reduce the toll of the complications of birth for women. However, birth in a hospital still offered little survival advantage to the low birth weight infant because not much could be done to manage the respiratory distress or hyaline membrane disease that reflected pulmonary immaturity. Despite this lack of success, transport services were organized in some cities, notably Chicago, to bring sick neonates born at home into the hospital for care.2

After World War II, many of the environmental causes of infant mortality past the first month of life had been controlled or reduced by sanitation, immunizations, and antibiotics. Deaths in the neonatal period began to dominate the rates of infant mortality with low birth weight infants accounting for the majority of these neonatal deaths.3 Thus, the problems of the low birth weight newborn received renewed attention. Until the late 1960s, however, the track record of infant special care units in improving infant outcomes was undistinguished.

Uncritical implementation of interventions poorly grounded in science led to practices that are now seen as useless and silly at best and, in some instances, extremely harmful.4 Not only were individual interventions of limited utility, the whole enterprise of special infant care was questionable as neonatal mortality rates remained unchanged for more than 15 years.3

In the late 1960s, however, basic scientific inquiry into the problems of the newborn began to bear fruit in empirically grounded and efficacious interventions. In particular, critical observations about hyaline membrane disease, the major cause of death among premature infants, led to more effective strategies for managing respiratory problems.5

While the capability to provide effective, exogenous surfactant, the missing chemical, would come much later (see the article by Horbar and Lucey in this journal issue), basic scientific discoveries led to more efficacious mechanical ventilation techniques.6 To underscore the recentness of this success, it should be realized that President Kennedy's son died of hyaline membrane disease in 1963, and the first report of this technique was not published until 1971.6

With the advent of more effective management of neonatal problems in the 1970s, the issue of assuring prompt access to infant care units emerged. At this time, access was severely limited by the small number of centers offering specialized newborn services, the few trained specialists, and the related complexity of care. The solution appeared to be region wide organization of referrals to the small number of available centers.

Regionalization

The concept of the regionalization of health services is not new. The first articulation of this concept in English was presented to the British Parliament in 1920 in the Report of the Consultative Council on Medical and Allied Services, generally referred to as the Dawson Report. Regionalization was considered to include an organized and integrated hierarchical array of medical services, both preventive and curative. At the base was primary care, consisting of those services most frequently used for common and/or simple health problems. Uncommon or more complex problems were referred to secondary or consultative care, and ultimately to tertiary, usually university-based services.7 Explicit in this model was a balance between ready access to care and the efficient deployment of resources at a population level.7

During the World War II era in the United States, several states and other jurisdictions experimented with regional plans.7 The first attempt to incorporate regional planning nationally occurred in the Hill-Burton Act (Public Law 79-725) in 1946 for hospital construction, and the Heart Disease, Cancer and Stroke Amendments of 1965 (Public Law 89-239) which authorized grants to establish Regional Medical Programs (RMPs) to facilitate access to diagnostic and therapeutic advances in the specified conditions. The voluntary nature of the arrangements, the lack of a clear mission, and the categorical nature of the planning effort limited their success.8-10

Subsequent planning legislation--the Comprehensive Health Planning and Public Health Service Amendments of 1966 and the National Health Planning and Resources

Development Act of 1974--did not emphasize regionalization as the model of organization.8, 10 However, they did encourage assessment of health services needs at the state and regional levels and the development of plans for increasing access to care. Further, some of the regulatory authority for approving major capital expenditures could be used to curtail unneeded expansion of expensive forms of health care such as duplicative intensive care facilities. In some areas, health professionals forged effective alliances with planning efforts to foster regionalized neonatal care plans.11 However, the general flaws built into planning legislation precluded universal effectiveness.12 In the wake of the failure of national planning efforts, alternative approaches emerged to the organization of health services generally.13

Regionalization and NICU Care

In the absence of strong national planning for all health services, increasing access to neonatal care relied on voluntary efforts led by health professionals, who noted the experience of a few major centers, and on a more general perception that neonatal care was becoming beneficial. In 1973, Schlesinger cited the improved survival documented in certain centers and recommended the models in Wisconsin, the Province of Quebec, and Arizona for moving sick neonates to special care.14 The specific rationale for such organizations was the dearth of physicians and nurses skilled in the new techniques and other support services as delineated carefully by Dwyer15 and endorsed by the American Medical Association House of Delegates.11

The major elements of such regional programs included the structure and function of neonatal intensive care units (NICUs), the formalization of arrangements with referring obstetric units, and transportation systems for sick neonates.11, 14,15 In this early view, regionalization essentially involved interhospital transfer of infants from community hospitals to the medical center and some reverse outreach educational services to the community hospitals on stabilization of the acutely ill newborn. In some instances, health professionals were able to use federal planning legislation to activate these regionalization efforts;11 in other instances, more informal arrangements among groups of hospitals occurred.

The regionalization of neonatal care represented only a small segment of regionalized services as envisioned by the Dawson model and, moreover, provided little threat to existing care arrangements. The mother remained in the care of her obstetrician. The newborn usually had no primary pediatrician. The limited number of highly trained NICU physicians and nurses precluded rapid increase in NICUs at the community level. Even among insured couples, coverage for expensive care for sick newborns might not be adequate, and thus, the transfer of such care provided little financial threat to the referring hospitals.

Evidence of the effectiveness of such regional models of neonatal intensive care is sparse. Arguments for its importance rest largely on decreases in neonatal mortality rates after the introduction of NICU care in geographically defined regions where it was not previously available14,16,17 and improvements in survival for infants with hyaline membrane disease among those managed through a formal referral system as compared with those managed through other arrangements.18

Regionalization and Perinatal Care

Evidence also accumulated that outcomes could be improved further by earlier identification of high-risk pregnancies and referral to tertiary perinatal centers before delivery. For example, very low birth weight infants born in hospitals with NICUs did better than those not born in such centers,19-21 even accounting for the availability of neonatal transfer.22 Additional evidence was seen in the more favorable outcomes of infants whose mothers were transported to perinatal centers before delivery compared with infants transported after birth.23-25

In response, the notion of regionalized care was expanded to include the prenatal period. Such regional systems would address the needs of all pregnant women in a population through systematic risk assessment and referral to the appropriate consultants when problems emerged. These systems would also assure community providers ready access to consultation, special laboratory facilities, and ongoing education. The intent was to improve perinatal care at all levels for a defined region based on the experience of several programs.26-28 The evolving concept of perinatal regionalization thereby broadened to include a large array of services (see Table 1) with a fully integrated system of consultation, referral, and transport, as advocated in several commentaries and editorials,11,27,29 and codified by a committee of the major pediatric, obstetric, and nursing organizations in a March of Dimes-sponsored publication entitled Toward Improving the Outcome of Pregnancy.30 This manifesto specified in detail the services required for level 1, 2, or 3 perinatal care as well as guidelines for delivery volume and/or geographic necessity for each level of care.

In contrast to the relatively sparse data on neonatal systems, more substantial evidence on the effectiveness of these comprehensive perinatal systems is available. To assess the effect of regionalization on previously less-well-organized areas, the Robert Wood Johnson Foundation conducted an eight-site, five-year demonstration program. The evaluation of that program revealed that regionalization occurred and that the rapidity of regionalization was closely correlated with the rate of decline in neonatal mortality, as measured by the proportion of low and very low birth weight infants born in tertiary centers. The sharp decreases in neonatal mortality were not offset by increases in infant morbidity. Unfortunately, the national movement toward regionalization had become so widespread that a specific effect of the demonstration program could not be detected when compared with the progress in similar control regions not funded by the foundation.31 Another Robert Wood Johnson Foundation program, aimed at improving care in 10 rural sites by fostering improved linkages with tertiary centers, also resulted in improved neonatal outcomes.32 In addition, reports accumulated on the success of individual programs and on specific aspects of regionalized programs.33-39

While clearly improving infant outcomes, the regional coordination of services and transfer of patients was not without adverse effects. These included:

- initial separation of the newborn from its family and the resulting anxiety and, in some instances, grief experienced by one or both parents,40,41
- prolonged neonatal hospital stays and the financial and emotional costs associated with frequent visiting,42

- disruption of established patient-physician relationships,43
- loss of local medical services,44
- disruption of continuity of care and parent-provider relationships through retrotransport to community hospitals to alleviate NICU crowding45 even though this is a cost-effective strategy for convalescent care.46,47

Despite these disadvantages, regionalization occurred, reinforced by the general impetus to central planning and scarcity of resources. Other reinforcements included more reliable funding through both public and private payers48 and, perhaps, the malpractice crises which made practitioners more cautious in the management of high-risk obstetric patients.49

The Current Era

In the early 1980s, changes in the availability of resources and cost containment strategies began to place stresses on regional programs. The current status is summarized in the following section.

Although state planning agencies and health departments could provide reinforcement to regionalization through funding and certification of need authorization, regional perinatal care could best be described as voluntary associations among hospitals and providers. In the 1970s these voluntary associations were reinforced by the impetus toward centralized planning noted above, the scarcity of skilled perinatal and neonatal personnel, the complexity and expense of well-equipped units, more reliable funding through public and private payers, and perhaps also the malpractice crisis. Beginning in the early 1980s, even as the evidence of effectiveness began to accumulate, other forces placed stress on regional programs.

Expansion of Perinatal and Neonatal Intensive Care

During the 1970s and 1980s, both the number of specialized physicians, or neonatologists, and the number of NICUs and NICU beds increased dramatically. This change in availability of NICU care has received little empirical examination, in part because of the difficulty of tracking the information. This dearth of information has been remedied with a directory of neonatologists prepared under the sponsorship of the Section on Perinatal Pediatrics of the American Academy of Pediatrics.

While data are still being accumulated, preliminary information reveals that, overall, about 3,000 neonatologists are active in the United States, or about 7.4 per 10,000 live births. In 1994, about 500 hospitals reported having a NICU for a total of about 12,000 NICU beds, or 3 per 1,000 live births.50 The number of neonatologists per 10,000 live births is at least twice that of several other industrialized countries51 and exceeds the upper bound estimate calculated by the American Academy of Pediatrics in 1985 of 5 per 10,000 live births.52 However, the rate of very low weight births has been increasing, and the birth weight at which survival is now more routine is decreasing. These trends indicate that the need for neonatologists may exceed 1985 estimates. To what extent the current status represents an excess needs to be examined further.

The availability of NICU beds is also difficult to assess. The reported number of about 3 per 1,000 live births exceeds the estimated need of one NICU bed per 1,000 live births. However, it is within the overall estimates of 5 to 6 total beds per 1,000 live births, which includes intermediate or convalescent beds.53-55 While these preliminary data are subject to some error and the shift in care patterns may indicate some increased need for resources over prior estimates, NICU care is no longer a scarce resource nationally, although access to care may not be uniform for all groups because of geographic factors and some of the financing issues discussed below.

Financing Neonatal Care

The growth of NICUs has occurred during an era when the financing of obstetric and newborn services was itself in rapid flux. Financing has become a dominant factor in determining both availability and access because of the exceedingly high cost of neonatal intensive care and the impact of inadequate reimbursement on regional neonatal services.

Private Insurance

Early studies of NICU care56 indicated incomplete private insurance coverage with a large pool of uncompensated care. More recent data reveal that, even for privately insured patients, most plans do not begin to cover the full costs of maternity care, and many women are uninsured. For those eligible, services may be covered by Medicaid, but reimbursement is often at considerably lower rates than are typical of private insurance.48 Thus, a substantial portion of NICU care remains uncompensated, and the costs of this care are shifted to other payers.48,57 Strong evidence indicates that uninsured newborns receive less care than those privately insured or on Medicaid, even when the numbers are adjusted for illness severity.58

Absent national health care reform, the current changes in private insurance coverage suggest that the problems of financing neonatal intensive care are likely to grow worse. Employed young couples are most likely to lack employer-based insurance because they have entry level jobs or work in small businesses. Even if the employed parent is covered, dependency coverage is decreasing. The result is that private insurance coverage for children has declined substantially.59 What coverage does exist may be exhausted by the catastrophic costs of NICU admission, as such care has been demonstrated to account for a substantial number of all episodes of catastrophic illness.60,61

Public Financing

Some portion of this financial burden may be offset by recent major expansions of public financing of perinatal care. First, the high cost of neonatal intensive care can result in rapid spend-down to medically needy status for Medicaid coverage, even for the insured population. Second, many states have expanded medical assistance coverage of pregnant women as a means of ensuring adequate prenatal care, and this coverage is automatically extended to their newborns.62 Likewise, recent changes in criteria for supplemental Social Security may provide support--both income and access to Medicaid--for children deemed disabled.63

Publicly financed health care is a fragile and vulnerable source of support, however. Eligibility requirements are based on income and vary by state. With the recent downturn in the economy, many states face severe economic constraints in providing for Medicaid patients. While the majority of Medicaid dollars go to support nursing home care for the elderly, few politicians are willing to face such a powerful lobby. Thus, attempts to reduce Medicaid costs focus on the smaller fraction going to poor women and children. Because neonatal intensive care represents a significant portion of hospital care for children, it has become a target for reducing Medicaid costs, as indicated by the recent Oregon waiver proposal that set birth weight limits for initiating intensive care.

Prospective Payment Systems

The shift to case-based reimbursement under Medicare does not directly affect newborns. However, the adoption of diagnosis-related groups (DRGs) by Medical Assistance (Medicaid) in several states has produced serious problems because the original neonatal DRGs were seriously flawed.64-67 Specifically, the original DRGs reflected only the experience of community-based hospitals and the limited data available in the small sample of hospitals used to derive the DRGs.

There are several problems related to the use of DRGs as the basis for reimbursement of NICU care. First, these DRGs performed poorly in explaining resource use because they lacked birth weight, a key predictor of cost. Second, for highly regionalized care such as NICUs, all outliers were concentrated in a few centers. A third serious flaw was the disincentive for back-transfer. While DRGs were adopted in only a few states, the threat of their use by other states and by private insurers sparked great concern among regional centers. This concern prompted the National Association of Children's Hospitals and Related Institutions (NACHRI) to develop pediatric modified DRGs in which the original seven DRGs were expanded to 46 categories, determined by birth weight and need for surgery and/or mechanical ventilation.68 Although the modified DRGs are an enormous improvement, they have not been broadly adopted by payers. Thus, the impact of case-based reimbursement in its more refined form remains to be determined. Other pressures on the arrangements of perinatal services come from the massive changes in organization that are being seen generally in health care. In particular, these changes involve rapid emergence of managed care and intense competition among providers to secure plan contracts.

Organization of Services

Managed Care

Managed care plans have expanded from the more traditional health maintenance organization (HMO) to include a broader array of service and financial arrangements. Significant elements of managed care plans include arrangements with selected care providers, utilization review, and strong financial incentives for members to use selected providers and to follow designated procedures.69 The major strategy to reduce costs is a reduction in hospital admissions, as well as more prudent purchasing of lower cost or discounted services. The extent to which such plans do reduce costs, the implications of

more active management of clinical care, and the relative advantages of various models remain open to question.70

Neonatal intensive care admissions are virtually all emergent so it may be difficult to reduce them. Where managed care may influence access to NICU services is its ability to channel obstetric and newborn patients to specific facilities and providers and, thereby, to have a major effect on reinforcing or weakening regionalized care (see Table 2). A major concern is that managed care organizations will direct all obstetric care into lower level hospitals because of their significantly lower operating cost, despite the strong evidence of better outcomes in higher level facilities. The increasing market penetration by managed care in many regions indicates that this will be an important factor in coming decades.

Competition

In view of the changes described above, both insurance plans and providers are now competing heavily for patients. Competition is particularly keen for obstetric patients because hospitals recognize that women make most of the medical care decisions and that a positive birth experience may ensure family loyalty to a particular institution. While competition may drive individual hospitals to upgrade their services, it has also spurred the rapid proliferation of NICUs, particularly for suburban areas where competition for well-insured patients is strongest. These NICUs are established to provide a sense of security in the availability of intensive care if needed but are often small and, therefore, inherently inefficient, although they may operate profitably by attracting a profitable case mix of insured patients. The loss of these patients has further eroded the financial viability of regional centers57 and has begun to redefine them as level 4, or "quaternary," centers, receiving a declining number of only the smallest infants or those with complex multispecialty needs. This reduced and very expensive population base cannot support the overhead costs of sustaining regional organization including outreach education, consultation, transport, and infant follow-up. The competition among hospitals has also curtailed the cooperative arrangements underlying regional perinatal organizations. Furthermore, the dispersion of patients into many small NICUs will significantly hinder research, medical education, and outcomes evaluation (see Table 3). While competition has also tended to sustain inefficient small obstetric services in suburban markets to draw the loyalty of women clients, in both inner cities and rural areas, competition may lead to closure of community obstetric services, thereby reducing access to prenatal care.

Deregionalization

The aggregate effect of these changes in manpower, facilities, technology diffusion, financing, competition, and health care organization has been a cessation or even reversal of the general trend toward regionalization. This deregionalization has been noted in several studies. The National Perinatal Information Center studied six regions using in-depth interviews with hospital executives, neonatologists, and obstetricians. While there was great variation from region to region, most agreed there was a general deterioration in perinatal regionalization, that competition had replaced cooperation, and that traditional levels of care were blurring as all facilities escalated the level of care provided.

These trends also occurred in many community hospitals where the volume of patients was inadequate to maintain professional skills or provide a cost-effective revenue base.71 another study of the Hartford region identified similar concerns, centered on the balance between competition and cooperation. It noted the potential for dispersing the NICU population into smaller competing NICUs versus a single unresponsive monopoly on regionalized services.72 Similar concerns have been voiced by others who have called for negotiated cooperation agreements in place of traditional regionalization schemes.73 Interestingly, deregionalization following National Health Service reforms in the United Kingdom has also produced adverse effects on perinatal care.74 These issues provoked the Committee on Perinatal Health to reconvene to formulate an agenda for regionalization in the 1990s and beyond.75 They recommended improvements in health education, prenatal care, system organization, access to inpatient and specialty services, documentation and evaluation, and adequate financing of perinatal care.

The reality of perinatal regionalization is that market forces are forcing hospital closures, consolidations, and mergers. Patients are increasingly channeled by payer-provider negotiations rather than historical regional designations. However, the long-term outcome may not be bad. Consolidated obstetric services are inherently safer and more efficient. Regionalized perinatal care is also inherently cost effective, utilizing graded levels of care according to need. The development of highly integrated vertical networks that eliminate redundant services may actually strengthen the regionalization of perinatal care. This level of integration, however, may not be achieved in many regions, and even where it is, the transition may cause serious dislocations for perinatal care.

Conclusion and Recommendations

The rapid proliferation of trained professionals and the diffusion of technology in a context of major organizational change and new financial pressures would appear to signal the unraveling of early regionalized models of delivering care. Little empirical evidence exists, however, to estimate the effect of these changes. Moreover, changes in access to NICU care in response to the various pressures noted above are unlikely to be uniform and will depend on demographics, geography, malpractice experience, and state regulatory environments. Several courses of action are recommended to assure access to appropriate levels of neonatal care.

Access and Equity

The first of these recommendations is for ongoing surveillance of access to NICU care through vital statistics and other record systems. Abundant evidence indicates that higher levels of care are associated with better outcomes.21,31,32,75 Shifts in births to lower level hospitals for cost reasons may have a significant impact on overall outcomes. Competition will close not only inefficient services but also poorly reimbursed ones. Hospitals caring for poor and underinsured populations will be stressed regardless of quality or efficiency. To the extent efficiency is also achieved through consolidation of existing facilities, the burden of seeking alternative services may be carried disproportionately by disadvantaged and/or rural communities. Thus, relevant public health and professional organizations should be routinely assessing births and birth-weight-adjusted mortality by hospital of delivery for the newborn population as a whole and for high- risk subgroups.

Quality of Care

The second recommendation is for rapid expansion in rigorous examination of the quality of NICU care. Even among designated tertiary hospitals, there have been instances where quality of NICU care has been questioned,76,77 and such quality differences in the past have been more likely to occur in areas serving largely minority populations.77 However, variations also occur in units where the level of practice is assumed to be high,78,79 suggesting that some portion of the variation may reflect practice patterns, as well as differences in the population that is served. The proliferation of small NICUs has raised additional questions about the extent to which such small units will have sufficient numbers of patients to maintain the skills of providers.77-80

To preserve quality in this rapidly changing health care environment, it is necessary first to measure it. This seemingly simple task has not yet been achieved for perinatal care. It is vital to develop comprehensive case mix adjustment tools77,81 and to pursue comparative outcomes research.78,79 Incorporated into these quality assessments must be explicit recognition of costs. The third-party payers will demand quality at the lowest price.

Adequate Reimbursement

Perinatal and neonatal services remain underfinanced even among populations with insurance. In the current competitive atmosphere, hospitals will be unable to subsidize these services. Besides the support of direct medical services, however, adequate support of other services formerly provided in regionalized networks is necessary. Particularly vulnerable are consultation services, outreach education, assessment of outcomes among discharged children, development and maintenance of information systems, and surveillance and planning activities. Adequate reimbursement must also reflect the increased costs of caring for many high-risk newborns, especially among the disadvantaged population.

Training

Finally, some equilibrium between the needs of training programs and the need for skilled neonatal professionals must be achieved. This equilibrium will require alterations in the size, number, and staffing of teaching hospitals. In addition, it may also require the provision of new training experiences to assure the ongoing assessment of neonatal practices as noted above.

In the absence of significant reductions in prematurity rates, NICU care will continue to be needed. Moreover, even with reduced rates of prematurity, such units are also critical to the well-being of children with malformations and acute complications of the newborn period. The current changes in neonatal care provide both exciting new opportunities to maximize its utility and grave challenges in assuring equity.

Evaluation of Neonatal Intensive Care Technologies

From The Future of Children Vol. 5 No. 1 Spring 1995

Abstract

The development and dissemination of neonatal intensive care technology has been associated with improved survival for critically ill newborn infants, particularly those with birth weights of less than 1,500 grams (3 pounds, 5 ounces). Despite these advances, there are concerns about the long-term health status of surviving infants and the costs of their initial and subsequent care. In this article, the authors review current evidence for the effectiveness of neonatal intensive care and discuss several approaches to evaluating neonatal intensive care technology. They discuss a four-step process originally proposed by Roper for assessing and improving neonatal intensive care practices which includes (1) monitoring of practices, outcomes, and costs; (2) analysis of variation in practices, outcomes, and costs; (3) assessment of the efficacy of individual interventions, and (4) feedback and education to alter clinical behavior. The authors conclude that organized networks of neonatal intensive care units can play a crucial role in this process.

The development and dissemination of neonatal intensive care technology has been associated with increasing survival for low birth weight infants, particularly those weighing less than 1,500 grams (3 pounds, 5 ounces) at birth. Other factors have also contributed to this trend, including the regionalization of perinatal care, the emergence of subspecialists in maternal-fetal medicine, neonatal medicine, and pediatric surgery, and diagnostic and therapeutic advances in high-risk obstetrics. Despite improvements in survival, however, there are continuing concerns about the high costs of neonatal intensive care and the quality of life of survivors. In this section discusses the evaluation of neonatal intensive care technologies and emphasize the role that organized networks of neonatal intensive care units can play in evaluating and continuously improving the effectiveness and efficiency of neonatal intensive care.

Background

Neonatal intensive care for critically ill newborns was introduced in the late 1960s when methods for providing assisted ventilation to small infants were first developed. Because neonatal intensive care units required specialized personnel and facilities beyond those available at most hospitals, national efforts were made to regionalize their location.1 This strategy was successful in increasing the availability of neonatal intensive care and resulted in improved survival rates for low birth weight infants.2 By 1976 there were more than 125 neonatal intensive care units in North America, primarily at major university medical centers.3 There are now reported to be more than 700 such units, including both level 2 and

level 3 nurseries.4 Clearly, there has been a dramatic increase in the number of neonatal intensive care units. As a result, the majority of newborns receiving intensive care are now treated in smaller non-university hospitals. This trend, called "deregionalization," is discussed in detail in the article by McCormick and Richardson in this journal issue.

Neonatal-perinatal medicine became a board-certified subspecialty of pediatrics in 1975. The training period consists of three years of general pediatric residency plus three years of neonatology fellowship in one of 106 approved training programs. All neonatologists who entered training programs after 1989 are required to take a recertification examination in general pediatrics and neonatology every seven years. A survey of perinatal centers performed in 1983 estimated that there were 1,509 physicians practicing neonatology in the United States.5 In 1993, the Accreditation Council for Graduate Medication Education listed 528 physicians in neonatal training programs and 2,498 board-certified neonatologists. There is no official estimate of the total number of pediatricians currently practicing neonatology, some of whom are not board certified, but a database maintained by Abbott Laboratories lists 3,740 individuals interested in neonatology. A survey is being carried out by the American Academy of Pediatrics to gather more accurate data on the number of neonatologists who are actually in practice. These data are important because questions have been raised as to whether there are currently too many neonatologists in the United States as compared with the number in other countries.6

The growth in the numbers of neonatologists and neonatal intensive care units has been accompanied by rapid expansion in the range and complexity of medical, surgical, and diagnostic services provided to critically ill newborns. In 1981, Sinclair and colleagues enumerated some of the specific preventive and therapeutic maneuvers included in neonatal intensive care programs.7 They concluded that, although the efficacy of some specific intensive care maneuvers had been validated in randomized controlled trials, the overall effectiveness of neonatal intensive care programs required further evaluation with rigorous scientific methods. Since that article was written, a large number of new intensive care techniques have been introduced. Also, neonatal intensive care has been provided to progressively smaller and less mature infants so that infants at 23 weeks gestational age and 400 grams (14 ounces) birth weight are now receiving intensive care at many institutions.

A representative list of the technologies and procedures that are included in current neonatal intensive care programs is shown in Box 1. This list is not exhaustive but does give an indication of the range of diagnostic and therapeutic measures which are used in modern neonatal intensive care. Most of the specific measures have still not been subjected to rigorous scientific testing, and there is considerable variation among neonatologists in how these techniques are used.

BOX 1

Neonatal Intensive Care Technologies and Procedures

1. **Environmental Control**

   incubators
   radiant warmers
   servo-controlled thermoregulation
   heat shields
   plastic wrap
   humidification
   control of noise and light

2. **Vascular Access**

   umbilical artery/vein catheters
   peripheral artery/vein catheters
   central venous catheters
   infusion and syringe pumps

3. **Physiologic Monitoring**

   temperature
   cardiorespiratory
   electrocardiogram
   thoracic impedance
   apnea/bradycardia alarms
   trend monitors
   systemic blood pressure
   oscillometric method
   indwelling artery catheter
   central venous pressure
   oxygenation/ventilation
   arterial blood sampling
   capillary blood sampling
   pulse oximetry
   transcutaneous PO2,CO2
   pulmonary function testing

4. **Laboratory Testing**

   micro sampling methods
   bedside glucose testing
   routine chemistry, hematology, serology
   microbiology
   pulmonary maturity
   genetic analysis
   metabolic screening

5. **Diagnostic Imaging**

   radiography
   ultrasonography
   Doppler echocardiography
   CT-scanning
   MRI scanning
   nuclear medicine scanning

6. **Nutritional Support**

   parenteral nutrition
   enteral feeding techniques
   special formula
   breast milk supplements
   vitamins
   minerals
   trace elements

7. **Blood Products**

   red blood cells
   white blood cells
   platelets
   plasma
   cryoprecipitate
   coagulation factors
   irradiation of blood products

8. **Respiratory Support**

   supplemental oxygen
   continuous positive airway pressure
   chest physiotherapy
   conventional ventilation
   high-frequency ventilation
   surfactant
   extracorporeal membrane oxygenation

9. **Delivery Room Resuscitation**
10. **Neonatal Pharmacotherapeutics**

    diuretics
    xanthines
    steroids
    indomethacin
    antimicrobials
    heparin
    vasopressors
    sedatives/analgesics

11. **Phototherapy**
12. **Neonatal Surgery/Anesthesia**
13. **Psychosocial Interventions**

    unlimited parental visiting
    parental involvement in care
    skin-to-skin contact
    infant stimulation
    reducing noxious stimuli
    nonnutritive sucking

14. **Neonatal Transport**

    skilled transport teams
    air/ground transport

15. **Other Diagnostic Testing**

    electroencephalogram
    evoked response audiometry

The Impact of Neonatal Intensive Care

Mortality

Several lines of evidence support the hypothesis that neonatal intensive care has resulted in decreased mortality. First, there have been marked declines in neonatal and infant mortality rates coincident with the introduction and refinement of neonatal intensive care.8-10 This decline has been almost entirely due to improvements in the survival of very low birth weight infants rather than a decrease in the number of very low birth weight infants.10 Between 1965 and 1975, neonatal mortality rates decreased by 35%. Because other factors known to affect survival at a given birth weight did not change during this period, Lee and colleagues concluded that improvements in perinatal medical care were responsible.8 A more recent drop in infant mortality has been associated with a specific neonatal intensive care practice.11- 13 Between 1989 and 1990, the infant mortality rate dropped by 6% (from 9.7 to 9.1/1,000 births). Kleinman estimated that as much as one-half of this change may have been due to the introduction of surfactant therapy, which reduces serious lung disease, into neonatal intensive care.11

The second line of evidence regarding the effect of neonatal intensive care on infant mortality is the observation showing that low birth weight infants born in hospitals with tertiary level neonatal intensive care units have lower mortality rates than infants born in hospitals without such units.14

Paneth and colleagues found that preterm low birth weight infants born in New York City were at a 24% lower risk of death if they were born at a hospital providing tertiary level neonatal intensive care.15 Similar findings have been reported for total population cohorts of infants from New York City,16 several states in the United States,17,18 and the Netherlands.19

Finally, increased access to neonatal intensive care--either because a new neonatal intensive care unit is opened20 or because regionalized neonatal services are instituted2--has been associated with decreases in neonatal mortality. In Hamilton-Wentworth County, Ontario, mortality for very low birth weight infants dropped by nearly 17% after a regional neonatal intensive care unit was opened in 1973.20

All of these findings suggest that neonatal intensive care has played a role in improving survival for low birth weight infants. Other factors, including regionalized transport

systems for high-risk women and infants, advances in obstetrical care and neonatal surgery, and improved training in maternal-fetal and neonatal medicine, have also had an effect.

Long-Term Outcomes

The impact of neonatal intensive care on long-term outcomes for low birth weight infants is more complex. (See the article by Hack, Klein, and Taylor in this journal issue for a detailed discussion of long-term developmental outcomes.) In a case study published in 1987, the Office of Technology Assessment concluded that "neonatal intensive care has contributed to improved long-term developmental outcomes for premature infants. The great decline in mortality among all subgroups of very low birth weight infants over the past 10 years, however, means there are now larger absolute numbers of both seriously handicapped and normal survivors."21 A recent review of population- based registries of cerebral palsy found that one unavoidable side effect of the increasing success of neonatal intensive care is a moderate rise in the childhood prevalence of cerebral palsy.22 In addition to neurobehavioral disabilities and poor school performance, children born at very low birth weight who survive are also at higher risk for a broad range of other adverse health outcomes at school age.23-27 As a result, survivors of neonatal intensive care have significantly increased medical care costs throughout childhood, which may pose a substantial financial burden to their families.28,29 These long-term consequences must be carefully balanced against the gains in survival in any evaluation of neonatal intensive care.

Extreme Immaturity

There is considerable uncertainty about the effectiveness of neonatal intensive care for extremely immature infants. Difficult questions arise as attempts are made to identify lower limits of birth weight and gestational age below which neonatal intensive care is either futile or does more harm than good for the individual infant, its family, and society. (For a discussion of these ethical issues, see the article by Tyson in this journal issue.) Based on infants born between 1982 and 1988, Hack and Fanaroff concluded that, with few exceptions, survival is limited to infants with birth weights of 600 grams (1 pound, 5 ounces) or more or to those whose gestational age is at least 24 weeks.30 They found no improvement in the outcomes for such infants between 1982 and 1988. Allen and colleagues, in a study of infants of 22 to 25 weeks gestation born from 1988 to 1991, found that no infants born at 22 weeks gestation survived as compared with 15% of infants born at 23 weeks, 56% born at 24 weeks, and 79% born at 25 weeks gestation.31 Only 2% of infants born at 23 weeks gestation survived without severe brain injury as compared with 21% of those born at 24 weeks and 69% of those born at 25 weeks of gestation. Allen and colleagues concluded that aggressive resuscitation and intensive care treatment are indicated for infants born at 25 weeks gestation, but not for those born at 22 weeks gestation. They recommend that, for infants born at 23 or 24 weeks gestation, discussions involving parents, health care providers, and society at large are required. In contrast, in 1991 the law in Japan was amended to lower the limit of viability from 24 to 22 weeks because of increasing numbers of survivors with gestational ages below 24 weeks.32,33 Questions about which infants should receive intensive care will become even more pressing as scarce health care resources are carefully scrutinized and reallocated.

Clinical Evaluation Science

Clinical evaluation science provides a natural framework for evaluating neonatal intensive care. This emerging field, otherwise known as outcome research or medical effectiveness research, uses a variety of analytic techniques to understand the relationships between the structure, process, outcomes, and costs of medical care.34 Clinical evaluation science attempts to identify and explain the variations in the practice and outcomes which have been observed to occur among regions, among hospitals, and among physicians. Ultimately, the goal is to change inappropriate practice patterns by disseminating information to physicians and patients. The Patient Outcome Research Teams sponsored by the Agency for Health Care Policy and Research are a major example of this strategy in action.35

Roper and colleagues have described a four-step process for assessing the effectiveness of medical care and improving clinical practice which illustrates many of the techniques of clinical evaluation science.36 This process includes (1) monitoring of practice, outcomes, and costs, (2) analysis of variations in practice, outcomes, and costs (3) assessment of the efficacy of individual interventions, and (4) feedback and education to alter behavior. We will discuss each of these steps as they apply to neonatal intensive care and describe the role that neonatal research networks can play in this process.

Monitoring

Monitoring the medical interventions, outcomes, and costs for large populations requires accurate and timely data collected using uniform definitions. A major barrier to monitoring neonatal intensive care on a large scale is the lack of adequate data sources. In the Medicare population, for which considerable effectiveness research has been done, monitoring is facilitated by the availability of a universal database of Medicare claims.

No similar national data sources are available for monitoring outcomes, interventions, and costs for perinatal patients. Studies in perinatal patients have, therefore, relied on vital statistics, linked birth and death certificates, state Medicaid files, medical record reviews, and hospital discharge abstracts.

Unfortunately, these sources often lack the clinical detail necessary to properly monitor neonatal intensive care. A pioneering example of how existing data sources can be used for monitoring neonatal care is the system developed by Williams, which uses linked birth and death certificates, for the state of California.37

The March of Dimes Birth Defects Foundation, in its publication, Toward Improving the Outcome of Pregnancy: The 90s and Beyond, recognizes that improved data sources will be crucial to the evaluation of neonatal intensive care.38 Comprehensive perinatal data systems at the state and regional level, which include vital statistics and information about clinical practice, will be needed. As integrated delivery systems are developed under health reform, there will be opportunities to create modern information systems which can be used to assess the effectiveness and costs of neonatal intensive care.

Neonatal Network Data Bases

Currently, databases maintained by neonatal research networks provide an important source of data for monitoring the practice and outcomes of neonatal intensive care. There are now at least eight such networks collecting information on infants receiving neonatal intensive care (see Box 2).

BOX 2

Neonatal Research Networks

1. **BAPM Perinatal Clinical Trials Group**

   British Association of Perinatal Medicine
   c/o Secretary BAPM Perinatal Trials Service
   NEPU, Radcliffe Infirmary
   Oxford, OX2 6HE UK

2. **Canadian Perinatal Clinical Trials Network ***

   W. Fraser, MDBR
   L'Hopital St. Francois d'Assise
   10 rue de L'Espinay Quebec, G1L 3L5 CANADA

3. **International Neonatal Network***

   W. O. Tarnow-Mordi, MD
   Department of Child Health
   Ninewells Hospital and Medical School
   Dundee, DD1 9SY UK

4. **National Perinatal Information Center***

   David E. Gagnon, MPH
   Executive Director
   One State Street, Suite 102
   Providence, RI 02908

5. **NICHD Neonatal Research Network**

   Linda Wright, MD
   NICHD/NIH
   Room 4B03, Bldg. 6100
   9000 Rockville Park
   Bethesda, MD 20892

6. **Perinatal Trials Service**

   National Perinatal Epidemiology Unit *
   Diana Elbourne, PhD
   NEPU, Radcliffe Infirmary
   Oxford, OX2 6HE UK

7. **Study Group for Complications of Perinatal Care***

   T. Macpherson, MD
   Department of Pathology
   Magee Women's Hospital
   Pittsburgh, PA 15213

8. **Tokyo Metropolitan Maternal & Child Health Service Center**

   Data Base Project
   M. Hirayama, MD
   Tokyo MCH Center
   Tokyo, JAPAN

9. **Vermont-Oxford Trials Network***

   Lynn Stillman
   Neonatal Research & Technology Assessment, Inc.
   52 Overlake Park
   Burlington, VT 05401.

Two examples of networks with ongoing databases are the Vermont-Oxford Trials Network 39 and the National Institute of Child Health and Human Development (NICHD) Neonatal Research Network.40 These networks perform randomized trials41-43 and maintain databases for observational studies. The Vermont-Oxford Trials Network consists of a broad range of university and non-university neonatal units. Membership is voluntary, most units are small, and participating investigators do not receive salary support for participation. The NICHD Neonatal Research Network consists of large university research centers with network-funded research personnel.

Both of these networks maintain databases for infants with birth weights below 1,500 grams (3 pounds, 5 ounces). In 1992, the Vermont- Oxford Trials Network collected information about more than 5,000 very low birth weight infants at 68 neonatal units. In 1993, it collected data on more than 6,600 infants at 84 neonatal units.

The NICHD Neonatal Research Network collected data on nearly 3,000 infants at 12 neonatal units in 1992. Combined, these networks represent approximately 20% of all very low birth weight infants born in the United States. Network databases such as these are now a major resource for monitoring the process and outcomes of neonatal intensive care.

Analysis of Variations

Since 1973, when Wennberg and Gittlesohn demonstrated that there were marked variations in the utilization of surgical procedures among hospital service areas within the state of Vermont, a large body of research has confirmed that both patterns of care and patient outcomes vary among geographic areas and hospitals in ways that cannot be explained by differences in the patient populations which are served.44 In addition to large differences in utilization rates for surgical procedures, diagnostic services, and hospital admissions, there is also wide variation in hospital mortality for a number of different medical conditions.45

In the following sections, we will review the data concerning variations in interventions and outcomes for neonatal intensive care and discuss approaches to risk adjustment for neonatal patients, which may be useful in determining the causes of the observed variations.

Variations in the Use of Interventions

Large variations in the use of prenatal corticosteroids exist despite their proven effectiveness in reducing morbidity and mortality among preterm infants. Corticosteroid treatment of women at risk for preterm delivery induces lung maturation in the fetus and improves neonatal outcomes.46 (For further discussion of the effectiveness of corticosteroids, see the article by Ricciotti in this journal issue.)

There is clear and convincing evidence from numerous randomized controlled trials that antenatal corticosteroid treatment not only reduces the risk of respiratory distress syndrome in preterm infants of treated women but also reduces the risk of death and intraventricular hemorrhage.47 Despite this evidence, many obstetricians prescribe antenatal steroids infrequently for women at risk for preterm delivery, and some obstetricians do not prescribe them at all. At 73 centers participating in the Vermont-Oxford Trials Network in either 1991 or 1992, 26% of the 8,749 infants weighing 501 to 1,500 grams (from 1 pound, 2 ounces to 3 pounds, 5 ounces), were born to women who had received antenatal steroids.48 Twenty-five percent of the centers in the network had treatment frequencies of 11% or less; 25% of centers had frequencies of 36% or more; only 10% of centers had frequencies of 60% or more. Data from the NICHD Neonatal Research Network also indicate wide variation in the use of antenatal steroid therapy for very low birth weight infants.40 Overall, 16% of infants in the NICHD Network were delivered to women who had received steroids with a range of 1% to 33%.

Reports from these two neonatal networks also document substantial variation among neonatal intensive care units (NICUs) in the use of a number of other postnatal interventions and procedures. Table 1 shows the overall frequencies for selected interventions and their interquartile ranges at 68 centers which participated in the Vermont-Oxford Trials Network in 1992.49

The variation persisted even within 250-gram birth weight categories. Data for variation in postnatal interventions are also provided by the NICHD Neonatal Research Network. Methods of delivery room management, use of phototherapy, exchange transfusions, indwelling vascular catheters, and parenteral nutrition all exhibited considerable variation among the NICHD Network Centers.40 The persistence of variation within relatively narrow birth weight categories suggests that the variation is due in large part to differences in practice styles among the units.

Variations in Outcomes After Neonatal Intensive Care

As previously discussed, neonatal intensive care has resulted in increased birth-weight-specific survival rates and a decrease in the overall infant mortality rate. Infants born at hospitals with level 3 neonatal intensive care units have lower neonatal mortality than infants born at hospitals without such units.15-19 Even among level 3 neonatal intensive care units, however, there are substantial variations in both mortality and morbidity among the survivors.

Avery and colleagues found that the incidence of chronic lung disease in infants weighing 700 to 1,500 grams (from 1 pound, 9 ounces to 3 pounds, 5 ounces) varied significantly among the eight institutions studied even after adjusting for birth weight, race, and gender.50 The investigators suggested that the observed variation was due to differences in respiratory care practices among the centers. Horbar, in a study of 11 neonatal intensive care units, found differences among centers both in the frequency of chronic lung disease and in neonatal mortality.51 Again, the differences persisted after adjustment for birth weight, race, and gender. Kraybill and colleagues, in a survey of 10 neonatal units in North Carolina, found significant differences among centers in the frequency of chronic lung disease.52 They also suggested that differences in respiratory care practices might explain the findings. Hack and colleagues, reporting for the NICHD Neonatal Research Network, indicate that there are large intercenter differences in morbidity, particularly with respect to chronic lung disease, necrotizing enterocolitis, intraventricular hemorrhage, and jaundice.40 Wide variation in most morbidities have also been documented for centers in the Vermont-Oxford Trials Network (see Table 2).49

These data suggest that there are differences among neonatal intensive care units with respect to short-term morbidity and mortality. While some of these differences may be due to differences in the way specific outcomes are diagnosed at the different centers, the extent to which they are due to differences in the quality of medical care is unknown. Data regarding variation in long-term neurodevelopmental outcomes and other morbidities among centers are not available.

Risk Adjustment

Variations in the outcomes of hospitalized patients have been used as indicators of the effectiveness of medical care. However, before inferences can be drawn from observed differences in mortality or other outcomes among hospitals, it is necessary to account for differences in case mix. Variation in hospital mortality has three major sources: the underlying risk of a hospital's patient population, the effectiveness and appropriateness of care provided at the hospital, and sampling variations (the likelihood that the mortality observed in the study group truly represents the experience in the total population).53 Statistical models for predicting mortality risk based on patient characteristics have been developed for use in a number of different clinical situations, including adult medical and intensive care, pediatric intensive care, and neonatal intensive care.54-58 These risk adjustment models can be used to compare the observed outcomes at a particular hospital with the outcomes that would be expected based on the demographic characteristics of the hospital's patients as well as the severity of their illnesses measured by physiologic and laboratory values. After differences in patient risk and sampling variations have been accounted for, residual variation in outcome is assumed to reflect differences in the effectiveness and/or appropriateness of medical care.

One of the earliest examples of risk adjustment for the evaluation of perinatal care was reported by Williams.37 He applied a model for predicting neonatal death based on birth weight, race, sex, and multiple birth to more than 3 million infants born at 504 hospitals in California during the years 1960 to 1973. After the model had been used to account for newborn risk and the effect of chance, there was still a twofold variation in mortality at these hospitals. This residual unexplained variation was presumably the result of differences in the effectiveness of perinatal care.

More recently, risk adjustment models have been developed specifically for neonatal intensive care. Richardson and colleagues have developed the Score for Neonatal Acute Physiology (SNAP), which is patterned after the Acute Physiology and Chronic Health Evaluation (APACHE) score used in adult intensive care and the PSI used in pediatric intensive care.59 The SNAP can be applied to all NICU admissions regardless of birth weight. The SNAP is predictive of neonatal mortality even within narrow birth weight strata and is correlated with other indicators of severity, including nursing workload, therapeutic intensity, and physician estimates of mortality risk. Furthermore, the SNAP increases the accuracy of neonatal mortality risk prediction when used along with birth weight, five-minute Apgar score, and size for gestational age.60 In the future, use of scoring systems such as the SNAP will help to refine the risk adjustment analyses and provide us with a clearer picture of variations in neonatal mortality across hospitals.

The International Neonatal Network has developed the Clinical Risk Index for Babies (CRIB), a scoring system for predicting mortality risk for infants weighing 1,500 grams (3 pounds, 5 ounces) or less.61 The CRIB score is based on birth weight, gestational age, maximum and minimum fraction of inspired oxygen, maximum base excess, and presence of congenital malformations. The score uses values obtained within 12 hours of admission. The CRIB score is more accurate than birth weight alone in predicting mortality risk, and higher scores are associated with an increased risk for major cerebral abnormality.

Because postadmission data may reflect the results of treatments provided in the neonatal intensive care unit rather than the infants' underlying risk, mortality prediction models

based only on admission data are preferred if the goal of risk adjustment is to identify differences in the effectiveness of care. Both the SNAP and the CRIB score use information collected during the first 12 to 24 hours after admission to the neonatal intensive care unit for predicting mortality risk.

Figure 1 shows the standardized neonatal mortality ratios (SNMRs) at 68 centers participating in the Vermont-Oxford Trials Network in 1992, and illustrates the existing variation in mortality rates in these centers. In this model, which is based on factors present at the time of admission, the observed variations cannot be attributed to the infant's birth weight, race, gender, health at birth, receipt of prenatal care, and location of the birth because the effects of these factors have been statistically controlled. The SNMR is the ratio of the number of observed deaths at a center to the number of deaths predicted based on the patient characteristics in the model. An SNMR of 1 means that a hospital has exactly the number of deaths which would be expected; values greater than 1 indicate that more deaths occurred than were expected; values less than 1 indicate that fewer deaths occurred than were expected. Although some hospitals have SNMRs that are less than 1 and others have SNMRs that are greater than 1, in most instances the 95% confidence limit includes the values of 1, which means that these hospitals do not appear to have too many or too few deaths. Improved predictor models which include major birth defects among the predictor variables are currently being developed.

Neonatal mortality prediction could serve several purposes. One purpose is the prediction of individual patient risk. It is unlikely that any model will be accurate enough to aid in patient care decisions such as when to withhold or withdraw life support. However, prediction of individual risk may be useful for identifying infants who died despite having a low predicted probability of death. These cases could then be chosen for audit as part of local quality improvement efforts.

A second purpose for neonatal risk prediction is the identification of outlier hospitals where the quality or effectiveness of care is low. Given the relatively small number of very low birth weight infants treated at individual neonatal intensive care units, the confidence intervals for estimates of measures like the SNMR will be large.62 This will severely limit the power of even very accurate statistical models to identify outlier hospitals. Aggregating cases over multiple years increases the ability to detect outliers. It remains to be proven, however, that targeting hospitals in this way accurately identifies units providing less effective care,63 as methods to adjust for the underlying risks and differences in the units remain imperfect.

A third purpose for neonatal risk prediction models is their use in studies of hospital characteristics associated with outcome. The power to detect differences in risk-adjusted mortality rates among groups of hospitals within large neonatal networks will be greater than the power to detect individual outliers. Several studies have already shown that hospital characteristics are associated with outcomes for adult and neonatal patients.37,64 Williams, in the study discussed above, found that, after adjusting for patient risk, hospitals with larger delivery services, urban hospitals, hospitals performing above-average numbers of cesarean sections, those recording Apgar scores, and hospitals with higher specialist-to-generalist ratios had lower mortality rates.37 Conversely hospitals with more Spanish-surnamed mothers and private proprietary hospitals had higher mortality rates. Paneth and

colleagues have shown that risk-adjusted neonatal mortality rates at level 3 hospitals are lower than at either level 1 or level 2 hospitals in New York City.15,16 The International Neonatal Network has also shown that mortality rates adjusted for risk using the CRIB score are lower in tertiary as opposed to nontertiary neonatal care units in the United Kingdom.57

We are currently using data from the Vermont-Oxford Trials Network to investigate whether hospital characteristics, services, and staffing patterns are associated with differences in mortality for very low birth weight infants. It is not known whether patient volume, teaching status, hospital ownership, and use of ancillary personnel such as neonatal nurse practitioners influence the costs and outcomes of neonatal intensive care. Because of trends toward deregionalization of care and changing patterns of referrals due to managed care, it will be increasingly important to understand how these factors affect both costs and outcome. Neonatal networks will be valuable laboratories for answering health services questions about the delivery of neonatal intensive care.

Assessment of Interventions

Randomized Controlled Trials

The third step in the process for evaluating and improving the effectiveness of neonatal intensive care is assessing the efficacy of specific interventions. The gold standard for evaluating the efficacy of an intervention is the randomized controlled trial. The National Perinatal Epidemiology Unit in the United Kingdom has demonstrated how large, simple randomized controlled trials (RCTs) can be applied to answer important questions in perinatal medicine.65 Most medical innovations lead to only small or moderate gains over standard treatment, but large trials are required to demonstrate such gains. For example, to have a reasonable chance of demonstrating that a new treatment reduces mortality from 25% to 20% requires a study that enrolls nearly 3,000 infants, many more infants than are generally admitted to any one NICU in a year. In the past, too many of the trials performed in neonatology were single-center studies enrolling relatively few patients. It is now clear that multicenter networks will be needed to perform the large trials required to demonstrate small, but clinically important, differences between treatments. The recent multicenter trials of surfactant therapy,66 high-frequency ventilation,67 and cryotherapy for retinopathy of prematurity68 are examples of how this approach can be used successfully to test new therapies for neonatal intensive care.

A number of new therapies and technologies that are now in the early stages of clinical development will require multicenter randomized clinical trials to demonstrate their safety and efficacy for treatment of low birth weight infants (see Table 3).69-82 Several of these treatments have already been tested in initial small trials or are currently being evaluated in multicenter trials.

It is instructive to compare the situation in neonatology with that in pediatric oncology. Eighty to ninety percent of children in the United States with cancer are cared for at institutions participating in one of two national collaborative networks (Children's Cancer Study Group or Pediatric Oncology Group), using strictly defined treatment protocols.83 These groups continually refine their treatment protocols based on the results of ongoing

randomized clinical trials. As a result, the outcomes for children with cancer have improved steadily.84 We should strive for a similar organizational structure in neonatal intensive care. Despite a central role in evaluating neonatal technologies, randomized trials will not be capable of answering all of the questions that arise about interventions in neonatal intensive care.

Feinstein has pointed out that randomized controlled trials are not feasible for studying multiple therapeutic candidates, minor changes in therapy, instabilities caused by rapid technological improvements in available treatment, long-term adverse side effects, studies of etiologic or other suspected "noxious" agents, and the diverse clinical roles of diagnostic technology.85 Additional methods will be required to address these issues. Observational studies based on large neonatal databases from multicenter networks will have a role in addressing those questions that cannot readily be answered using randomized trials.

Meta-Analysis: Combining Data from Many Randomized Trials

The evaluation of specific interventions requires a synthesis of all the available evidence. Traditionally, such a synthesis took the form of a qualitative literature review. Recently, statistical techniques for combining the findings of individual studies have come into widespread use. The formal overview, or meta-analysis, arrives at a summary measure of effect size by combining the results of individual trials.86 Meta- analysis provides a powerful tool for evaluating the evidence from randomized controlled trials. However, investigators must approach meta- analysis with the same methodologic rigor as any other research. Overviews should include all relevant trials which meet predefined inclusion criteria. The results of the trials are extracted from published reports and, in some instances, supplemented with unpublished data obtained from the investigators. These results are then tabulated, and summary measures of effect size are calculated. Several different statistical methods for determining the summary measures are available.87

The method of meta-analysis has been extensively applied to synthesizing the results of randomized trials in perinatal medicine. Formal meta- analyses, or overviews, have been included in the Oxford Database of Perinatal Trials, which contains a bibliography of all randomized trials in prenatal medicine published since 1940.88,89 Several obstetrical overviews90 and neonatal overviews have also been published.91

These reference works will be updated and published in electronic format, providing extensive statistical summaries of the available evidence for perinatal interventions. The highly respected Cochrane Collaboration has been established to coordinate and disseminate overviews of randomized trials which can be used to inform evidence- based decision-making. An example of a recent meta-analysis is the overview by Mercier and Soll of the effects of natural surfactant therapy for the treatment of respiratory distress syndrome (see Figure 2).92 This overview is based on 12 separate randomized trials. Taken together, these trials indicate that surfactant therapy reduces the risks for serious lung diseases and mortality.

The individual trials did not each demonstrate these results. Only by pooling the evidence from all of the trials do such clear conclusions emerge. Formal overviews such as this one are powerful tools for evaluating the efficacy and safety of specific interventions.

A novel form of meta-analysis has recently been described for combining the results of randomized trials and medical practice databases. This method--called cross-design synthesis--identifies studies conducted using similar research designs, assesses the potential biases associated with each design, makes secondary adjustments of study results to correct for known biases, and develops models for synthesizing results which minimize hidden biases.93 This untested method may prove useful in the future because it combines the strengths of randomized trials for producing unbiased comparisons with the ability of patient data bases to include a broad range of patients treated in real-world conditions.

Economic Evaluation

Faced with limited reserves and the need to choose among alternative programs, policymakers must consider not only whether neonatal intensive care is effective but also whether it is worth the cost. Increasingly, analysts have come to rely on cost-effectiveness analyses to evaluate medical care and interventions.94 In cost-effectiveness analyses, an estimate is made of the incremental costs of an improvement in health status (such as the cost of an additional year of life), attributable to a particular intervention and compared with the incremental costs of other interventions.

Cost-effectiveness analysis was one technique used in the most comprehensive economic evaluation of neonatal intensive care which was based on patients receiving intensive care in Hamilton-Wentworth County, Ontario, between 1973 and 1977.95 In addition to measuring all of the costs flowing from neonatal intensive care, such as health care and special services received by survivors after discharge, the study attempted to measure the condition of survivors based on physical function, role function, social and emotional function, and health problems. These outcome data were used to adjust life years gained by NICU survivors by a factor that takes into account the quality of life for those who survived with disabilities. The resulting units are called quality-adjusted life-years (QALYs). For infants weighing from 1,000 to 1,499 grams (between 2 pounds, 3 ounces and 3 pounds, 5 ounces), the cost (in 1978 Canadian dollars) was $59,500 per additional survivor, $2,900 per life-year gained, and $3,200 per QALY gained. For infants weighing from 500 to 999 grams (between 1 pound, 2 ounces and 2 pounds, 3 ounces), the costs were $102,500 per additional survivor, $9,300 per life-year gained, and $22,400 per QALY gained.

These cost-effectiveness ratios have little intrinsic meaning by themselves but can be compared with ratios for other major health interventions. Figure 3 shows the cost per QALY, adjusted to 1986 U.S. dollars, for neonatal intensive care in the two birth weight groups and for other selected health care interventions.96 Several interventions-- including coronary bypass surgery for single-vessel disease, school tuberculin testing, continuous ambulatory peritoneal dialysis, hospital hemodialysis, and liver transplantation--all have higher estimated costs per QALY gained than neonatal intensive care for infants weighing from 500 to 999 grams (between 1 pound, 2 ounces and 2 pounds, 3 ounces). For example, a liver transplant costs $250,000 for each QALY gained while NICU care for a moderately low birth weight infant costs less than $10,000 for each QALY.

The Office of Technology Assessment, in its 1987 evaluation of neonatal intensive care, concluded: "Neonatal intensive care results in both increased survival and increased costs. Moreover, neonatal intensive care becomes more expensive as it is employed in increasingly marginal cases. The worth of a life saved, however, is ultimately a value judgment involving ethical and social considerations. The results from cost-effectiveness studies alone cannot guide decisions regarding who should receive care."21

These conclusions are still valid today. In addition, advances in neonatal intensive care have influenced both the costs and the outcomes of this care. Since the Canadian study was done, survival rates for infants weighing less than 1,000 grams (2 pounds, 3 ounces) have increased. A recent report from the province of Alberta, Canada, suggests that the condition of NICU survivors may also be improving.97 The introduction of surfactant therapy has changed both outcomes and costs.12,13 It is estimated that use of surfactant among very low birth weight infants has resulted in a 30% decrease in mortality and a similar decrease in use of hospital resources.13 Several other investigators have concluded that surfactant therapy is cost-effective, but definitive analyses are still required.13,98-103 An economic evaluation of neonatal intensive care based on patients treated in the 1990s is urgently needed.

Ultimately policymakers and society will have to decide whether resources should be allocated to neonatal intensive care as opposed to other purposes. Joyce and colleagues put this choice into perspective by comparing the cost-effectiveness of different strategies to reduce infant mortality.104 They estimated that, if there was a direct causal relationship between prenatal care and infant mortality, it would cost between $30 and $40 (1984 U.S. dollars) to save an additional life by expanding the number of women who receive prenatal care in the first trimester, as opposed to $2,000 or $3,000 to save an additional life by expanding the number of low birth weight infants who receive neonatal intensive care.

Unfortunately, there is growing evidence that providing access to quality prenatal care alone is insufficient to reduce low birth weight.

Changing Physician Behavior

The final step in the process of evaluating and improving the effectiveness and efficiency of neonatal intensive care involves changing physicians' practices. Greco and Eisenberg have recently reviewed the general methods that can be used to alter the practice behavior of physicians.105 These include (1) educational processes such as continuing medical education and practice guidelines, (2) feedback of information comparing individual physician practices and patient outcomes with benchmark standards, (3) continuous quality improvement programs and other efforts to engage physicians in change, (4) administrative interventions, and (5) financial incentives or penalties. In general, whether an intervention is successful depends on the particular circumstances in which it is used; combinations of methods appear to be the most effective.

Neonatal networks have the potential to influence practice patterns of neonatologists using several of these approaches. Membership in a database that produces benchmarking reports, participation in meetings, communication with other network members, and the use of

standardized research protocols supplies many elements needed to change neonatologists' behavior.

Participation in multicenter randomized clinical trials may itself be an educational process capable of causing changes in practice. Surfactant therapy for neonatal respiratory distress syndrome was rapidly adopted in nearly all neonatal intensive care units in North America soon after surfactants were commercially released in 1991. The strength of the experimental evidence and advertising by commercial sponsors were partly responsible for the rapid acceptance of surfactant therapy. The fact that hundreds of neonatal units actually participated in the randomized controlled trials conducted in the preceding decade also played a role. Information from neonatal network databases has the potential to influence physician behavior and neonatal intensive care practices.106,107 The Vermont-Oxford Trials Network currently provides members with reports containing feedback on how local practices and outcomes compare with those of the total network. These reports are intended for use in continuous quality improvement programs. The reports include data on risk-adjusted mortality, length of hospital stay, and adverse outcomes such as intraventricular hemorrhage (bleeding in the brain), chronic lung disease, necrotizing enterocolitis (severe damage to the intestines), nosocomial infection (infections acquired in the hospital), and retinopathy of prematurity (impaired vision or blindness). It will be important to evaluate how these reports are actually used by the members of the network and to determine whether such feedback leads to changes in physician behavior and improvements in the quality of neonatal intensive care.

The Role of Parents in Evaluating Neonatal Intensive Care

Parents and families must play a critical role in evaluating neonatal intensive care. Assessments of the benefits and costs of neonatal intensive care should incorporate the views and experiences of a broad range of families whose infants received intensive care. A recent conference attended by neonatologists and parents who had personal experience with neonatal intensive care developed a set of "Principles for Family-Centered Neonatal Care," which will help parents and professionals work together.108 Two of these principles focus directly on issues relating to the evaluation of neonatal intensive care. One principle urges that new treatments be introduced only in the context of properly controlled trials and states, "Experienced parents should have a voice in determining the research agenda, in establishing outcomes of interest, and in educating other parents about the need for ethically and scientifically sound research in neonatology." The other principle states, "Parents and professionals must work together to promote meaningful long-term follow-up for all high risk NICU survivors."

Only a small percentage of infants receiving neonatal intensive care are currently enrolled in formal follow-up studies, and there are many unanswered questions about the quality of life, particularly for extremely low birth weight survivors.109,110 Those follow-up data that are available concentrate primarily on defining the incidence of neurologic deficits. A more complete evaluation of societal and familial costs and benefits is needed which takes into account the experience and opinions of parents and families and examines a broad range of health outcomes.111 An evaluation of this kind will require collaboration between professionals and the parents and families whose infants have been cared for in neonatal intensive care units. There is great interest in developing simple report cards by which

patients can compare or judge results of various therapies. The New York State Department of Health is a leader in this field. Since 1991, it has supplied data to the public ranking cardiac surgical services and individual surgeons.112 Other states have begun publishing similar data. This movement is bound to spread to neonatology. Comparative data will be of little value, however, unless they are carefully gathered and reported by a neutral source in a format that parents can understand. Neonatal networks will be capable of compiling the necessary data. Creative new ideas for presenting information, such as the use of interactive videodisks, may help to explain the information to parents.

Conclusion

Nearly 15 years ago, Sinclair and colleagues concluded that, although the efficacy of specific neonatal intensive care interventions had been demonstrated, the overall effectiveness and efficiency of neonatal intensive care programs required validation in randomized controlled trials.7 Such trials have not yet been done. It is unlikely that they will be for several reasons. First, there is widespread agreement that neonatal intensive care saves lives. Second, there is considerable disagreement about what to include in a standard package of neonatal intensive care given the multitude of elements that make up modern intensive care and the marked variations in practice which currently exist. Third, diagnostic and therapeutic technologies are changing so rapidly that any package of services would quickly become obsolete as new tests and treatments were introduced. Although the randomized controlled trial will remain the gold standard by which all new therapies must be judged, a broader range of methods drawn from clinical evaluation science will be needed if the effectiveness of neonatal intensive care as a whole is to be monitored and continuously improved. The proper question is no longer "Does neonatal intensive care work?" but rather "How can neonatal intensive care be made more effective and efficient?" Neonatal research networks will play an important role in finding the answers and applying them.

---

1. National Committee on Perinatal Health. Toward improving the outcome of pregnancy. White Plains, NY: National Foundation-March of Dimes, 1976.
2. McCormick, M.C., Shapiro, S., and Starfield, B.H. The regionalization of perinatal services: Summary of the evaluation of a national demonstration program. Journal of the American Medical Association (1985) 253:799-804.
3. Butterfield, L.J. Organization of regional perinatal programs. Seminars in Perinatology (1977) 1:217-33.
4. American Hospital Association. Hospital statistics. Chicago: AHA, 1989.
5. Merenstein, G.B., Rhodes, P.G., and Little, G.A. Personnel in neonatal pediatrics: Assessment of numbers and distribution. Pediatrics (1985) 76:454-56.
6. Silverman, W.A. Is neonatal medicine in the United States out of step? Pediatrics (1993) 92:612-13.
7. Sinclair, J.C., Torrance, G.W., Boyle, M.H., et al. Evaluation of neonatal-intensive care programs. New England Journal of Medicine (1981) 305:489-94.
8. Lee, K.S., Paneth, N., Gartner, L.M., et al. Neonatal mortality: An analysis of the recent improvement in the United States. American Journal of Public Health (1980) 70:15-21.
9. Williams, R.L., and Chen, P.M. Identifying the sources of the recent decline in perinatal mortality rates in California. New England Journal of Medicine (1982) 306:207-14.
10. Buehler, J.W., Kleinman, J.C., Hogue, C.J.R., et al. Birth weight- specific infant mortality, United States, 1960 and 1980. Public Health Reports (1987) 102:151-61.
11. Hilts, P.J. U.S. reports drop in infant deaths. New York Times. April 6, 1991, at A1.

12. Horbar, J.D., Wright, E.C., Onstad, L., et al. Decreasing mortality associated with the introduction of surfactant therapy: An observational study of neonates weighing 601 to 1300 grams at birth. Pediatrics (1993) 92:191-96.
13. Schwartz, R.M., Luby, A.M., Scanlon, J.W., and Kellogg, R.J. Effect of surfactant on morbidity, mortality, and resource use in newborn infants weighing 500 to 1500 g. New England Journal of Medicine (1994) 30:1476-80.
14. Paneth, N. Technology at birth. Editorial. American Journal of Public Health (1990) 80:791-92.
15. Paneth, N., Kiely, J., Wallenstein, S., and Susser, M. The choice of place of delivery: Effect of hospital level on mortality in all singleton births in New York City. American Journal of Diseases of Childhood (1987) 141:60-64.
16. Paneth, N., Kiely, J.L., Wallenstein, S., et al. Newborn intensive care and neonatal mortality in low-birth-weight infants: A population study. New England Journal of Medicine (1982) 307:148-55.
17. Gortmaker, S., Sobol, A., Clark, C., et al. The survival of very low-birth weight infants by level of hospital at birth: A population study of perinatal systems in four states. American Journal of Obstetrics and Gynecology (1985) 152:517-24.
18. Mayfield, J.A., Rosenblatt, R.A., Baldwin, L.M., et al. The relation of obstetrical volume and nursery level to perinatal mortality. American Journal of Public Health (1990) 80:819-23.
19. Verloove-Vanhorick, S.P., Verwey, R.A., Ebeling, M.C.A., et al. Mortality in very preterm and very low birthweight infants according to place of birth and level of care: Results of a national collaborative survey of preterm and very low birthweight infants in the Netherlands. Pediatrics (1988) 81:404-11.
20. Horwood, S.P., Boyle, M.H., Torrance, G.W., and Sinclair, J.C. Mortality and morbidity of 500- to 1,499-gram birth weight infants live-born to residents of a defined geographic region before and after neonatal intensive care. Pediatrics (1982) 69,5:613-20.
21. U.S. Congress, Office of Technology Assessment. Neonatal intensive care for low birthweight infants: Costs and effectiveness. Health Technology Case Study 38. OTA-HCS-38. Washington, DC: OTA, 1987.
22. Bhushan, V., Paneth, N., and Kiely, J.L. Impact of improved survival of very low birth weight infants on recent secular trends in the prevalence of cerebral palsy. Pediatrics (1993) 91:1094-1100.
23. McCormick, M.C. The contribution of low birth weight to infant mortality and childhood morbidity. New England Journal of Medicine (1985) 312:82-90.
24. McCormick, M.C. Long-term follow-up of infants discharged from neonatal intensive care units. Journal of the American Medical Association (1989) 261:1767-72.
25. McCormick, M.C., Brooks-Gunn, J., Workman-Daniels, K., et al. The health and developmental status of very low-birth-weight children at school age. Journal of the American Medical Association (1992) 267:2204- 8.
26. Hack, M., Taylor, G., Klein, N., et al. School-age outcomes in children with birth weights under 750g. New England Journal of Medicine (1994) 331:753-59.
27. Saigal, S., Rosenbaum, P., and Stoskopf, B. Comprehensive assessment of the health status of extremely low birth weight children at eight years of age: Comparison with a reference group. Journal of Pediatrics (1994) 125:411-17.
28. Shankaran, S., Cohen, S.N., Linver, M., and Zonia, S. Medical care costs of high-risk infants after neonatal intensive care: A controlled study. Pediatrics (1988) 81:372-78.
29. McCormick, M.C., Bernbaum, J.C., Eisenberg, J.M., et al. Costs incurred by parents of very low birth weight infants after the initial neonatal hospitalization. Pediatrics (1991) 88:533-41.
30. Hack, M., and Fanaroff, A. Outcomes of extremely-low-birth-weight infants between 1982 and 1988. New England Journal of Medicine (1989) 321:1642-47.
31. Allen, M.C., Donohue, P.K., and Dusman, A.E. The limit of viability--Neonatal outcome of infants born at 22 to 25 weeks' gestation. New England Journal of Medicine (1993) 329:1597-601.
32. Nishida, H., and Ishizuka, M.E. Survival rate of extremely low birthweight infants and its effect on the amendment of the Eugenic Protection Act in Japan. Acta Pediatrica Japonica (1992) 34:612-16.
33. Nishida, H. The viability limit of gestation for the fetus and premature neonates. Asian Medical Journal (1992) 35:487-94.
34. Aday, L.A., Begley, C.E., Lavison, D.R., and Slater, C.H. Evaluating the medical care system: Effectiveness, efficiency and equity. Ann Arbor, MI: Health Administration Press, 1993.
35. Raskin, I.E., and Maklau, C.W. Medical treatment effectiveness research: A view from inside the Agency for Health Care Policy and Research. Evaluation and the Health Professions (1991) 14:161-86.

36. Roper, W.L., Winkenwerder, W., Hackbarth, G.M., and Krakauer, H. Effectiveness in health care: An initiative to evaluate and improve medical practice. New England Journal of Medicine (1988) 319:1197-1202.
37. Williams, R.L. Measuring the effectiveness of perinatal medical care. Medical Care (1979) 17:95-110.
38. National Committee on Perinatal Health. Toward improving the outcome of pregnancy: The 90s and beyond. White Plains, NY: March of Dimes Birth Defects Foundation, 1993.
39. Investigators of the Vermont-Oxford Trials Network Database Project. The Vermont-Oxford Trials Network: Very low birth weight outcomes for 1990. Pediatrics (1993) 91:540-45.
40. Hack, M., Horbar, J.D., Malloy, M.H., et al. Very low birth weight outcomes of the National Institute of Child Health and Human Development Neonatal Network. Pediatrics (1991) 87:587-97.
41. The Vermont-Oxford Trials Network. A multicenter randomized trial comparing synthetic surfactant to modified bovine surfactant extract in the treatment of neonatal respiratory distress syndrome. Pediatric Research (1994) 35:259A.
42. Fanaroff, A., Wright, E., Korones, S., et al. A controlled trial of prophylactic intravenous immunoglobulin (IVIG) to reduce nosocomial infections in VLBW infants. New England Journal of Medicine (1994) 330:1107-13.
43. Horbar, J.D., Wright, L.L., and Soll, R.F. A multicenter randomized trial comparing two surfactants for the treatment of neonatal respiratory distress syndrome. Journal of Pediatrics (1993) 123:757-66.
44. Wennberg, J., and Gittlesohn, A. Small area variations in health care delivery. Science (1973) 182:1102-8.
45. Health Care Financing Administration. Medicare hospital information 1988, 1989, 1990. Vol. 55. Technical supplement. Washington, DC: U.S. Department of Health and Human Services, 1992.
46. Ballard, P.L. Glucocorticoid effects in vivo. In Monographs in endocrinology. Vol. 28: Hormones and lung maturation. P.L. Ballard, ed. Berlin: Springer-Verlag, 1986, pp. 24-71.
47. Crowley, P. Promoting pulmonary maturity. In Effective care in pregnancy and childbirth. I. Chalmers, M. Enkin, M. Keirse, eds. Oxford: Oxford University Press, 1989, pp. 746-64.
48. Horbar, J.D. Antenatal corticosteroid administration and neonatal outcomes for infants 501 to 1500 grams: Vermont-Oxford Trials Network 1991-1992. Program and abstracts of the NIH Consensus Development Conference on the Effect of Corticosteroids for Fetal Maturation on Perinatal Outcomes. Bethesda, MD: National Institute of Health, 1994, pp. 47-52.
49. The Vermont-Oxford Trials Network 1992 Annual Report. Burlington, VT: Neonatal Research and Technology Assessment, 1993.
50. Avery, M.E., Tooley, W.H., and Keller, J.B. Is chronic lung disease in low birth weight infants preventable? A survey of eight centers. Pediatrics (1987) 79:26-30.
51. Horbar, J.D., McAuliffe, T.L., and Adler, S.M. Variability in 28- day outcomes for very low birth weight infants: An analysis of 11 neonatal intensive care units. Pediatrics (1988) 82:554-59.
52. Kraybill, E.N., Bose, C.L., and D'Ercole, A.J. Chronic lung disease in infants with very-low-birthweight: A population based study. American Journal of Diseases of Children (1987) 141:784-88.
53. Jencks, S.F., Daley, J., Draper, D., et al. Interpreting hospital mortality data: The role of clinical risk adjustment. Journal of the American Medical Association (1988) 260:3611-16.
54. Hadorn, D.C., Keeler, E.B., Rogers, W.H., and Brook, R.H. Assessing the performance of mortality prediction models. Santa Monica, CA: RAND, 1993.
55. Pollack, M.M., Ruttiman, U.E., Getson, P.R., et al. Accurate prediction of the outcome of pediatric intensive care: A new quantitative method. New England Journal of Medicine (1987) 316:134-39.
56. Richardson, D.K., Gray, J.E., McCormick, M.C., et al. Score for neonatal acute physiology: A physiologic severity index for neonatal intensive care. Pediatrics (1993) 91:617-23.
57. International Neonatal Network. The CRIB (clinical risk index for babies) score: A tool for assessing initial neonatal risk and comparing performance of neonatal intensive care units. Lancet (1993) 342:193-98.
58. Horbar, J.D., Onstad, L., Wright, E., et al. Predicting mortality risk for infants weighing 501 to 1500 grams at birth: A National Institutes of Health Neonatal Research Network report. Critical Care Medicine (1993) 21:12-18.
59. Richardson, D.K., Gray, J.E., McCormick, M.C., et al. Score for neonatal acute physiology: A physiologic severity index for neonatal intensive care. Pediatrics (1993) 91:617-23.
60. Richardson, D.K., Phibbs, C.S., Gray, J.E., et al. Birth weight and illness severity: Independent predictors of neonatal mortality. Pediatrics (1993) 91:969-75.

61. See note no. 57, International Neonatal Network, for more information about the CRIB score.
62. Horbar, J.D. Birthweight-adjusted mortality rates for assessing the effectiveness of neonatal intensive care. Medical Decision Making (1992) 12:259-64.
63. Park, R.E., Brook, R.H., and Kosecoff, J. Explaining variations in hospital death rates. Journal of the American Medical Association (1990) 264:484-90.
64. Hartz, A.J., Krakauer, H., Kuhn, E.M., et al. Hospital characteristics and mortality rates. New England Journal of Medicine (1989) 321:1720-25.
65. National Perinatal Epidemiology Unit 1991 Report. Oxford: National Perinatal Epidemiology Unit, 1992.
66. Soll, R.F., and McQueen, M.C. Respiratory distress syndrome. In Effective care of the newborn infant. J.C. Sinclair and M.B. Bracken, eds. Oxford: Oxford University Press, 1992, pp. 325-55.
67. HIFI Study Group. High-frequency oscillatory ventilation compared with conventional mechanical ventilation in the treatment of respiratory failure in preterm infants. New England Journal of Medicine (January 12, 1989) 320:88-93.
68. Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter trial of cryotherapy for retinopathy of prematurity: Preliminary results. Pediatrics (1988) 81:697-706.
69. Shannon, K. Recombinant erythropoietin in anemia of prematurity: Five years later. Pediatrics (1993) 92:614-16.
70. Shenai, J.P., Kennedy, K.A., Chytil, F., and Stahlman, M.T. Clinical trial of vitamin A supplementation in infants susceptible to bronchopulmonary dysplasia. Journal of Pediatrics (1987) 111:269-77.
71. Hallman, M., Bry, K., Hoppu, K., et al. Inositol supplementation in premature infants with respiratory distress syndrome. New England Journal of Medicine (1992) 326:1233-39.
72. Yeh, T.F., Torre, J.A., Rastogi, A., et al. Early postnatal dexamethasone therapy in premature infants with severe respiratory distress syndrome: A double-blind, controlled study. Journal of Pediatrics (1990) 117:273-82.
73. La Force, W.R., and Brudno, S. Controlled trials of beclomethasone dipropionate by nebulization in oxygen and ventilator-dependent infants. Journal of Pediatrics (1993) 122:285-88.
74. Traystman, R.J., Kirsch, J.R., and Koehler, R.C. Oxygen radical mechanisms of brain injury following ischemia and reperfusion. Journal of Applied Physiology (1991) 71:1185-95.
75. Valaes, T., Petmezaki, S., Henschke, C., et al. Control of jaundice in preterm newborns by an inhibitor of bilirubin production: Studies with tin-mesoporphyrin. Pediatrics (1994) 93:1-11.
76. Eibi, M.M., Wolf, H.M., Furnkrantz, H., and Rosenbranz, A. Prevention of necrotizing enterocolitis in low-birth-weight infants by IgA-IgG feeding. New England Journal of Medicine (1988) 319:1-7.
77. Lester, B.M., Trunick, E.Z. Introduction: Guidelines for stimulation with preterm infants. Clinics in Perinatology (1990) 17:xv- xvii.
78. Abman, S.H., Kinsella, J.P., Shaffer, M.S., and Wilkening, R.B. Inhaled nitric oxide in the management of a premature newborn with severe respiratory distress and pulmonary hypertension. Pediatrics (1993) 92:606-9.
79. Revenis, M.E., Glass, P., and Short, B.L. Mortality and morbidity rates among lower birth weight infants (2000 to 2500 grams) treated with extracorporeal membrane oxygenation. Journal of Pediatrics (1992) 121:452-58.
80. Greenspan, J.S., Wolfson, M.R., Rubenstein, S.D., and Shaffer, T.H. Liquid ventilation of human preterm neonates. Journal of Pediatrics (1990) 117:106-11.
81. Bancalari, E. Mechanical ventilation--New strategies. Program/Syllabus Hot Topics '93 in Neonatology. Columbus, OH: Ross Laboratories, 1993, pp. 119-32.
82. Phelps, D.L. Retinopathy of prematurity. Current Problems in Pediatrics (September 1992) 22,8:349-71.
83. Bleyer, W.A. The impact of childhood cancer in the United States and the world. CA:A Cancer Journal for Clinicians (1990) 40:355-67.
84. Kramer, S., Meadows, A.T., Pastore, G., et al. Influence of place of treatment on diagnosis, treatment, and survival in three pediatric solid tumors. Journal of Clinical Oncology (1984) 2:917-23.
85. Feinstein, A.R. An additional basic science for clinical medicine: IV. The development of clinimetrics. Annals of Internal Medicine (1983) 99:843-48.
86. Sacks, H.S., Berrier, J., Reitman, D., et al. Meta-analyses of randomized controlled trials. New England Journal of Medicine (1987) 316:450-55.

87. Bracken, M.B. Statistical methods for analysis of effects of treatment on overviews of randomized trials. In Effective care of the newborn infant. J.C. Sinclair and M.B. Bracken, eds. Oxford: Oxford University Press, 1992, pp. 13-18.
88. A classified bibliography of controlled trials in perinatal medicine, 1940-1984. Oxford: Oxford University Press, 1985.
89. Chalmers, I. Oxford database of perinatal trials. Version 1.2, Spring 1992 disk issue 7. Oxford: Oxford University Press, 1992.
90. Chalmers, I., Enkin, M., and Keirse, M., eds. Effective care in pregnancy and childbirth. Vols. 1 and 2. Oxford: Oxford University Press, 1989.
91. Sinclair, J.C., and Bracken, M.B., eds. Effective care of the newborn infant. Oxford: Oxford University Press, 1992.
92. Mercier, C.E., and Soll, R.F. Clinical trials of natural surfactant extract in respiratory distress syndrome. Clinics in Perinatology (1993) 20:711-35.
93. Korper, S., Mosteller, F., and Weissman, N. Cross-design synthesis: A new form of meta-analysis for combining results from randomized clinical trials and medical-practice databases. International Journal of Technology Assessment in Health Care (1993) 9:440-49.
94. Racine, A.D., Joyce, T.J., and Grossman, M. Effectiveness of health services for pregnant women and infants. The Future of Children (Winter 1992) 2,2:40-57.
95. Boyle, M.H., Torrance, G.W., Sinclair, J.C., and Horwood, S.P. Economic evaluation of neonatal intensive care of very-low-birth-weight infants. New England Journal Medicine (1983) 308:1330-37.
96. Detsky, A.S. Are clinical trials a cost-effective investment? Journal of the American Medical Association (1989) 262:1795-1800.
97. Robertson, C., Sauve, R.S., and Christianson, H.E. Province-based study of neurologic disability among survivors weighing 500 through 1249 grams at birth. Pediatrics (1994) 93:636-40.
98. Mugford, M., Piercy, J., and Chalmers, I. Cost implications of different approaches to the prevention of respiratory distress syndrome. Archives of Diseases of Childhood (1991) 66:757-64.
99. Maniscalco, W.M., Kendig, J.W., and Shapiro, D.L. Surfactant replacement therapy: Impact on hospital charges for premature infants with respiratory distress syndrome. Pediatrics (1989) 83:1-6.
100. Tubman, T.R.J., Halliday, H.L., and Normand, C. Cost of surfactant replacement treatment for severe neonatal respiratory distress syndrome: A randomized controlled trial. British Medical Journal (1990) 301:842- 45.
101. Egberts, J. Estimated costs of different treatments of the respiratory distress syndrome in a large cohort of preterm infants of less than 30 weeks of gestation. Biology of the Neonate (1992) 61(suppl. 1):59-65.
102. Merritt, T.A., Hallman, M., Vaucher, Y., et al. Impact of surfactant treatment on cost of neonatal intensive care: A cost benefit analysis. Journal of Perinatology (1990) 10:416-19.
103. Soll, R.F., Jacobs, J., Pashko, S., and Thomas, R. Cost effectiveness of beractant in the prevention of respiratory distress syndrome. PharmacoEconomics (1993) 4:278-86.
104. Joyce, T., Corman, H., and Grossman, M. A cost-effectiveness analysis of strategies to reduce infant mortality. Medical Care (1988) 26:348-60.
105. Greco, P.J., and Eisenberg, J.M. Changing physicians' practices. New England Journal of Medicine (1993) 329:1271-74.
106. Wirtschafter, D.D., Jones, K.R., and Thomas, J.T. Using health care outcomes to improve patient care in the NICU. Journal of Quality Improvement (1994) 10:57-65.
107. Holthof, B., and Prins, P. Comparing hospital perinatal mortality rates: A quality improvement instrument. Medical Care (1993) 31:801-7.
108. Harrison, H. The principles for family-centered neonatal care. Pediatrics (1993) 92:643-50.
109. McCormick, M.C. Has the prevalence of handicapped infants increased with improved survival of the very low birth weight infant? Clinics in Perinatology (1993) 20:263-77.
110. Robertson, M.R.C. Should we look after babies less than 800 grams? Archives of Diseases of Childhood (1993) 68:326-29.
111. Saigal, S., Feeny, D., Furlong, W., et al. Comparison of the health-related quality of life of extremely low birth weight children and a reference group of children at age eight years. Journal of Pediatrics (1994) 125:418-25.
112. Cardiac surgery in New York State. Albany: New York State Department of Health.

Childhood Immunizations

(from the ANA's "Every Child by Two" program)

Abstract

Childhood immunizations, particularly for those under the age of two, are a major health issue. Since the measles epidemic in 1989-1991, the American Nurses Association/ Foundation has collaborated with Every Child By Two (ECBT) to protect the nation's youngest from the ravages of vaccine preventable disease. Immunizations are the first line of prevention for infants and children. Healthy People 2000, together with the Presidential Administration's Childhood Immunization Initiative have mandated a goal of 90% immunizations for children under the age of two by the year 2000. As a nation, we are very close to meeting that goal.

.

Immunizing Infants and Children

This century has seen a dramatic decrease in morbidity and mortality from infectious disease (*Table 1*). Vaccine for diphtheria was introduced in the early part of the century, and was a hallmark for protecting children as well as adults from death and the devastating effects of infectious disease. Shortly thereafter, pertussis and tetanus toxoid were introduced and diphtheria, tetanus and pertussis become the first combination vaccine (dTTP). Polio vaccine became available in the mid-1950s and significantly allayed parental fears that the disease would disable their children. Measles, rubella and mumps vaccine followed in the 1960's.

Table 1: Changes in Vaccine Preventable Disease in the United States

Disease	Year Vaccine Introduced	Peak Yearly Incidence	1997 Incidence	Percent Change
Diphtheria	1925	206,939	5	-99.99%
Measles	1960	894,134	135	-99.98%
Mumps	1967	152,209	612	-99.60%
Pertussis	1925	265,269	5519	-97.92%
H. Influenzae	1988	28,000	165	-99.18%
Poliomyelitis	1954	21,269	0	-100.00%
Rubella	1966	47,686	161	-99.72%
Tetanus Toxoid	1925	1,560***	43	-98.27%

***Mortality

Although many of these diseases were considered "common" childhood illnesses, complications often resulted in significant morbidity and mortality. Hepatitis B was introduced in 1986 as the first recombinant vaccine to provide long-term protection. It was a major breakthrough in providing protection from liver disease and cancer, which costs many thousands of lives each year (Grossman 1995). Although the first dose of this vaccine is administered to infants prior to leaving the hospital, there are two additional doses that are needed. It is recommended that children not immunized prior to 1992, when Hepatitis B became a part of the Advisory Committee for Immunization Practices (ACIP) schedule, now receive this vaccination. Several states now require Hepatitis B for school entry. It is largely the adolescent population that has not been immunized against Hepatitis B. Efforts are currently underway to develop programs in middle and high schools.

Many providers never see a child with meningitis due to the introduction of haemophilus influenzae type b (Hib) vaccine in 1989. The newest vaccine is varicella (chicken pox), introduced in 1996. This vaccine is now recommended by the ACIP. Concurrent with the writing of this continuing education program, rotavirus vaccine was approved by the Food and Drug Administration (FDA). This vaccine is specific to infant diarrhea. In October, 1999 rotavirus vaccine was voluntarily withdrawn from the list of available vaccines due to a potential association between the available vaccine and intussusception (bowel obstruction). Research is ongoing to verify/dispel that association. Other vaccines are anticipated in the next few years, namely pneumococcus conjugate, which will successfully immunize infants against otitis media. It is also anticipated that some of the current vaccines will be eliminated with the global eradication of certain diseases, such as polio and measles. The Centers for Disease Control and Prevention (CDC) is diligently working with many organizations to eradicate polio worldwide by the year 2000 and possibly eradicate measles worldwide in the next ten years.

Eighty percent of the recommended vaccines for children should be given before the age of two. This affords protection during the period of time when children are most susceptible to infectious disease. Most children are fully immunized at school age; however, there are no formal legislative mandates indicating that children be immunized by their second birthday, when they are most vulnerable to the devastating effects of vaccine preventable disease.

In 1992, only 55.3% of children under the age of two had received four DTaPs, three polio and one MMR (4:3:1) (CDC 1997). It was these statistics that initiated President Clinton's Childhood Immunization Initiative (CII). In 1993, the rate rose to 67.1%, and in 1994, it had risen to 72.5%. These rates did not include the Hib vaccine. At this time, we are close to reaching a 90% level; however, there is still a long way to go, with many cities identified by CDC as Pockets of Need (PON) where immunization rates are less than 75%. These cities include: New York City, Los Angeles, Chicago, Houston, Detroit, Philadelphia, San Diego, Dallas, San Antonio, Phoenix and Miami.

The CII identified many initiatives in order to meet the needs of the under-served, undocumented and uninsured children. There has been a significant growth of many partnerships among public and private agencies as well as the development of state and local immunization coalitions. The work of these partnerships has begun to achieve a dramatic increase in immunization rates for children less than two years of age. By their second birthday, children should have received four doses of diphtheria/tetanus/pertussis

(DTaP), four doses of Haemophilus influenza type b, three polio (IPV/OPV), three Hepatitis B (HepB), measles/mumps/ rubella (MMR) and varicella. DTaP is the preferred vaccine for all doses in the vaccination series because it is more effective than DTaP (89% effective in preventing WHO-defined pertussis when given as a three-dose primary series). The goal is to achieve a 90% vaccination level for all infants by the year 2000. Reaching this goal is only the first step in ensuring that young children in the United States are protected from preventable infectious diseases.

In 1994, the Vaccine for Children (VFC) program provided free vaccines for providers to immunize those children who meet certain economic criteria. The Vaccines for Children (VFC) program is a federally funded program. It supplies vaccine at no cost to public and private health care providers who enroll and agree to immunize eligible children in their medical practice or clinic. The VFC program was created by the Omnibus

Budget Reconciliation Act (OBRA) of 1993 and began on October 1, 1994. The VFC program was designed to:

- reduce the cost of vaccines for a physician or medical practice.
- create fewer barriers for parents to immunize their children.
- save parents about $340 per child in expenses for vaccines.
- keep children in their medical home when they qualify for VFC.

Availability of these vaccines allows all children to be immunized in any setting regardless of ability to pay. Any child from birth through 18 years age is eligible to receive VFC supplied vaccine if he/she meets at least one of the following criteria:

- The child does not have health insurance.
- The child is enrolled in Medicaid (including Medicaid HMOs).
- The child is a Native American or Alaskan Native.

Current Recommendations

Development of new vaccines, revised recommendations on timing and dosage, as well as the introduction of combination vaccines, has necessitated yearly revision of the vaccine guidelines for children. These are generated by the ACIP, the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP).

These guidelines are the accepted standard for immunization of infants and children. Children with specialized health care needs may require additional immunizations as is the case with asthmatics needing influenza and pneumococcal vaccine and the HIV positive determining the benefit versus the risk of MMR. Table 2 indicates the acceptable minimum interval between doses, which is helpful when planning an immunization schedule for children whose immunizations are delayed. Table 3 is the Recommended Childhood Immunization Schedule for the United States for the period January - December 2000.

Table 2: Minimum Interval Between Vaccine Doses for Children under Two Years of Age

Vaccine	Minimum age by first dose*	Dose (1 to 2)*	Dose (2 to 3)*	Dose (3 to 4)*
DTaP, DTP, DT†	6 weeks	4 weeks	4 weeks	6 months
HbOC	6 weeks	1 month	1 month	§
PRP-T	6 weeks	1 month	1 month	§
PRP-OPM	6 weeks	1 month	§	--
Polio¶	6 weeks	4 weeks	4 weeks**	††
MMR	12 months§§	1 month	--	--
Hepatitis B	birth	1 month	5 months¶¶	--
Varicella	12 months	4 weeks	--	--

*These minimum acceptable ages and intervals may not correspond with the optimal recommended ages and intervals for vaccination. See tables 3-5 in the ACIP's General Recommendations on Immunization and ACIP's "Recommended Childhood Immunization Schedule, United States, January-December 1998" for the current recommended routine and accelerated vaccination schedules.

†The total number of doses of diphtheria and tetanus toxoids should not exceed six each before the seventh birthday.

§The booster dose of Hib vaccine which is recommended following the primary vaccination series should be administered no earlier than 12 months of age and at least 2 months after the previous dose of Hib vaccine (Tables 3 and 4 of ACIP's General Recommendations on Immunization).

¶Sequential IPV/OPV, all-OPV, or all-IPV.

**For unvaccinated adults at increased risk of exposure to poliovirus with <3 months but >2 months available before protection is needed, three doses of IPV should be administered at least 1 month apart.

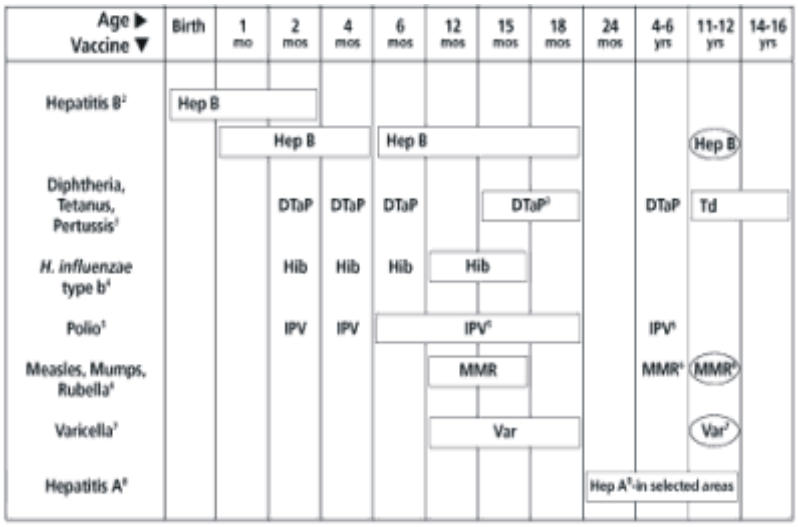
††If the third dose is given after the third birthday, the fourth (booster) dose is not needed.

§§Although the age for measles vaccination may be as young as 6 months in outbreak areas where cases are occurring in children <1 year of age, children initially vaccinated before the first birthday should be revaccinated at 12-15 months of age and an additional dose of vaccine should be administered at the time of school entry or according to local policy. Doses of MMR or other measles-containing vaccines should be separated by at least 1 month.

¶¶This final dose is recommended at least 4 months after the first dose and no earlier than 6 months of age. For children not vaccinated at birth, the recommended interval is first dose at elected date, second dose 1 month later, third dose 5 months after second dose.

Recommended Childhood Immunization Schedule
United States, January - December 2000

Vaccines[1] are listed under routinely recommended ages. Bars indicate range of recommended ages for immunization. Any dose not given at the recommended age should be given as a "catch-up" immunization at any subsequent visit when indicated and feasible. Ovals indicate vaccines to be given if previously recommended doses were missed or given earlier than the recommended minimum age.



Approved by the Advisory Committee on Immunization Practices (ACIP), the American Academy of Pediatrics (AAP), and the American Academy of Family Physicians (AAFP)

[1] This schedule indicates the recommended ages for routine administration of currently licensed childhood vaccines as of 11/1/99. Additional vaccines may be licensed and recommended during the year. Licensed combination vaccines may be used whenever any components of the combination are indicated and its other components are not contraindicated. Providers should consult the manufacturers' package inserts for detailed recommendations.

[2] **Infants born to HBsAg-negative mothers** should receive the 1st dose of hepatitis B (Hep B) vaccine by age 2 months. The 2nd dose should be at least 1 month after the 1st dose. The 3rd dose should be administered at least 4 months after the 1st dose and at least 2 months after the 2nd dose, but not before 6 months of age for infants.

Infants born to HBsAg-positive mothers should receive hepatitis B vaccine and 0.5 mL hepatitis B immune globulin (HBIG) within 12 hours of birth at separate sites. The 2nd dose is recommended at 1 month of age and the 3rd dose at 6 months of age.

Infants born to mothers whose HBsAg status is unknown should receive hepatitis B vaccine within 12 hours of birth. Maternal blood should be drawn at the time of delivery to determine the mother's HBsAg status; if the HBsAg test is positive, the infant should receive HBIG as soon as possible (no later than 1 week of age).

All children and adolescents (through 18 years of age) who have not been immunized against hepatitis B may begin the series during any visit. Special efforts should be made to immunize children who were born in or whose parents were born in areas of the world with moderate or high endemicity of hepatitis B virus infection.

[3] The 4th dose of DTaP (diphtheria and tetanus toxoids and acellular pertussis vaccine) may be administered as early as 12 months of age, provided 6 months have elapsed since the 3rd dose and the child is unlikely to return at age 15 to 18 months. Td (tetanus and diphtheria toxoids) is recommended at 11 to 12 years of age if at least 5 years have elapsed since the last dose of DTP, DTaP, or DT. Subsequent routine Td boosters are recommended every 10 years.

[4] Three Haemophilus influenzae type b (Hib) conjugate vaccines are licensed for infant use. If PRP-OMP (PedvaxHIB or ComVax [Merck]) is administered at 2 and 4 months of age, a dose at 6 months is not required. Because clinical studies in infants have demonstrated that using some combination products may induce a lower immune response to the Hib vaccine component, DTaP/Hib combination products should not be used for primary immunization in infants at 2, 4, or 6 months of age unless FDA-approved for these ages.

[5] To eliminate the risk of vaccine-associated paralytic polio (VAPP), an all-IPV schedule is now recommended for routine childhood polio vaccination in the United States. All children should receive four doses of IPV at 2 months, 4 months, 6 to 18 months, and 4 to 6 years. OPV (if available) may be used only for the following special circumstances:

1. Mass vaccination campaigns to control outbreaks of paralytic polio.
2. Unvaccinated children who will be traveling in <4 weeks to areas where polio is endemic or epidemic.
3. Children of parents who do not accept the recommended number of vaccine injections. These children may receive OPV only for the third or fourth dose or both; in this situation, health care professionals should administer OPV only after discussing the risk for VAPP with parents or caregivers.
4. During the transition to an all-IPV schedule, recommendations for the use of remaining OPV supplies in physicians' offices and clinics have been issued by the American Academy of Pediatrics (see Pediatrics, December 1999).

[6] The 2nd dose of measles, mumps, and rubella (MMR) vaccine is recommended routinely at 4 to 6 years of age but may be administered during any visit, provided at least 4 weeks have elapsed since receipt of the first dose and that both doses are administered beginning at or after 12 months of age. Those who have not previously received the second dose should complete the schedule by 11-12 years old.

[7] Varicella (Var) vaccine is recommended at any visit on or after the first birthday for susceptible children, i.e., those who lack a reliable history of chickenpox (as judged by a

health care professional) and who have not been immunized. Susceptible persons 13 years of age or older should receive 2 doses, given at least 4 weeks apart.

[8] Hepatitis A (Hep A) is shaded to indicate its recommended use in selected states and/or regions; consult your local public health authority. (Also see MMWR Morb. Mortal Wkly Rep. Oct. 01, 1999;48(RR-12); 1-37).

Barriers to Infant Immunization

Although the safety and efficacy of infant/childhood immunizations have been proven, there are still many barriers that prevent protecting vulnerable population groups from preventable diseases. These multiple barriers are currently addressed in these areas:

- economic and cultural risk factors
- provider practices
- families
- inadequate knowledge

Economic and Cultural Risk Factors

Demographic and social support variables indicate that children are at risk for many diseases. Data from the CDC National Immunization Survey indicates that children living below the poverty level and that Black and Hispanic children had immunization rates below the national average (CDC 1997). A study in Baltimore found that children of teenage mothers, children in large families, and children whose mothers lack social support systems had lower immunization rates at age two. Most of these mothers believed that immunizations protected their children from disease and that these diseases had serious consequences; however, these parents also believed that timing of immunizations did not matter (Strobino, Keane, Holt, Hughart and Guyer 1996).

A study of Mexican American mothers by Guendelman, English and Chavez (1995) found that children of mothers who smoked, drank alcohol, were unaware of child safety measures, had a stressful event since birth of the child, lived in chaotic households, or were new to their neighborhood had lower immunization rates. A large study of public and private patients in Texas by Suarez, Simpon and Smith (1997) found that immunization rates for families with private insurance and those using public clinics were the same, but families with Medicaid coverage had lower immunization rates. Families receiving Aid to Families with Dependent Children (AFDC) also had lower rates. Similarly, Houseman, Butterfoss, Morrow and Rosenthal (1997) found that mothers with fewer resources found it more difficult to succeed in obtaining immunizations for their children. Other identified risk factors include low parental educational level, low socioeconomic status, inability to access appropriate transportation, nonwhite race, single parent family, lack of parental care, and a late start on the immunization series (Pruitt, Kline and Kovaz 1995). Knowledge of these risk factors for inadequate immunization must be incorporated into strategies to increase rates.

Provider Practices

Policies and procedures in office settings can be barriers to timely immunization. Missed opportunities are the most significant barrier among clinicians. Many reasons are given for this (Szilagyi et al. 1996): immunization status is not evaluated at each well child and acute care visit, immunizations are not given when the need is identified, immunizations are delayed for non-valid contraindications, all vaccines needed are not given at one visit and immunizations are not provided in the absence of a complete physical exam. Watson (1996) found that 78% of a group of public and private patients did not bring an immunization record to a visit. This percentage was the same for both well and sick child visits to a provider.

Focus groups conducted (Houseman et al. 1997) identified additional practice setting barriers. These were:

- Parents were unable to obtain appointments in a timely manner, with some experiencing delays of 4-6 weeks. Families in stressed households found it difficult to effectively plan that far in advance.
- There were inflexible office schedules with immunizations only being administered by appointment, during a physical exam with no weekend or evening coverage.
- The office environment was frequently non-conducive with long waits for small children in crowded waiting rooms.
- Phone access was often difficult with frequent busy signals and being left on hold for long periods of time. These were considered inconvenient by many poor households without phones.
- Attitudes of staff in offices were frequently insensitive, with many mothers from low-income families feeling that staff treated them in a condescending manner, particularly if their child was behind schedule. They also felt that they were not given adequate explanations and information.
- Personal safety concerns were expressed about the location of some clinics.
- Parents had misconceptions about the safety of vaccines and their contraindications (*Tables 4-5*). Minor and serious side effects caused some parents to delay immunizations.

Table 4: General Contraindications and Precautions to Vaccinate

True Contraindications	Non-Contraindications
□ Anaphylactic reaction to vaccine, or vaccine constituent (eg. eggs, yeast) □ Severe illness with or without fever □ Known altered immune state	□ Mild to moderate local reaction following a dose of an injectable antigen (eg. low-grade fever, mild acute illness with or without a fever.)

Table 5: Events Reportable to the National Vaccine Injury Compensation Program Following Vaccination

Vaccine	Adverse Event	Interval from vaccination (n)
Tetanus in any combination	□ Anaphylaxis or anaphylactic shock	7 days
same as above	□ Brachial neuritis	23 days
Pertussis in any combination	□ Anaphylaxis or anaphylactic shock	7 days
same as above	□ Encephalopathy	7 days
Measles, mumps, rubella in any combination	□ Anaphylaxis or anaphylactic shock	7 days
same as above	□ Encephalopathy	15 days
Rubella in any combination	□ Chronic arthritis	42 days
Measles in any combination in an immunodeficient recipient	□ Thrombocytopenic purpura	30 days
same as above	□ Vaccine-strain measles viral infection	6 months
OPV	□ Paralytic polio or vaccine-strain polio viral infection	
same as above	- in a non-immunodeficient recipient	30 days
same as above	- in an immunodeficient recipient	6 months
same as above	- in a vaccine-associated community case	No limit

Strategies to Eliminate Barriers

In order to effectively achieve a 90% immunization level for our nation's children under the age of two, it is important to strengthen provider practices, educate parents and provide access to the under served, the uninsured, and the undocumented. Every child is important and will be served by these efforts. The following strategies should be operationalized.

Avoid Missed Opportunities to Immunize. In every setting — office, clinic, school, home, emergency room — health care providers can assess each child's immunization status. If immunizations are needed, immunize immediately, and if not possible, assist the

parent to make arrangements for the child to be immunized as soon as possible. Develop referral mechanisms in practice settings.

Educate Staff and Parents. Information as well as continuing education programs should be available for staff in all settings to acquaint them with the Standards for Pediatric Immunization Practice (*Table 6*). Current vaccine administration guidelines are provided annually by the ACIP and are available in professional journals and directly on the CDC Internet site. As new vaccines become available, updates and inservice programs must be provided to all practitioners.

Table 6: Standards for Pediatric Immunization Practice

- Immunization services are readily available.
- There are no barriers or unnecessary prerequisites to the receipt of vaccines.
- Immunization services are available free or for a minimal fee.
- Providers utilize all clinical encounters to screen for needed vaccines and when indicated, vaccinate.
- Providers educate parents and guardians about immunization in general terms.
- Providers question parents or guardians about contraindications and, before vaccinating a child, inform them in specific terms about the risks and benefits of the vaccinations their child is to receive.
- Providers follow only true contraindications.
- Providers administer simultaneously all vaccine doses for which a child is eligible at the time of each visit.
- Providers use accurate and complete recording procedures.
- Providers co-schedule immunization appointments in conjunction with appointments for other child health services.
- Providers report adverse events following vaccination promptly, accurately, and completely.
- Providers operate a tracking system.
- Providers adhere to appropriate procedures for vaccine management.
- Providers conduct semiannual audits to assess immunization coverage levels and to review immunization records in the patient populations they serve.
- Providers maintain up-to-date, easily retrievable medical protocols at all locations where vaccines are administered. Providers practice patient-oriented and community-based approaches.
- Vaccines are administered by properly trained persons.
- Providers receive ongoing education and training regarding current immunization recommendations.

Parents also need education. They should be provided with the necessary information about reactions within 48 hours post inoculation that may require additional medical intervention. Although serious adverse events are rare, children who are seriously or fatally injured as a result of immunization can seek compensation through the National Vaccine Injury

Compensation Program (*Table 5*). It is required that these be reported using the Vaccine Adverse Events Reporting System form available in all provider practices.

Identify Children in Need. Development of protocols for identification of children in need of immunization is imperative. Gill and Fisher (1997) found that three steps were useful in increasing immunization rates in a primary care setting: use of a tracking sheet recording the child's record, all dosages and contraindications, placing a stamp on each progress note for sick and well visits with nurses checking for immunizations on the progress note and alerting physicians. Reasons for non-administration of vaccine also were recorded.

Evaluate Existing Policies and Procedures. Office operation/environment can prove to be a barrier to infant immunization. Hughart et al. (1997) found that providing immunizations outside of regular well-child care visits would not necessarily decrease attendance at visits for well-child care. Office protocols should be developed to enable providers to automatically administer immunizations under standing orders (Gill and Fisher 1997).

Utilize a Tracking System. Computerized tracking systems can yield data to remind parents about appointments, to identify children with delayed immunizations, and to monitor and evaluate the practice efforts to reach the children in that particular practice. These programs will send postcards to parents as reminders. Alemi et al. (1996) found that the use of computer-generated telephone reminders to the parents' home was a very effective strategy to improve immunization rates.

Nursing Role in Immunization Practice

The leadership role undertaken by nurses in immunizing children is well-documented. They practice in multiple settings, are the largest number of health care providers and collaborate with many other professionals and groups. They are vital to the mobilization and outreach efforts of state coalitions, are frequently the first person seen by consumers in any health care setting, and have developed innovative programs for the immunization of children throughout the United States (ANA 1993). Their knowledge base, advocacy role and conceptual framework of health promotion and disease prevention provide a strong basis for their role in immunizing children.

Community health nurses in home care settings, clinics, and schools can assess children for immunization status and immunize siblings at school settings. Nurses have been effective advocates linking immunization sites with other services such as Women Infants and Children (WIC) and Aid For Dependent Children (AFDC). Nurses have an opportunity to educate providers about registries and develop the needed linkages with provider practices in states. As educators, nurses utilize students in clinic settings, teach childhood immunizations, physical assessment, and also work in faculty practice settings/nurse-run clinics to make certain that children in all settings receive appropriate health care.

Conclusion

As we enter a new century, health care in America will undergo major changes, revisions and challenges. The health of children must remain a major priority. Their first line of defense against disease is immunizations. We are close to reaching a major goal of assuring

that all children receive timely immunizations by the time they are two years of age. We must not allow the ravages of another measles or other epidemic to take the lives of our children. The next few years will be critical in this effort. Nurses have a significant challenge ahead to maintain their leadership role in the delivery of vaccine, to educate consumers, to collaborate with others to develop innovative strategies to eliminate barriers and to develop policies that will mandate that all children be immunized by their second birthday. Anything less than a total commitment to this effort on the part of all health care providers is unacceptable.

References

Alemi, F., Alemagno, S., Goldhagen, J., Ash, L., Finkelstein, B., Lavin, A., Butts, & Ghadiri, A. (1996). Computer reminders improve on-time immunization rates. Medical Care, 34 (10 supp), OS45-OS51.

American Nurses Association (1994). Urban and Rural Immunization Initiatives. Washington, D.C.: ANA Publishing.

Centers for Disease Control and Prevention (CDC) (1997). Vaccination coverage by race/ethnicity and poverty level among children aged 19-35 months - United States, 1996. MMWR, 46, 963-968.

Gill, J. & Fisher, J. (1997). Improving childhood immunizations in a family practice office. Delaware Medical Journal, 69 (1) , 13-16.

Grossman, M. (1995). Immunization: Past successes, future challenges. Infectious Disease Clinics of North America, 9, 325-333.

Guendelman, S., English, P., & Chavez, G. (1995). The effects of maternal health behaviors and other risk factors on immunization status among Mexican-American infants. Pediatrics 95, 823-828.

Houseman, C., Butterfoss, F., Morrow., & Rosenthal, J. (1997). Focus groups among public, military, and private sector mothers: Insights to improve the immunization process. Public Health Nursing, 14, 235-243.

Hughart, N., Vivier, P., Ross, A., Strobina, D., Holt., E., Hou, W. & Guyer, B. (1997). Archives of Pediatric and Adolescent Medicine, 151, 690-695.

Kimmel, S., Madlon-Kay, D., Burns, I. & Admire, J. (1996). Breaking the barriers to childhood immunization. American Family Physician, 53, 1648-1656.

Pruitt, R., Kline, P. & Kovaz, R. (1995). Perceived barriers to childhood immunizations among rural populations. Journal of Community Health Nursing, 12 (2), 65-72.

Strobino, D., Keane, V., Holt, E., Hughart., N. & Guyer, B. (1996). Parental attitudes do not explain under immunization. Pediatrics, 98, 1076-1083.

Suarez, L., Simpson. D. & Smith, D. (1997). The impact of public assistance factors on the immunization levels of children younger than 2 years. American Journal of Public Health, 87, 845-848.

U. S. Department of Health and Human Services. (1993). Standards for Pediatric Immunization Practice. Centers for Disease Control and Prevention (CDC). Atlanta: National Immunization Program.

Neonatal Nutrition

.At this time, we would like to have you review information relating to infant nutrition. We begin with an often controversial subject, Breast-feeding:

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Policy Statement

Pediatrics **Volume 100, Number 6** **December 1997, pp 1035-1039**

Breast-feeding and the Use of Human Milk (RE9729)

AMERICAN ACADEMY OF PEDIATRICS

Work Group on Breast-feeding

ABSTRACT. This policy statement on breast-feeding replaces the previous policy statement of the American Academy of Pediatrics, reflecting the considerable advances that have occurred in recent years in the scientific knowledge of the benefits of breast-feeding, in the mechanisms underlying these benefits, and in the practice of breast-feeding. This document summarizes the benefits of breast-feeding to the infant, the mother, and the nation, and sets forth principles to guide the pediatrician and other health care providers in the initiation and maintenance of breast-feeding. The policy statement also delineates the various ways in which pediatricians can promote, protect, and support breast-feeding, not only in their individual practices but also in the hospital, medical school, community, and nation.

ABBREVIATION. AAP, American Academy of Pediatrics

HISTORY AND INTRODUCTION

From its inception, the American Academy of Pediatrics (AAP) has been a staunch advocate of breast-feeding as the optimal form of nutrition for infants. One of the earliest AAP publications was a 1948 manual, *Standards and Recommendations for the Hospital Care of Newborn Infants*. This manual included a recommendation to make every effort to have every mother nurse her full-term infant. A major concern of the AAP has been the development of guidelines for proper nutrition for infants and children. The activities, statements, and recommendations of the AAP have continuously promoted breast-feeding of infants as the foundation of good feeding practices.

THE NEED

Extensive research, especially in recent years, documents diverse and compelling advantages to infants, mothers, families, and society from breast-feeding and the use of human milk for infant feeding. These include health, nutritional, immunologic, developmental, psychological, social, economic, and environmental benefits.

Human milk is uniquely superior for infant feeding and is species-specific; all substitute feeding options differ markedly from it. The breast-fed infant is the reference or normative model against which all alternative feeding methods must be measured with regard to growth, health, development, and all other short- and long-term outcomes.

Epidemiologic research shows that human milk and breast-feeding of infants provide advantages with regard to general health, growth, and development, while significantly decreasing risk for a large number of acute and chronic diseases. Research in the United States, Canada, Europe, and other *developed* countries, among predominantly middle-class populations, provides strong evidence that human milk feeding decreases the incidence and/or severity of diarrhea,[1-5] lower respiratory infection,[6-9] otitis media,[3,10-14] bacteremia,[15,16] bacterial meningitis,[15,17] botulism,[18] urinary tract infection,[19] and necrotizing enterocolitis.[20,21] There are a number of studies that show a possible protective effect of human milk feeding against sudden infant death syndrome,[22-24] insulin-dependent diabetes mellitus,[25-27] Crohn's disease,[28,29] ulcerative colitis,[29] lymphoma,[30,31] allergic diseases,[32-34] and other chronic digestive diseases.[35-37] Breast-feeding has also been related to possible enhancement of cognitive development.[38,39]

There are also a number of studies that indicate possible health benefits for mothers. It has long been acknowledged that breast-feeding increases levels of oxytocin, resulting in less postpartum bleeding and more rapid uterine involution.[40] Lactational amenorrhea causes less menstrual blood loss over the months after delivery. Recent research demonstrates that lactating women have an earlier return to prepregnant weight,[41] delayed resumption of ovulation with increased child spacing,[42-44] improved bone remineralization postpartum[45] with reduction in hip fractures in the postmenopausal period,[46] and reduced risk of ovarian cancer[47] and premenopausal breast cancer.[48]

In addition to individual health benefits, breast-feeding provides significant social and economic benefits to the nation, including reduced health care costs and reduced employee absenteeism for care attributable to child illness. The significantly lower incidence of illness in the breast-fed infant allows the parents more time for attention to siblings and other family duties and reduces parental absence from work and lost income. The direct economic benefits to the family are also significant. It has been estimated that the 1993 cost of purchasing infant formula for the first year after birth was $855. During the first 6 weeks of lactation, maternal caloric intake is no greater for the breast-feeding mother than for the nonlactating mother.[49,50] After that period, food and fluid intakes are greater, but the cost of this increased caloric intake is about half the cost of purchasing formula. Thus, a saving of >$400 per child for food purchases can be expected during the first year.[51,52]

Despite the demonstrated benefits of breast-feeding, there are some situations in which breast-feeding is not in the best interest of the infant. These include the infant with galactosemia,[53,54] the infant whose mother uses illegal drugs,[55] the infant whose mother has untreated active tuberculosis, and the infant in the United States whose mother has been

infected with the human immunodeficiency virus.[56,57] In countries with populations at increased risk for other infectious diseases and nutritional deficiencies resulting in infant death, the mortality risks associated with not breast-feeding may outweigh the possible risks of acquiring human immunodeficiency virus infection.[58] Although most prescribed and over-the-counter medications are safe for the breast-fed infant, there are a few medications that mothers may need to take that may make it necessary to interrupt breast-feeding temporarily. These include radioactive isotopes, antimetabolites, cancer chemotherapy agents, and a small number of other medications. Excellent books and tables of drugs that are safe or contraindicated in breast-feeding are available to the physician for reference, including a publication from the AAP.[55]

THE PROBLEM

Increasing the rates of breast-feeding initiation and duration is a national health objective and one of the goals of Healthy People 2000. The target is to "increase to at least 75% the proportion of mothers who breast-feed their babies in the early postpartum period and to at least 50% the proportion who continue breast-feeding until their babies are 5 to 6 months old." [59] Although breast-feeding rates have increased slightly since 1990, the percentage of women currently electing to breast-feed their babies is still lower than levels reported in the mid-1980s and is far below the Healthy People 2000 goal. In 1995, 59.4% of women in the United States were breast-feeding either exclusively or in combination with formula feeding at the time of hospital discharge; only 21.6% of mothers were nursing at 6 months, and many of these were supplementing with formula.[60]

The highest rates of breast-feeding are observed among higher-income, college-educated women >30 years of age living in the Mountain and Pacific regions of the United States.[60] Obstacles to the initiation and continuation of breast-feeding include physician apathy and misinformation,[61-63] insufficient prenatal breast-feeding education,[64] disruptive hospital policies,[65] inappropriate interruption of breastfeeding,[62] early hospital discharge in some populations,[66] lack of timely routine follow-up care and postpartum home health visits,[67] maternal employment[68,69] (especially in the absence of workplace facilities and support for breast-feeding),[70] lack of broad societal support,[71] media portrayal of bottle-feeding as normative,[72] and commercial promotion of infant formula through distribution of hospital discharge packs, coupons for free or discounted formula, and television and general magazine advertising.[73,74]

The AAP identifies breast-feeding as the ideal method of feeding and nurturing infants and recognizes breast-feeding as primary in achieving optimal infant and child health, growth, and development. The AAP emphasizes the essential role of the pediatrician in promoting, protecting, and supporting breast-feeding and recommends the following breast-feeding policies.

RECOMMENDED BREASTFEEDING PRACTICES

1. Human milk is the preferred feeding for all infants, including premature and sick newborns, with rare exceptions.[75-77] The ultimate decision on feeding of the infant is the mother's. Pediatricians should provide parents with complete, current information on the benefits and methods of breast-feeding to ensure that the feeding

decision is a fully informed one. When direct breast-feeding is not possible, expressed human milk, fortified when necessary for the premature infant, should be provided.[78,79] Before advising against breast-feeding or recommending premature weaning, the practitioner should weigh thoughtfully the benefits of breast-feeding against the risks of not receiving human milk.

2. Breast-feeding should begin as soon as possible after birth, usually within the first hour.[80-82] Except under special circumstances, the newborn infant should remain with the mother throughout the recovery period.[80,83,84] Procedures that may interfere with breast-feeding or traumatize the infant should be avoided or minimized.
3. Newborns should be nursed whenever they show signs of hunger, such as increased alertness or activity, mouthing, or rooting.[85] Crying is a ***late*** indicator of hunger.[86] Newborns should be nursed approximately 8 to 12 times every 24 hours until satiety, usually 10 to 15 minutes on each breast.[87,88] In the early weeks after birth, nondemanding babies should be aroused to feed if 4 hours have elapsed since the last nursing.[89,90] Appropriate initiation of breast-feeding is facilitated by continuous rooming-in.[91] Formal evaluation of breast-feeding performance should be undertaken by trained observers and fully documented in the record during the first 24 to 48 hours after delivery and again at the early follow-up visit, which should occur 48 to 72 hours after discharge. Maternal recording of the time of each breast-feeding and its duration, as well as voidings and stoolings during the early days of breast-feeding in the hospital and at home, greatly facilitates the evaluation process.
4. No supplements (water, glucose water, formula, and so forth) should be given to breast-feeding newborns unless a medical indication exists.[92-95] With sound breast-feeding knowledge and practices, supplements rarely are needed. Supplements and pacifiers should be avoided whenever possible and, if used at all, only after breast-feeding is well established.[93-98]
5. When discharged <48 hours after delivery, all breast-feeding mothers and their newborns should be seen by a pediatrician or other knowledgeable health care practitioner when the newborn is 2 to 4 days of age. In addition to determination of infant weight and general health assessment, breast-feeding should be observed and evaluated for evidence of successful breast-feeding behavior. The infant should be assessed for jaundice, adequate hydration, and age-appropriate elimination patterns (at least six urinations per day and three to four stools per day) by 5 to 7 days of age. All newborns should be seen by 1 month of age.[99]
6. Exclusive breast-feeding is ideal nutrition and sufficient to support optimal growth and development for approximately the first 6 months after birth.[100] Infants weaned before 12 months of age should not receive cow's milk feedings but should receive iron-fortified infant formula.[101] Gradual introduction of iron-enriched solid foods in the second half of the first year should complement the breast milk diet.[102,103] It is recommended that breast-feeding continue for at least 12 months, and thereafter for as long as mutually desired.[104]
7. In the first 6 months, water, juice, and other foods are generally unnecessary for breast-fed infants.[105,106] Vitamin D and iron may need to be given before 6 months of age in selected groups of infants (vitamin D for infants whose mothers are vitamin D-deficient or those infants not exposed to adequate sunlight; iron for those who have low iron stores or anemia).[107-109] Fluoride should not be administered to infants during the first 6 months after birth, whether they are breast- or formula-fed. During the period from 6 months to 3 years of age, breast-fed infants (and formula-

fed infants) require fluoride supplementation only if the water supply is severely deficient in fluoride (<0.3 ppm).[110]

8. Should hospitalization of the breast-feeding mother or infant be necessary, every effort should be made to maintain breast-feeding, preferably directly, or by pumping the breasts and feeding expressed breast milk, if necessary.

ROLE OF PEDIATRICIANS IN PROMOTING AND PROTECTING BREASTFEEDING

To provide an optimal environment for breast-feeding, pediatricians should follow these recommendations:

1. Promote and support breast-feeding enthusiastically. In consideration of the extensive published evidence for improved outcomes in breast-fed infants and their mothers, a strong position on behalf of breast-feeding is justified.
2. Become knowledgeable and skilled in both the physiology and the clinical management of breast-feeding.
3. Work collaboratively with the obstetric community to ensure that women receive adequate information throughout the perinatal period to make a fully informed decision about infant feeding. Pediatricians should also use opportunities to provide age-appropriate breast-feeding education to children and adults.
4. Promote hospital policies and procedures that facilitate breast-feeding. Electric breast pumps and private lactation areas should be available to all breast-feeding mothers in the hospital, both on ambulatory and inpatient services. Pediatricians are encouraged to work actively toward eliminating hospital practices that discourage breast-feeding (eg, infant formula discharge packs and separation of mother and infant).
5. Become familiar with local breast-feeding resources (eg, Special Supplemental Nutrition Program for Women, Infants, and Children clinics, lactation educators and consultants, lay support groups, and breast pump rental stations) so that patients can be referred appropriately.[111] When specialized breast-feeding services are used, pediatricians need to clarify for patients their essential role as the infant's primary medical care taker. Effective communication among the various counselors who advise breast-feeding women is essential.
6. Encourage routine insurance coverage for necessary breast-feeding services and supplies, including breast pump rental and the time required by pediatricians and other licensed health care professionals to assess and manage breast-feeding.
7. Promote breast-feeding as a normal part of daily life, and encourage family and societal support for breast-feeding.
8. Develop and maintain effective communications and collaboration with other health care providers to ensure optimal breast-feeding education, support, and counsel for mother and infant.
9. Advise mothers to return to their physician for a thorough breast examination when breast-feeding is terminated.
10. Promote breast-feeding education as a routine component of medical school and residency education.
11. Encourage the media to portray breast-feeding as positive and the norm.

12. Encourage employers to provide appropriate facilities and adequate time in the workplace for breast-pumping.

CONCLUSION

Although economic, cultural, and political pressures often confound decisions about infant feeding, the AAP firmly adheres to the position that breast-feeding ensures the best possible health as well as the best developmental and psychosocial outcomes for the infant. Enthusiastic support and involvement of pediatricians in the promotion and practice of breast-feeding is essential to the achievement of optimal infant and child health, growth, and development.

Parenteral Nutrition in the Neonatal and Pediatric Patient

Advances in medical and surgical technology have allowed for the successful management of congenital and acquired diseases in the pediatric patient, as well as better outcomes in premature births.[1,2] However, adequate nutrition is essential for the survival and growth of this population.[3] Optimal use of parenteral nutrition has resulted in a substantial reduction in mortality among critically ill infants. Unlike the adult population, endogenous nutrient reserves are limited in the pediatric populations and can be quickly depleted with the metabolic stresses from surgical procedures or disease.[4,5] In addition, good nutrition is an essential factor in the growth and development of the pediatric patient.[6]

Within the pediatric population, nutritional needs differ by age, from the premature or low birth weight neonate to the adolescent. Low birth weight or premature neonates are at the highest risk for mortality and represent the largest percentage of the pediatric population who receive parenteral nutrition.[7,8] For the purposes of this review, the term neonate will apply to this high risk group.

Age groups within the pediatric population[7,9]

Premature or preterm	Birth before 37 weeks of gestation
Neonate	Birth to 4 weeks of age
Infant	1 month to 2 years of age
Child	2 to 12 years of age
Adolescent	12 to 16 years of age

Definitions by weight[7]

Low birth weight (LBW)	Infants weighing less than 2500 g
Moderately low birth weight (MLBW)	Infants weighing 1500 to less than 2500 g
Very low birth weight (VLBW)	Infants weighing less than 1500 g
Extremely low birth weight (ELBW)	Infants weighing less than 1000 g

Indications for Parenteral Nutrition in Pediatric Patients

Nutrition needs of the neonate and pediatric patient differ significantly from adults.[10] Smaller body size, more rapid growth, immature organ systems, and more variable fluid requirements are factors that can influence the nutritional needs of the pediatric patient, especially the neonate.

Indications for parenteral nutrition

- Low birth weight.
- Major surgery.
- Gastrointestinal tract anomalies.
- Inflammatory bowel disease.
- Respiratory disorders.
- Sepsis.
- Burns.
- Major trauma.
- Malignancies.

Other conditions that make parenteral nutrition necessary include conditions which may result in a hypercatabolic state, such as burns, trauma or malignancies.

In addition, infants born prematurely do not accumulate nutrient stores. In the neonate unable to take oral feedings, endogenous nutrient stores may be depleted within 3 to 4 days without parenteral nutrition, resulting in protein-calorie malnutrition or vitamin and trace element deficiencies. Following is a list of signs and symptoms associated with these conditions:

Vitamin/trace element deficiencies

- Changes in oral mucosa.
- Growth retardation.
- Skin lesions.
- Pale conjunctiva.

- Pallor.

Protein-calorie malnutrition

- Muscle wasting.
- Edema.
- Scaly skin.
- Dry/brittle hair.

Nutritional Assessment

Weight, height, daily fluid balance, and visceral proteins as well as physical examination are all used in nutritional assessment of the pediatric patient. These measures can be used to identify malnutrition or other deficiencies as well as to monitor response to parenteral nutrition.[11]

Measurements used in nutritional assessment: [11]

Weight

- Performed daily for all pediatric patients on parenteral nutrition.
- Infant should wear same amount of clothing for each weighing.
- Same scales should be used.
- Weight should be taken at the same time each day.

Intake and output

- Measured daily.

- Intake includes all fluids received (maintenance and replacement fluids as well as medications).
- Output includes all fluids lost (urine, stool, nasogastric or gastrostomy tube drainage, emesis, and wound drainage).

Growth curves

- Standardized charts based on height, weight, and head circumference values derived from general pediatric population.
- Use as preliminary assessment of nutritional status.
- Can be used to differentiate between acute active and chronic malnutrition.
- Also used to assess growth and response to parenteral nutrition.

Anthropometric measurements (subcapsular and triceps skinfold thickness, midarm muscle circumference)

- Estimates body fat and muscle mass.
- Used less frequently than height and weight measurements.
- Compared to population standards.
- Site and technique need to be consistent to reduce variability.

Visceral proteins

	Half-Life
Serum albumin	20 days
Transferrin	7 days
Prealbumin	2 days
Retinol-binding protein	2 days

Fluid/Water Requirements

Maintaining appropriate fluid balance in the pediatric patient is essential. Dehydration, hypernatremia and hyperosmolarity may occur if fluid intake is inadequate. Excess fluid administration may result in fluid overload, manifesting as pulmonary or peripheral edema or congestive heart failure, especially in the neonate with pulmonary, renal or cardiovascular abnormalities.[11] Differences in body water composition and immature renal function are two factors that make the neonate more susceptible to dehydration and electrolyte imbalances than older infants or adults.[5] In comparison to adults, water accounts for a much larger percentage of body weight in neonates, as much as 80%, with a greater proportion as extracellular fluid. As a result, daily fluid requirements are higher in the neonate than in adults. These requirements are increased with decreased birth weight, especially during the first days of life.[12]

Fluid/Water Loss

Most insensible or evaporative water loss in the neonate and infant occurs via the skin and respiratory tract, with about two-thirds due to losses from the skin. In the neonate, immature skin allows for greater water permeability. In addition, neonates and infants have a high surface area to body weight ratio and more highly vascular skin than older children or adults. All these physiologic factors contribute to high evaporative water losses, especially during the few first days of life.[12,13] Environmental factors also contribute to insensible fluid losses in the neonate. Exposure to warmer temperatures will increase insensible losses, as will low humidity. Use of radiant warmers or phototherapy may increase insensible losses by as much as 50%. However, plastic heat shields may reduce insensible water loss by 10% to 30%.

Conditions influencing insensible water losses

- Surrounding temperature.
- Humidity level.
- Radiant warmers.
- Phototherapy.

- Plastic shields.
- Infant age and body weight.
- Body temperature.
- Skin integrity.

Fluid Requirements:[10]

Weight	Fluid volume per 24 hours*
Premature, < 2 kg	150 mL/kg
Neonates and infants, 2-10 kg	100 mL/kg for the first 10 kg
Infants and children, 10-20 kg	1000 mL + 50 ml/kg over 10 kg
Children, >20 kg	1500 mL + 20 ml/kg over 20 kg

*fluid intake in premature or low birth weight neonates must be carefully monitored during the first few days of life; fluids should be initiated at 75 to 100 ml/kg and increased cautiously.

Energy Requirements

As with fluids, the energy needs of pediatric patients are balanced between energy intake and energy loss plus storage for growth.[13] Energy requirements for the neonate are higher than those of the full term infant, with the neonate requiring more energy for protein synthesis and growth.

Energy requirements in kilocalories for parenteral nutrition [10,14]

Age	Caloric Need - kcal/kg/day
Preterm neonates	120-140
<6 months	90-120
6-12 months	80-100
1-7 years	75-90
7-12 years	60-75

12-18 years	30-60
Factors increasing caloric requirements [10]	
Fever	12% increase for each degree >37°C
Major surgery	20% to 30% increase
Severe sepsis	40% to 50% increase
Long-term growth failure	50% to 100% increase

Energy is supplied in the form of carbohydrates and fat. Protein is administered for tissue synthesis and repair. Most calories for energy (nonprotein calories) are supplied as carbohydrates, most commonly dextrose, with fat administered to avoid essential fatty acid deficiency.[10]

Macronutrient	Amount required[10]
Carbohydrates	0.4 to 1.5 g/kg/hr
Protein*	1 to 2.5 g protein/kg/day (1 g protein = 0.16 g nitrogen)
Fat	1 to 4 g/kg/day**

* for every gram of nitrogen, 150 to 300 nonprotein calories (as dextrose and fat) should be provided to prevent utilization of protein calories for energy

**up to 3 g/kg/day for premature neonates; 0.5 to 1 g/kg/day will prevent essential fatty acid deficiency in neonates

---

Nitrogen/Protein/Amino Acids

Amino acids, which are characterized by their nitrogen content, are the primary component for synthesis of structural (skeletal muscle) and functional (visceral proteins, enzymes, etc.) proteins. Protein requirements in neonates are greater than those needed by older infants or

adults, and these requirements decline with age.[15] During the third trimester, the fetus undergoes rapid growth and accumulates body proteins and stores of other nutrients, such as glycogen, fat, and minerals.[5] However, neonates born prematurely do not accumulate these nutrient stores and require early supplementation in the form of parenteral nutrition. Without parenteral nutrition, endogenous nutrient stores in the neonate unable to tolerate oral feedings may be depleted within three to four days.

As in adults, protein requirements are increased in the neonate, infant and child secondary to stress. However, unlike the adult, the pediatric patient has additional protein requirements for growth and development. In addition to requiring higher amounts of protein, different types of amino acids are needed by neonates. Amino acids have been classified as essential, nonessential or conditionally (or acquired) essential. Essential amino acids cannot be synthesized by the human body and are needed to maintain and promote cell growth.[5] The nonessential amino acids are available as metabolites of other amino acids or precursors via enzymatic degradation. In older infants, tyrosine and cysteine are synthesized from phenylalanine and methionine.

However, in the neonate the enzymatic pathways for synthesis of these and other amino acids are immature. Use of standard amino acid solution in neonates has resulted in excesses of methionine, phenylalanine, and glycine.[16] Therefore, in the neonate, certain amino acids (cysteine, taurine, tyrosine and histidine) are considered conditionally essential or acquired essential amino acids, since the neonate lacks the enzymes necessary for their production. [5,16] For this reason, 10% lipid emulsions are avoided in pediatric patients.

Essential Amino acids:	Nonessential Amino Acids:	Conditionally or Acquired Essential Amino Acids:
Isoleucine	Alanine	· Cysteine
· Leucine	· Aspartic acid	· Tyrosine
· Lysine	· Asparagine	· Taurine
· Methionine	· Glutamic acid	· Histidine
· Phenylalanine	· Glycine	
· Threonine	· Proline	
· Tryptophan	· Serine	
· Valine	· Histidine	

Carbohydrates

Dextrose is most commonly used to supply carbohydrate calories in parenteral nutrition. Each gram of hydrous dextrose supplies 3.4 kcal.[13] (anhydrous glucose provides 4.0 kcal/g.) Solutions of 10% to 12.5% can usually be administered by peripheral infusions. However, these lower concentrations of dextrose may require large volumes of fluid and maximal fat administration to achieve adequate calories, especially for neonates with high energy needs. Central vein administration allows for hypertonic solutions of dextrose to be administered, supplying more calories with smaller fluid volumes.

Fat (Lipid) Emulsions and Essential Fatty Acids

Use of lipids in parenteral nutrition will prevent the development of essential fatty acid deficiency, provide a non-carbohydrate source of calories, and provide the pediatric patient with a more physiologic diet.[15] Use of 35% carbohydrates, 50% fat, and 15% protein (the approximate composition of breast milk) is considered to be an ideal distribution of calories for the newborn; however, fat is usually administered at 35% to 40%, since the neonate may not be able to tolerate a high level of intravenous fat. Lipids given as 4% of calories will prevent essential fatty acid deficiency in the neonate.[10] Mild essential fatty acid deficiency may be present in the neonate and can develop within days in the full term infant who receives only dextrose-amino acid solutions.[17] Use of lipids in combination with dextrose also results in enhanced protein retention, and more efficient utilization of calories, with more energy available for growth and storage.[1,13]

Intravenous lipid emulsions in the United States are composed of long-chain triglycerides derived from soybean or safflower oils and contain the essential fatty acids, linoleic acid and linolenic acid, along with egg yolk phospholipids. Both 10% and 20% emulsions are available for direct infusion. The 20% emulsion provides approximately 2.0 kcal/mL as compared to 1.1 kcal/mL for the 10%, with the 20% providing more calories in a smaller volume. In addition, there are differences in the triglyceride content between the two emulsions; the 10% emulsion contains 10 g/dL of triglycerides and the 20% contains 20 g/dL. However, each emulsion contains the same amount of phospholipids (1.2 gm/dL), resulting in phospholipid/triglyceride ratios of 0.12 and 0.06 for the 10% and 20% emulsions, respectively.[3,19] Since phospholipids inhibit lipoprotein lipase, the enzyme responsible for clearance of fat, a 2 gm/kg/d dose of triglycerides from a 10% emulsion results in a greater increase in cholesterol levels than 4 gm/kg/d of a 20% emulsion, because of the higher ratio of phospholipid/triglyceride in a 10% emulsion.[3,18-20]

Electrolytes, Vitamins, Trace Elements

Electrolytes

The electrolyte requirements of the pediatric patient may be influenced by a number of factors. In the neonate, immature kidney function may result in excess water and sodium losses during the first days of life.[13,15] Other conditions, such as diarrhea, vomiting or drug therapy may result in greater potassium and magnesium losses. Calcium and phosphorous

needs may also be greater in the neonate, due to rapid skeletal bone development. Dosage of each electrolyte must be made on an individual basis.

RECOMMENDED DAILY ELECTROLYTE REQUIREMENTS FOR NEONATES[14]

Electrolyte	Recommended daily dosing range
Calcium	3-4 mEq/kg
Magnesium	0.3-0.5 mEq/kg
Phosphorus	1-2 mmol/kg
Potassium	1-4 mEq/kg
Sodium	2-5 mEq/kg
Chloride	1-5 mEq/kg

RECOMMENDED DAILY ELECTROLYTE REQUIREMENTS FOR INFANTS AND CHILDREN[14]

Electrolyte	Recommended daily dosing range
Calcium	1-2.5 mEq/kg
Magnesium	0.3-0.5 mEq/kg
Phosphorus*	0.5-1 mmol/kg
Potassium	2-3 mEq/kg
Sodium	2-6 mEq/kg
Chloride	2-5 mEq/kg

* Due to valance charge with pH, phosphorus is ordered in millimoles rather than milliequivalents.

Vitamins and Trace Elements (Micronutrients)

Recommendations for vitamins and trace elements in parenteral nutrition for neonates and infants have been made by the American Society for Clinical Nutrition (ASCN).[21] Although trace elements are found only in small amounts in the body (<0.01% of body weight), they are essential nutrients for growth and development. Currently, the ASCN recommends the addition of zinc for parenteral nutrition of less than 4 weeks duration.

After 4 weeks, other trace elements are needed. However, for the neonate, trace elements should be included at the initiation of parenteral nutrition. As with other nutrients, deficiencies may develop quickly in this population since body stores are low.[13,15] It is important to note that many of the available trace element combinations do not conform to ASCN recommendations; therefore, it is important to monitor trace elements when using these combination preparations.

ASCN RECOMMENDATIONS FOR VITAMIN SUPPLEMENTS FOR PEDIATRIC PARENTERAL NUTRTITION [21]

Fat Soluble Vitamins	Term infants and children (per day)	Premature infants (dose/kg body weight)
Vitamin A	2300 IU	1643 IU
Vitamin D	400 IU	160 IU
Vitamin E	7 IU	2.8 IU
Vitamin K	200 mcg	80 mcg

Water Soluble Vitamins	Term infants and children (per day)	Premature infants (dose/kg body weight)
Ascorbic Acid	80 mg	25 mg
Folic acid	140 mcg	56 mcg
Niacin	17 mg	6.8 mg
Vitamin B2 (Riboflavin)	1.4 mg	0.15 mg
Vitamin B1 (Thiamine)	1.2 mg	0.35 mg
Vitamin B6 (Pyridoxine)	1.0 mg	0.18 mg
Vitamin B12 (Cyanocobalamin)	1.0 mcg	0.3 mcg
Pantothenic acid	5 mg	2.0 mg
Biotin	20 mcg	6.0 mcg

ASCN RECOMMENDATIONS FOR TRACE ELEMENT SUPPLEMENTS TO PEDIATRIC PARENTERAL NUTRITION[21]

Trace element	Term infant (mcg/kg/day)	Preterm infant (mcg/kg/day)	Children (mcg/kg/day) {max mcg/day}
Zinc	250 (< 3 months) 100 (>3 months)	400	50 {5000}
Copper	20	20	20 {300}
Selenium	2.0	2.0	2 {30}
Manganese	1.0	1.0	1 {50}
Molybdenum	0.25	0.25	0.25 {5}
Iodide*	1.0	1.0	1 {1}
Chromium	0.20	0.20	0.2 {5}

* Not included in PN supplements: sufficient amounts are absorbed via iodinated skin preparations.

Access Site and Maintenance

Parenteral nutrition can be delivered either via the peripheral or the central vein. Choice of the route of administration of parenteral nutrition is dependent on the state of the infant's endogenous nutrient stores and energy needs, and the expected duration of parenteral nutrition.[17] Because of the high osmolarity and risk of phlebitis, dextrose solutions given via the peripheral vein should not exceed a concentration of 10% to 12.5%.[2,5,12] The peripheral route may be appropriate for larger weight infants who are likely to tolerate enteral feeding within one to two weeks and who have adequate nutrient stores. Peripheral parenteral nutrition should supply enough calories and nutrients to adequately maintain existing body composition, providing up to 80 to 90 kcal/kg per day of dextrose, amino acids and lipids.

However central line access may be necessary for infants or neonates with fluid restriction, those who are expected to require parenteral nutrition for longer periods, or those who need additional calories for tissue repair as well as growth. Parenteral nutrition has also been administered via umbilical artery and venous catheters.[17,22,23] Umbilical artery catheters are frequently used in neonates for monitoring blood gases and arterial blood pressure. Although this route of administration has not been recommended because of the risk of thrombosis, recent studies have suggested that umbilical artery catheters may be safely used for administration of parenteral nutrition to neonates if venous access is needed for other purposes.

Central Catheter Types Often Used in the Pediatric Population[24]

- Peripherally inserted central catheters (PICC).
    - Silastic central venous catheter.

    - 20-30 centimeters in length.
- Permanent right atrial catheters (PRAC).
    - Silicone rubber catheters
    - 70-90 centimeters in length.
    - 0.15 to 1.9 mL total volume.
    - Attached Luer-lock external connection.
    - Dacron "cuff" for tissue ingrowth to secure catheter in place.
- Totally implantable venous access device (TIVAD).
    - Subcutaneous port or reservoir attached to catheter.

Monitoring and Complications

Preventing adverse effects during parenteral nutrition requires a close familiarity with the nutritional requirements of the pediatric patient and awareness of the potential complications associated with parenteral nutrition. Potential complications may be metabolic, infectious or catheter-related in nature.[15] Many complications can be averted by proper monitoring of the patient's response to therapy using physical and laboratory assessments.

Suggested monitoring for parenteral nutrition[20]

Parameter	Frequency
Laboratory measurement	
Serum electrolytes	3-4 times/week initially, then weekly
Serum urea nitrogen	3 times/week initially, then weekly
Calcium, magnesium, phosphorous	3 times/week initially, then weekly
Glucose	2 times/day
Protein	Weekly
Liver function tests	Weekly
Hematocrit	Weekly
Urine glucose	Daily
Serum triglycerides	4 hours after a dose increase initially, then weekly
Physical assessment	
Weight and height	Daily

Intake/output	Daily
Anthropometric measurements	Weekly
Growth curves	Weekly

Metabolic complications may result from:

- Inappropriate administration of dextrose, protein or lipid.
- Hepatic complications.
- Imbalances and disorders of fluid and electrolytes.
- Vitamin or trace element deficiencies.[10]

Dextrose-Related Complications

Hypo- and hyperglycemia are common problems found with the administration of parenteral nutrition.[11,13,15] Neonates are more prone to hypo- or hyperglycemia than older infants and children. Neonates have inadequate stores of glycogen and a limited ability for glycogenolysis, due to poor enzyme activity. Hypoglycemia frequently occurs when parenteral nutrition solutions are stopped. For this reason, infusion rates should be tapered down prior to discontinuation of the nutrition solution.

Hyperglycemia is a more common problem in the neonate. Immature alpha-cell and beta-cell function, slow release of insulin and a diminished tissue response all contribute to the development of hyperglycemia. In addition, hepatic glucose output is not reduced in response to external glucose. For this reason, parenteral nutrition solutions should be started with low dextrose concentrations or at slow infusion rates.

High blood glucose concentrations result in an increase in serum osmolarity and the development of osmotic diuresis and dehydration, and increase the risk of intracranial hemorrhage.[11,13,15] Blood glucose should be monitored routinely and the glucose intake reduced if hyperglycemia occurs.

Protein-Related Complications

Blood urea nitrogen (BUN), the laboratory parameter that indicates effective utilization of protein, should be monitored. Azotemia, with a BUN/Creatinine ratio greater than 10, in the absence of renal insufficiency, may suggest the need for additional fluid. [27] Elevations in BUN due to azotemia should be differentiated from other conditions, such as dehydration or renal insufficiency, which may also increase BUN.[11]

Lipid-Related Complications

Use of lipid emulsions has been associated with certain complications in the neonate, including hyperlipidemia, hyperbilirubinemia and changes in pulmonary function when the rate of administration is too fast.

Too rapid infusion of lipid emulsions may result in hyperlipidemia in the neonate. The ability of the neonate to effectively clear and utilize intravenous lipids is dependent on enzyme systems that vary with both weight and gestational age.[11,15] Lipid emulsions should be infused over 24 hours, at an initial rate of 0.5 g/kg/day in neonates. Serum triglycerides should be monitored and the rate increased based on the neonate's tolerance, usually at 0.5 g/kg per day, up to a total of 3.5 to 4.0 g/kg per day.

Hyperbilirubinemia is another potential complication of the use of parenteral nutrition in neonates. Hyperbilirubinemia and jaundice occur frequently because the liver enzymes needed to conjugate bilirubin are reduced in the immature liver.[11] When lipids are infused more quickly than they can be cleared from the blood, free fatty acid concentrations are increased. Bilirubin and free fatty acids both compete for binding to albumin. This displacement of bilirubin by free fatty acids results in higher serum concentrations of bilirubin and an increased risk of kernicterus.

Lipid emulsions may also cause changes in pulmonary function in the neonates. Partial arterial oxygen pressure (PO_2) levels may be lowered due to changes in pulmonary microcirculation in neonates with respiratory-distress syndrome.[11] Reducing the fat to carbohydrate ratio may minimize the adverse effects of lipids. Lipid emulsions may undergo oxidation following prolonged exposure to light resulting in the formation of lipid hydroperoxides.[27] These lipid hydroperoxides are presumed to be toxic to the newborn.[28] Protecting the lipid and administration tubing from light may avoid the formation of peroxides.[29]

Hepatic Effects

Cholestasis (or cholestatic jaundice) is the most common and serious metabolic complication seen with parenteral nutrition in the neonate.[11,13,20] It usually occurs after 2 to 6 weeks of parenteral nutrition and may ultimately result in biliary cirrhosis or end-stage liver disease. Mild hepatomegaly and elevations in conjugated bilirubin are seen, followed by increases in serum alkaline phosphatase and transaminases. The exact cause of the hepatic effects of parenteral nutrition are unknown, but may be related to administration of amino acids, lack of enteral feedings and calorie overload. Secretion of gastrointestinal hormones (gastrin and cholecystokinin) are decreased during the fasting state, resulting in an inhibition of bile secretion and a disruption in the enterohepatic circulation. Use of enteral feedings as early as possible, even in minimal amounts, stimulates hormone production and bile secretion.[11] When continued parenteral nutrition is needed, steps in the management of cholestasis include:

- Avoid excess calorie intake (overfeeding).
- Provide a mix of calories (dextrose, protein, and lipids) in appropriate ratios.
- Provide some enteral stimulation (when possible).
- Cycle parenteral nutrition infusion over fewer than 24 hours (when possible).

Electrolytes and Trace Element Deficiencies

Most deficiencies of electrolytes and trace elements are secondary to improper supplementation and monitoring. Excess fluid loss, from vomiting, diarrhea, wounds or

other secretions, may result in additional electrolyte losses and loss of some trace elements, such as zinc. Careful monitoring of electrolytes and fluid losses is necessary to avoid deficiencies. Adequate calcium intake is essential for bone growth. However, administration of appropriate amounts of calcium may be hindered by incompatibilities with other electrolytes, primarily phosphorous.[11] Addition of L-cysteine to amino acid solutions improves the solubility of both calcium and phosphorous, allowing greater concentrations in the parenteral nutrition solution.

Electrolyte Body Fluid Composition in Neonates (in mmol/L)[13]

	Na+	K+	C1-
Bile	120-140	5-15	90-120
Gastric Secretions	20-80	5-20	100-150
Small intestine	100-140	5-15	90-120
Ileostomy Fluid	45-135	3-15	20-120
Diarrhea	10-90	10-80	10-110

Catheter-Related Complications

Catheter-related complications, which may be either technical or infectious in nature, are related to the disease state of the infant, nursing care, and type of catheter being used. The immature immune system of the premature infant also contributes to the risk of infection. Similar to complications seen in adult patients, pneumothorax, hemothorax, air embolism, cardiac perforation or damage to arteries or vein may occur following improper placement of the catheter in the pediatric patient. Formation of thrombus or fibrin clots, dislodgement of the catheter tip or formation of precipitates are also potential catheter-related complications. [11] The risk of some of these complications may be reduced by proper placement of the catheter with radiologic confirmation of its position. After insertion, the position of the catheter may be secured by suturing the catheter where it enters the skin followed by careful inspection of the catheter at each dressing change.[16] Proper catheter maintenance is also essential to lessen the likelihood of catheter occlusion.

The incidence of sepsis associated with central venous access has been reported to be up to 45% in pediatric patients, higher than the incidence seen in adult patients.[11] Factors which influence the risk of infectious complications include length of time the catheter is in place, number of lumens, and the type of catheter used. PICC lines have an incidence of catheter-related infections lower than 2% in parenteral nutrition therapy. The central line infection

rate ranges from 5% to 25%. Steps which may reduce the risk of catheter-related infections include:

- Proper aseptic technique when changing intravenous solutions.
- Use of sterilizing ointment or solution around connections.
- Changing of catheter insertion site dressings every two to three days.
- Close monitoring for signs of infection (fever, increased irritability, redness at catheter insertion site).

Transition to Enteral Feedings

While parenteral nutrition provides the neonate and infant with nutrients to sustain life and promote growth, its use can have negative physiologic effects on the gastrointestinal tract.[10,20,25,26] Enteral starvation results in decreased secretion of gastrointestinal hormones, atrophy of gastric mucosa, a decline in gastrointestinal motility, and an increase in the incidence of intestinal ulceration. These effects result in a decline in the digestive and absorptive capabilities of the gastrointestinal tract and a loss of protective effects, increasing the risk for systemic bacterial infections. To minimize these effects, enteral feeding should be initiated as soon as possible. Even the use of small volumes of enteral feedings (minimal enteral feeding) as a supplement to parenteral nutrition, will stimulate the gastrointestinal tract functions.

It is important to monitor the infant for signs of intolerance to enteral feedings. Diarrhea is generally indicative of poor absorption and may be avoided by a reduction in rate of feeding or strength of formula.

Transition to enteral feedings[10]

- Determine energy, protein, micronutrient, and fluid requirements.
- Determine the hourly volume of formula needed to meet these requirements.
- Initiate feedings using small volume of 1/4 to 1/2 strength as a 24-hour continuous enteral feeding.
- Titrate volume every 12 hours as tolerated; reduce parenteral nutrition to 50% of its original rate when 50% of the needed hourly volume of enteral feedings are tolerated.
- Reduce parenteral nutrition to 25% of its original rate when 75% of the needed hourly volume of enteral feedings are tolerated.
- Advance to full strength of enteral feeding when full hourly volume is tolerated.
- Discontinue parenteral nutrition when full strength feedings are tolerated.

Hyperbilirubinemia in the Healthy Term Newborn

Healthy term newborns are now routinely discharged less than 48 hours after birth. The presence of significant jaundice is the most common reason for infant readmission to the hospital during the first week of life. Clinicians should recognize the risk factors for significant jaundice, make sure babies are appropriately followed and treated, and provide adequate support and education to caregivers

Jaundice is the most common clinical problem in newborns, observed during the first week of life in approximately 60% of term infants and in 80% of preterm infants.[1,2] Much debate has surrounded the evaluation and treatment of jaundice, particularly due to the potential deleterious neurologic effects from elevated serum bilirubin levels.[1-10] Documentation of kernicterus in healthy term newborns with no evidence of hemolysis and no cause for hyperbilirubinemia other than breast-feeding has raised concern among those in the pediatric and primary care community.[4,5,10,11]

With the advent of early discharge from the hospital, care of neonatal jaundice has been transformed to an outpatient problem. It has become the responsibility of the outpatient medical community to provide early detection and treatment of neonatal hyperbilirubinemia to ensure optimal management of infants.[12]

Recognizing that practices were changing and that no attempt had been made to use evidence-based practice to recommend strategies for managing jaundiced infants, the American Academy of Pediatrics (AAP) developed guidelines for the management of hyperbilirubinemia in the healthy term infant and published them in 1994.[2]

Etiology and Clinical Manifestations

Bilirubin is largely produced by the breakdown of red blood cells (RBCs). In the fetus, the placenta eliminates most of the lipid-soluble bilirubin. In the newborn, bilirubin must be conjugated, or chemically changed, in the liver to a water-soluble form before it can be excreted in the bile.[13] In the adult, bilirubin passes into the small bowel where bacteria reduces or converts it to urobilinogen. Urobilinogen is excreted in the stool; virtually no bilirubin is absorbed from the gastrointestinal tract.[10]

The fetal gut is sterile, however, and although bacteria form after delivery, they do not reduce bilirubin to urobilinogen. Conjugated bilirubin cannot pass through the intestinal mucosa, but because it is not reduced to urobilinogen and remains in the bowel, it is deconjugated and becomes available for resorption.[10]

Jaundice refers to the yellow color of the skin, sclera, mucous membranes, and body fluids when bile pigment (bilirubin) is present as a result of excess bilirubin in the blood.[13] Jaundice is first seen on the face and progresses caudally to the trunk and extremities.[1,10,13] In newborns, jaundice is detected by digitally blanching the skin, which reveals the underlying color of the skin and subcutaneous tissue.[1,10]

Bilirubin Toxicity

Bilirubin appears to be poisonous to cells, although the exact mechanism of its toxic effect is unknown.[10] Toxic levels of unconjugated bilirubin may cause infants to develop kernicterus, a condition characterized by encephalopathy, opisthotonos, hearing loss, and in many cases death.[14] Signs and symptoms of bilirubin toxicity include vomiting, lethargy, poor feeding, high-pitched crying, hypotonic state, respiratory distress, and temperature instability.[1,9,11]

Conditions that may make the infant's brain more susceptible to toxic levels of unconjugated bilirubin include factors that allow bilirubin to leave the circulation, such as hypoalbuminemia; displacement of bilirubin (by drugs or other anions) from its binding sites on albumin; and factors that increase the permeability of the blood-brain barrier.[1,2,10]

RAPID READ

Jaundice is the most common clinical problem in newborns, observed during the first week of life in approximately 60% of term infants and in 80% of preterm infants. Jaundice is first seen on the face and progresses caudally to the trunk and extremities. In newborns, jaundice is detected by digitally blanching the skin, which reveals the underlying color of the skin and subcutaneous tissue.

Toxic levels of unconjugated bilirubin may cause infants to develop kernicterus, a condition characterized by encephalopathy, opisthotonos, hearing loss, and in many cases death. Conditions that may make the infant's brain more susceptible to toxic levels of unconjugated bilirubin include factors that allow bilirubin to leave the circulation, such as hypoalbuminemia; displacement of bilirubin (by drugs or other anions) from its binding sites on albumin; and factors that increase the permeability of the blood-brain barrier.

Although nonhemolytic jaundice in healthy term newborns has generally been thought to be benign, case reports have appeared of healthy term newborns having no risk factors, other than breast-feeding, who developed kernicterus.[4,5] Because newborns are now routinely discharged before the bilirubin peak, primary care providers may see infants on days 4 through 7 with serum bilirubin levels greater than 25 to 30 mg/dl.[10]

Debate surrounds the question of whether neurotoxicity occurs at lower bilirubin levels without abnormal clinical signs and symptoms during the newborn period.[6,10] In the late 1960s and throughout the 1970s, reports from the Collaborative Perinatal Project, a study of 53,000 pregnant women and their offspring, linked moderate increases in serum bilirubin to increased neurologic abnormalities and decreased developmental and IQ scores.[15-17] This large study was not restricted to healthy or term newborns.[10]

A recent reanalysis of the study data showed that elevated neonatal bilirubin levels seem to have little effect on IQ, hearing loss, or definite neurologic abnormalities. An association between higher bilirubin levels and mild, nonspecific motor abnormalities may exist.[7]

The effects of moderately elevated bilirubin levels are not known. Recent literature suggests that bilirubin may have protective properties as a physiologic antioxidant.[12]

Physiologic Jaundice

Normally, the level of indirect bilirubin in umbilical cord blood is 1 to 3 mg/dl and rises at a rate of less than 5 mg/dl/24 hours. Jaundice becomes apparent between the second and fourth days of life, when bilirubin usually peaks (or in breast-fed infants, between the third and fifth days)[11] at 5 to 6 mg/dl; it decreases to 2 mg/dl between the fifth and seventh days.[1] It is hypothesized that this normal appearance of jaundice, called physiologic jaundice,

results from several processes: the breakdown of fetal RBCs; increased enterohepatic circulation of bilirubin, which causes increased bilirubin load on liver cells; decreased uptake of bilirubin from plasma; a decrease in the liver's ability to conjugate bilirubin; and defective bilirubin excretion.[1,10]

Some 6% to 7% of full-term infants have total bilirubin levels above 12.9 mg/dl. Less than 3% have levels greater than 15 mg/dl.[1] Breast-fed infants are three times more likely than formula-fed infants to have serum bilirubin levels above 12 mg/dl during the first few days of life.[11]

Idiopathic or breast-feeding associated jaundice is far more common than jaundice of any pathologic cause. Bilirubin production in breast-fed infants is no greater than in formula-fed infants.[18] Suggested causes of jaundice associated with breast-feeding include decreased bilirubin clearance by the liver and increased intestinal resorption of bilirubin. Decreased bilirubin clearance is affected by the decreased caloric intake in early breast-feeding and by weight loss in the first few days after birth, both of which are associated with elevated bilirubin levels.[19,20] The breast milk of some mothers is believed to contain inhibitory substances. Genetic factors may also play a role.

The increased intestinal resorption of bilirubin is most responsible for breast-feeding associated jaundice. Factors include delayed passage of meconium and decreased formation of urobilinogen, both of which enhance the resorption of bilirubin in the intestine. An increase in beta-glucuronidase, an enzyme that reduces bilirubin to an unconjugated (absorbable) form, may be a contributing factor in breast-feeding associated jaundice. Bile acid abnormalities may also play a role in the intestinal resorption of bilirubin.[10]

Differential Diagnosis

Jaundice can have many causes, and the time of onset is important in determining etiology. Jaundice that appears within the first 24 hours of life may be caused by erythroblastosis fetalis (Rh incompatibility) or other hemolytic anemia, including ABO incompatibility. It may also be caused by concealed hemorrhage, congenital viral infection, or sepsis. Early jaundice can be significant in the diagnosis of sepsis.

Hemolytic anemia caused by Rh incompatibility is rare since the advent of Rh_o(D) immune globulin (RhoGAM). ABO incompatibility is more common. Some 20% of all pregnancies are associated with mother-fetus ABO incompatibility, but the incidence of severe hemolytic disease is low. ABO hemolytic disease results from the action of anti-A or anti-B antibodies of the mother with type O blood on the fetal type A or type B erythrocyte.

Immunoglobulin (Ig) A, IgM, and IgG fractions of plasma contain the anti-A and anti-B antibodies, but only the anti-G antibodies cross the placenta and produce disease. Newborns of mothers with high levels of IgG anti-A or anti-B titers tend to have ABO hemolytic disease. The diagnosis of ABO hemolytic disease is supported by indirect hyperbilirubinemia, jaundice during the first 24 hours of life, a type A or type B baby born to a type O mother, an increased number of spherocytes in the blood, and increased erythrocyte production as evidenced by reticulocytosis or an elevated erythrocyte creatine concentration.[21]

Other maternal minor group antibodies such as anti-E, anti-C, and anti-Kell can cause hemolytic disease. Anti-Kell antibodies can cause severe hemolytic disease and neonatal death.[22] Management of ABO incompatibility is directed primarily toward preventing hyperbilirubinemia. Phototherapy reduces the need for exchange transfusion.[23]

Physiologic jaundice usually appears on the second or third day of life. Hyperbilirubinemia of the newborn occurs when physiologic bilirubin levels are exceeded.

Jaundice that appears in the first week is usually physiologic, associated with breast-feeding, or caused by increased bilirubin production from bruising or a cephalhematoma. Jaundice noted initially after the first week of life may be caused by septicemia, congenital atresia of the bile ducts, congenital viral infections, metabolic disorders such as hypothyroidism or galactosemia, hemolytic anemias, or congenital deficiencies of enzymes glucose-6-phosphate dehydrogenase, glutathione synthetase, reductase, or peroxidase.[1]

In infants with jaundice that persists beyond the second or third week of life, a direct bilirubin level must be obtained to rule out the possibility of cholestatic (obstructive) jaundice. Parents or caretakers must be asked whether the child has dark urine or light-colored stools.

RAPID READ

Jaundice can have many causes, and the time of onset is important in determining etiology. Jaundice that appears within the first 24 hours of life may be caused by two forms of hemolytic anemia: erythroblastosis fetalis (Rh incompatibility) or ABO incompatibility. It may also be caused by concealed hemorrhage, congenital viral infection, or sepsis. Early jaundice can be significant in the diagnosis of sepsis. Physiologic jaundice usually appears on the second or third day of life. Jaundice that appears in the first week is usually physiologic, associated with breast-feeding, or caused by increased bilirubin production from bruising or a cephalhematoma. Jaundice noted initially after the first week of life may be caused by septicemia, congenital atresia of the bile ducts, congenital viral infections, metabolic disorders, or congenital deficiencies. In infants with jaundice that persists beyond the second or third week of life, a direct bilirubin level must be obtained to rule out the possibility of cholestatic (obstructive) jaundice.

Diagnosing the cause of hyperbilirubinemia requires careful consideration of the maternal and infant history, the physical examination, and laboratory findings. Table 1 lists factors that warrant further assessment of the jaundiced infant.[1,2,10,24]

Table 1.
Factors Suggesting a Nonphysiologic Cause of Jaundice

- Jaundice appearing within the first 24 hours of life
- Total serum bilirubin rising more than 5 mg/dl/24 hour
- Total serum bilirubin >15 mg/dl in a full-term infant
- Jaundice persisting after the second week of life
- Direct-reacting bilirubin >1 mg/dl at any time

- Family history of hemolytic disease
- Pallor, hepatomegaly, splenomegaly
- Failure of phototherapy to lower bilirubin
- Excessive weight loss
- Signs of kernicterus

Risk Factors for Indirect Hyperbilirubinemia

- Indirect hyperbilirubinemia has numerous risk factors (see Table 2).[1,2,6,10] Infants with multiple risks are more likely to have elevated indirect bilirubin levels. Infants without risk factors rarely develop levels greater than 12 mg/dl.[1]

Table 2.
Risk Factors for Indirect Hyperbilirubinemia

- Sibling with hyperbilirubinemia in the newborn period
- Decreasing gestational age
- Breast-feeding, caloric deprivation
- Significant weight loss after birth
- Maternal diabetes
- Race (Asian, Native American)
- Drugs (oxytocin)
- Altitude
- Polycythemia
- Male sex
- Cutaneous bruising, cephalhematoma
- Delayed stooling
- Trisomy-21

Significant jaundice is the most common reason for an infant to be readmitted to the hospital in the first week of life.[25] Identifying infants who are at higher risk for hyperbilirubinemia and predicting the ideal time to institute treatment (such as phototherapy to prevent high bilirubin levels), potential detrimental sequelae, and to avoid the need for exchange transfusion is difficult even for health care providers who are knowledgeable about risk factors.[26]

Management

The main treatment modalities that have been advocated for hyperbilirubinemia in the newborn are exchange transfusion, phototherapy, and, in cases in which breast-feeding was thought to contribute to jaundice, nursing cessation.[1,2,10,24]

Exchange transfusion was developed in the 1950s as a method for reducing the risk of death or injury in infants born with hemolytic disease.[27] In hemolytic disease, the sensitized RBCs and bilirubin are removed and replaced with group O Rh-negative (bilirubin-free) blood.[13]

Phototherapy, first described in 1958,[28] reduces serum bilirubin concentration in the newborn via exposure to sunlight (for mildly jaundiced infants) or artificial blue light, which alters bilirubin to a readily excreted form.[13] Refinements in phototherapy in the late 1980s brought about the fiberoptic delivery of blue light.

This form of delivery, commonly used in the home setting, is equally effective if used properly. Other advantages include low cost, reduction of parent-child separation, and reduction of breast-feeding cessation.[10]

RAPID READ

Normally, the level of indirect bilirubin in umbilical cord blood is 1 to 3 mg/dl and rises at a rate of less than 5 mg/dl/24 hours. Jaundice becomes apparent between the second and fourth days of life (or in breast-fed infants, between the third and fifth days) when bilirubin usually peaks at 5 to 6 mg/dl; it decreases to 2 mg/dl between the fifth and seventh days. Some 6% to 7% of full-term infants have total bilirubin levels above 12.9 mg/dl. Less than 3% have levels greater than 15 mg/dl. Breast-fed infants are three times more likely than formula-fed infants to have serum bilirubin levels above 12 mg/dl during the first few days of life. Idiopathic or breast-feeding associated jaundice is far more common than jaundice of any pathologic cause. Bilirubin production in breast-fed infants is no greater than in formula-fed infants. Suggested causes of jaundice associated with breast-feeding include decreased bilirubin clearance by the liver and increased intestinal resorption of bilirubin. Decreased bilirubin clearance is affected by the decreased caloric intake in early breast-feeding and by weight loss in the first few days after birth, both of which are associated with elevated bilirubin levels**.**

The AAP recommends not interrupting breast-feeding in jaundiced healthy term newborns and encourages continued frequent breast-feeding--at least 8 to 10 feedings every 24 hours. Supplementation with water or glucose water does not lower the bilirubin level in jaundiced, healthy breast-feeding infants. Other options include supplementing breast-feeding with formula or interrupting breast-feeding temporarily and substituting it with formula. Either option can be accompanied by phototherapy.[2] A recent study compared newborns who developed nonhemolytic hyperbilirubinemia and feeding methods. This study consisted of three groups including infants who were formula-fed, breast-fed, and primarily breast-fed with formula supplementation. All three groups received phototherapy. The infants who were breast-fed and supplemented with formula reduced their bilirubin concentration faster than the other two groups. This study supports the theory that breast-feeding with formula supplementation in addition to phototherapy is efficacious in treating hyperbilirubinemia.[29]

The AAP has issued guidelines for treating hyperbilirubinemia in the healthy term newborn. The group recommends including ABO and Rh typing and a blood screen for unusual isoimmune antibodies in prenatal screening. If the mother has not undergone prenatal blood grouping or is Rh negative, tests from the infant's cord blood should include a direct Coombs' test, blood type, and Rh type. Institutions are encouraged to save cord blood for future testing, especially when the mother's blood type is O. Infants who develop jaundice in the first 24 hours of life should undergo a total serum bilirubin evaluation. The pattern of early newborn discharge from the hospital makes it prudent that all neonates

discharged within 48 hours of birth receive follow-up care by a health care professional in an office or clinic or at home within 2 to 3 days of discharge. (See Figure Part 1 and Figure Part 2.)

Figure. Part 1
Algorithm Management of Hyperbilirubinemia in the Healthy Term Infant

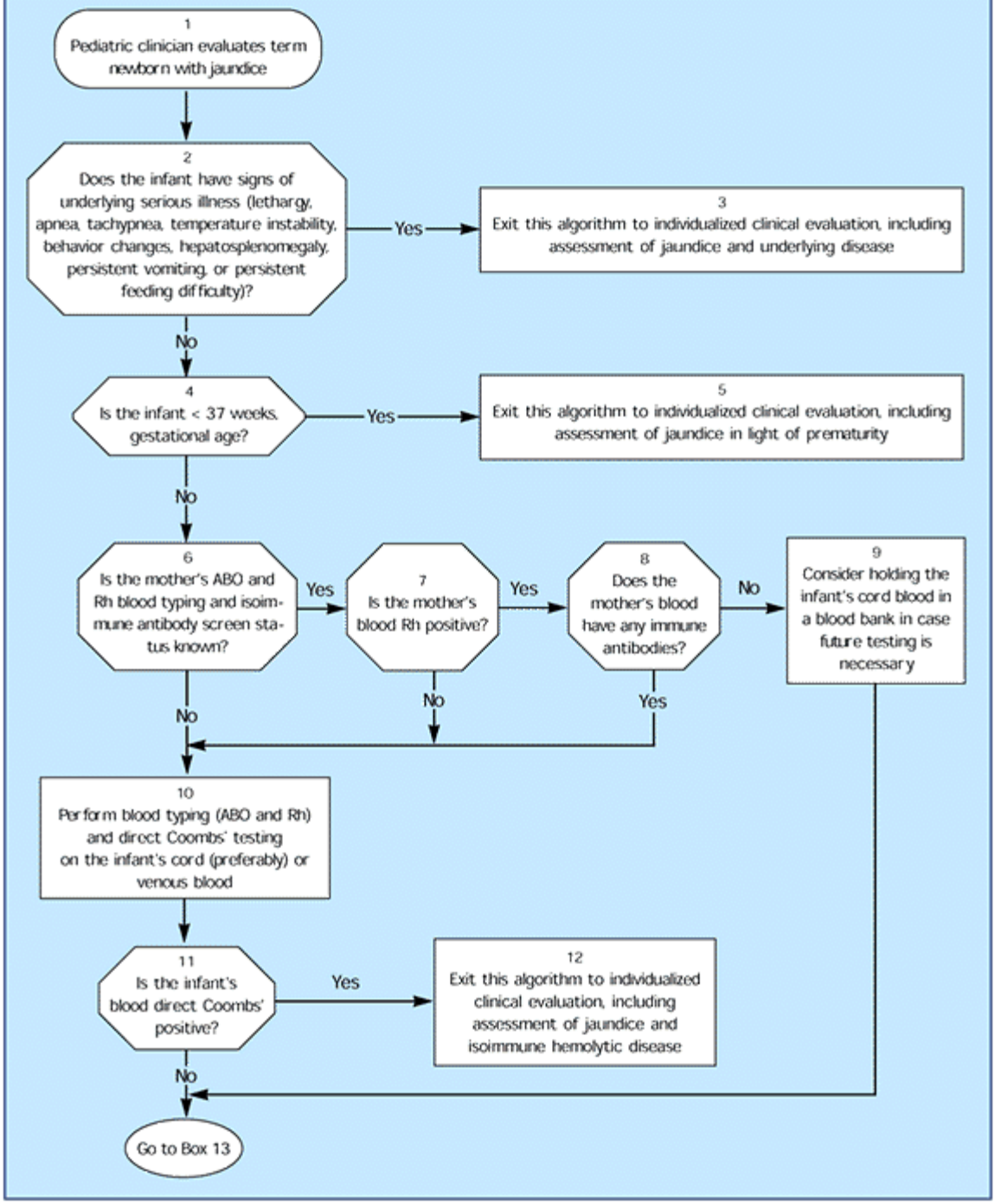


Figure. Part 3

Algorithm Management of Hyperbilirubinemia in the Healthy Term Infant

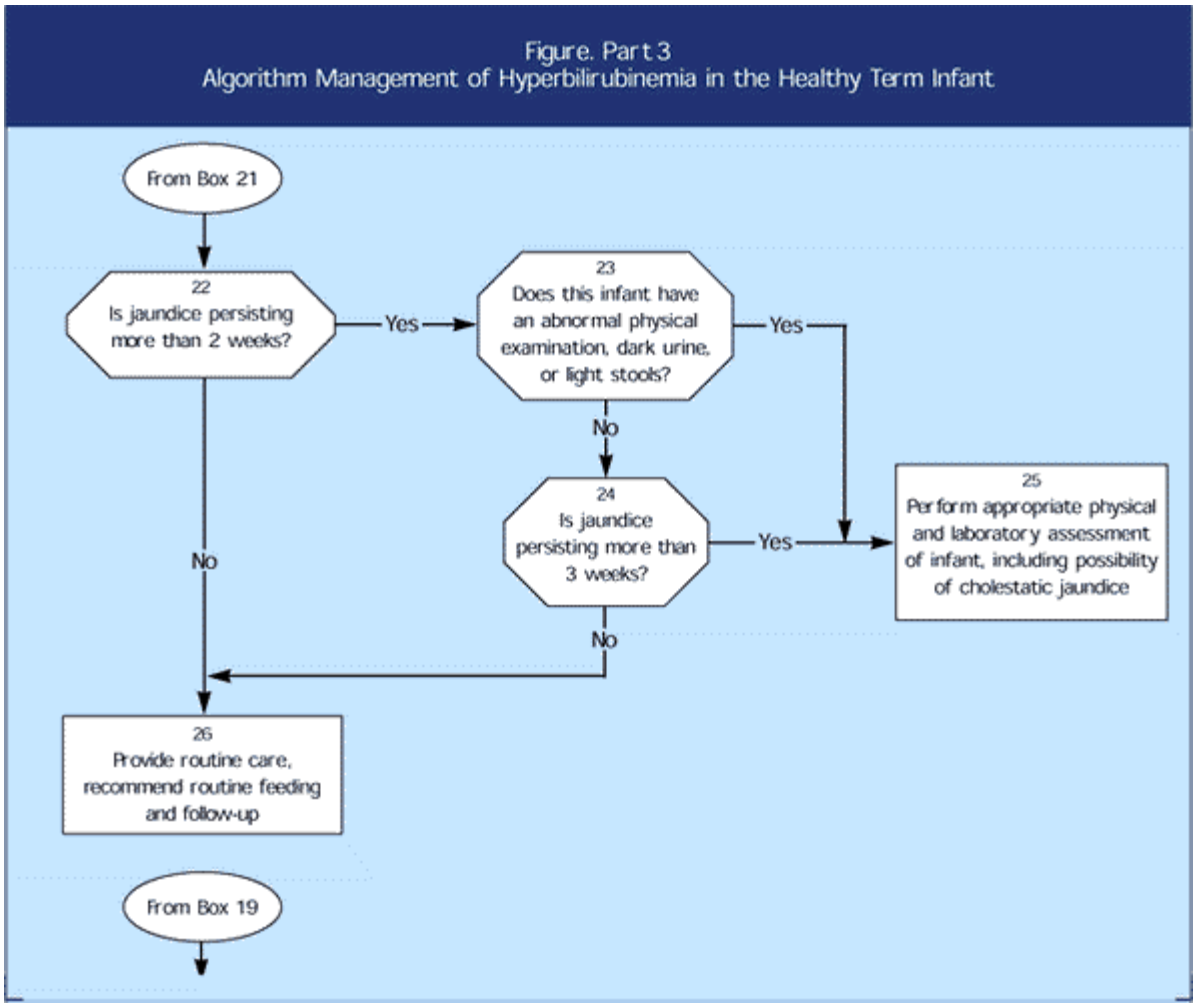


Table 3.

Management of Hyperbilirubinemia in the Healthy Term Infant

TSB Level, mg/dl(micromole/liter)

Age, hours	Consider Phototherapy+	Phototherapy	Exchange Transfusion if Intensive Phototherapy Fails++	Exchange Transfusion and Intensive Phototherapy

≤ 24	--	--	--	--
25-48	≥ 12(170)	≥ 15(260)	≥ 20(34)	≥ 25(430)
49-72	≥ 15(26)	≥ 18(310)	≥ 25(430)	≥ 30(510)
>72	≥ 17(290)	≥ 20(340)	≥ 25(430)	≥ 30(510)

[+]Phototherapy at these total serum bilirubin levels is a clinical option, meaning that the intervention is available and may be used *on the basis of individual clinical judgment.*

[++]Intensive phototherapy should decrease the total serum bilirubin level 1 to 2 mg/dl within 4 to 6 hours, and the level should continue to fall and remain below the threshold level for exchange transfusion. If this does not occur, it is considered a failure of phototherapy.

Reproduced by permission of Pediatrics 1994. Practice parameter: Management of hyperbilirubinemia in the healthy term newborn; 94(4):563-65.

The AAP guidelines for management of hyperbilirubinemia in the healthy term infant, written as an algorithm and as a table, offer a range of acceptable evaluation and treatment practices based on the infant's age as measured in hours.[2]

The rate of total serum bilirubin rise and the infant's age help determine how often to monitor bilirubin levels and whether to begin phototherapy. The provider may appropriately choose to observe rather than to treat with repeated phototherapy and total serum bilirubin testing. If the infant requires intensive phototherapy, this can be achieved by using special blue tubes in standard fluorescent phototherapy units or increasing the infant's body surface area exposure by placing him or her on a fiberoptic blanket while also using a standard phototherapy system. A decline in the total serum bilirubin of 1 to 2 mg/dl within 4 to 6 hours of intensive phototherapy can be expected; the level should continue to decline. When the total serum bilirubin level falls to 14 to 15 mg/dl, phototherapy may be discontinued.[2]

While receiving phototherapy, infants should be monitored for fluid and weight loss and for hyperthermia. Insensible water loss is increased in the full-term infant during phototherapy.[30] Skin temperature increases significantly as well; however, these complications can be avoided by using servocontrolled incubators. Weight gain is less in infants who receive phototherapy during the first week of life than in those who do not, but their growth catches up during the next 2 weeks.[10]

Newer Treatments for Severe Hyperbilirubinemia

Less commonly used pharmacologic treatment for severe hyperbilirubinemia includes the administration of phenobarbital, which accelerates the normal metabolic pathways for bilirubin clearance, and the administration of agar, which inhibits the enterohepatic circulation of bilirubin. Synthetic metalloporphyrins, still in experimental use only, inhibit the production of bilirubin. The use of high-dose I.V. immunoglobulin is being studied to reduce the need for exchange transfusion in infants with isoimmune hemolytic disease.[11] These treatments, which require consultation with or referral to a physician, are not indicated for the healthy term newborn without hemolytic disease.

A simple, noninvasive method to measure increased RBC destruction in newborns has had promising results. Clinically important hemolysis has been identified before the development of anemia or hyperbilirubinemia by measuring carbon monoxide production, an index of bilirubin production.[10] The device determines the end-tidal carbon monoxide concentration by sampling expired air with a small nasal catheter.[12]

RAPID READ

The main treatment modalities that have been advocated for hyperbilirubinemia in the newborn are exchange transfusion, phototherapy, and, in cases in which breast-feeding was thought to contribute to jaundice, nursing cessation. The rate of total serum bilirubin rise and the infant's age help determine how often to monitor bilirubin levels and whether to begin phototherapy. The provider may appropriately choose to observe rather than to treat with repeated phototherapy and total serum bilirubin testing. A decline in the total serum bilirubin of 1 to 2 mg/dl within 4 to 6 hours of intensive phototherapy can be expected; the level should continue to decline. When the total serum bilirubin level falls to 14 to 15 mg/dl, phototherapy may be discontinued. While receiving phototherapy, infants should be monitored for fluid and weight loss and for hyperthermia. Weight gain is less in infants who receive phototherapy during the first week of life than in those who do not, but their growth catches up during the next 2 weeks.

Case Study

K.A. was a well newborn delivered vaginally and without complications to a healthy woman. Born at 39 weeks and 1 day on March 31, 1996, 12:25 a.m., he weighed 7 lbs. 1 oz and was 20 inches long. He was breast-fed and had a 22-month-old sibling who had mild jaundice in the newborn period that did not require treatment.

The initial assessment, conducted by a staff pediatrician 12 hours after birth, was normal. An evaluation on day 2 of life, 32 hours after birth, and just before hospital discharge, revealed jaundice.

Follow-up with health care provider in 2 to 3 days was recommended.

Upon follow-up check on April 4, 1996, the infant was noted to be significantly jaundiced with icterus. Record review showed that the mother had O+ blood and the infant had A+

blood. A Coombs' test performed on cord blood was negative. Stat total bilirubin level was obtained and found to be 21.4. A home phototherapy blanket was instituted later that evening.

On April 5, 1996, bilirubin had decreased to 19 mg/dl. Phototherapy was continued and the bilirubin level on April 6 was 15 mg/dl. Phototherapy was continued for another 24 hours and discontinued when total bilirubin level reached 12.4 mg/dl.

Conclusion

Jaundice in the healthy term newborn is common. In rare cases, bilirubin reaches toxic levels within the first week of life.[1,4,5,10,11] Untreated infants may develop kernicterus.[4,5,11] Lower levels of hyperbilirubinemia may place infants at risk for mild, nonspecific neurologic abnormalities. Even those who are knowledgeable about risk factors for hyperbilirubinemia may find it difficult to predict which infants are at increased risk.[5]

The need for research to determine the effects of moderate increases in bilirubin on the healthy infant's developing neurologic system persists. Breast-feeding associated jaundice or idiopathic jaundice is far more common than jaundice with pathologic causes. On an ongoing basis, it is necessary for clinical practitioners to recognize risk factors for the development of significant jaundice, to provide thorough follow-up for newborns discharged from the hospital, and to support and educate caregivers.

For many pediatric patients, parenteral nutrition is a lifesaving intervention, providing energy for growth and tissue repair when the gastrointestinal tract cannot be used. This is especially true for preterm or low birth weight neonates, who represent the highest percentage of the pediatric population requiring parenteral nutrition. Familiarity with the nutritional requirements, complications, and methods of monitoring parenteral nutrition in the pediatric patient will help to minimize the risks to this population.

References

While individual sections in this course had their own list of References, the primary references utilized throughout this course were:

- Barnhart SL, Czervinske MP, Perinatal and Pediatric Respiratory Care, W.B. Saunders Co., May 2008,
- Egan's Fundamentals of Respiratory Care,Mosby; 8 edition (June 11, 2003)
- Neonatal/Pediatric Respiratory Care: A Critical Care Pocket Guide, Dana F. Oakes, RespiratoryBooks.com; 5th edition (January 1, 2004)
- Thibeault DW, Gregory GA, Neonatal Pulmonary Care, Appleton-Century-Crofts, 20 Oct 2005.
- Neonatal and Pediatric Pharmacology: Therapeutic Principles in Practice, Jacob V. Aranda, Sumner J. Yaffe, Lippincott Williams and Wilkins, 2004
- Wong's Nursing Care of Infants and Children, Hockenberry, Marilyn J, and Wilson, David, and Rentfro, Anne Rath C.V. Mosby 8th, 2006

Neonatal Exam

Select the ***best*** answer to each of the following items. Mark your responses on the Answer form.

1. During development, fetal nutrition, oxygenated blood, excretion, respiration, and protection are provided by_____.

a. the lungs
b. surfactant
c. elastin
d. the placenta

2. During the _____ phase, which begins at about 4-6 weeks of gestational age, the lung begins as a bud from the foregut.

a. pseudoglandular
b. canalicular
c. saccular
d. embryonic

3. During the _____ phase, weeks 17 to 28, the gas exchanging area of the lung develops.

a. pseudoglandular
b. canalicular
c. saccular
d. embryonic

4. During the _____ phase, which lasts from about week 7 to week 16, the predominant feature involves the formation of conducting airways.

a. pseudoglandular
b. canalicular
c. saccular
d. embryonic

5. The prenatal lungs do not function as gas exchange organs, but they do serve important purposes:

a. The lung is a primary source of amniotic fluids.
b. Lungs act as reservoirs of carbohydrates needed for the organism's energy.
c. They produce surfactant beginning at about 24 weeks
d. All of the above

6. An absence of fetal breathing movements or a lack of adequate space for lung growth may also cause _____.

a. hypoplasia
b. hyperplasia
c. asphyxia
d. euphrasia

7. During lung development, _____ is the dominant connective tissue in airways.

a. fibrogen
b. collagen
c. surfactant
d. muscle

8. Diaphragm is formed at _____ week’s development of the fetus

a. three
b. five
c. eight
d. sixteen

9. _____ is the active agent in the alveoli that cuts surface tension and reduces the need for high pressures to open the alveoli on inspiration.

a. Lamellar

b. Fistula
c. Collagen
d. Surfactant

10. The term _____ , which is often used interchangeably with toxemia, means a toxemia of late pregnancy, which is characterized by hypertension, edema and proteinuria.

a. pre-eclampsia
b. premature
c. placenta
d. placebo

11. The neonate's _____ should be examined at birth for odor, color, consistency, and the presence of meconium.

a. placenta
b. amniotic fluid
c. amniocentesis
d. diaphragm

12. The average _____ in early gestation is 140 beats per minute, dropping to an average of 120/min near term.

a. fetal pulse
b. respiration rate
c. fetal heart rate
d. none of the above

13. The goal regarding neonates' _____ is to achieve and maintain a neutral thermal environment (NTE), an environment that allows the infant to maintain its internal temperature without increasing oxygen consumption.

a. Apgar measurement
b. heart rate measurement
c. aspiration

d. thermoregulation

14. The _____ scoring system, was developed as an objective way to evaluate the general status of the newborn at one minute and five minutes after birth.

a. FHR
b. Apgar
c. Surfactant
d. Shake-test

15. Meconium is present in the amniotic fluid of nearly _____ of all infants at birth, and of those, between 20-25% go on to suffer some form of significant pulmonary disorder.

a. 2%
b. 10%
c. 20%
d. 45%

16. _____ is called for to eliminate airway obstructions, and placement of a nasogastric tube is needed to evacuate swallowed meconium and stomach contents.

a. Thoracic surgery
b. Mouth-to-mouth resuscitation
c. Aggressive suctioning
d. Thermoregulation

17. Diaphragmatic hernia, which occurs in about _____ births, is an extreme emergency and must be treated and corrected immediately upon diagnosis.

a. 1 in 20
b. 1 in 220
c. 1 in 2,200
d. 1 in 22,000

18._____, also known as hyaline membrane disease, is one of the most predominant lung problems experienced by neonates. It mainly strikes infants under 35 weeks old, affecting the younger newborns more than older infants.

a. APG
b. SIDS
c. ARC
d. RDS

19. When interpreting a chest x-ray in the neonate, the entire film should be examined, and not just the chest. Use of the _____ approach ensures that all areas of the film are systematically examined.

a. ABC
b. RDS
c. ARC
d. SIDS

20. _____ is a technique for pulmonary bypass, used to support patients with severe respiratory and/or cardiac failure who are not responsive to conventional therapy.

a. FHR
b. ARC
c. SIDS
d. ECMO

21. _____ is the accumulation of lymphatic fluid in the pleural space.

a. Chylothorax
b. Tracheoesophageal fistula
c. Pulmonary hypoplasia
d. Alveolarization

22. The purpose of the neonatal resuscitation is to reverse _____ before irreparable damage occurs.

a. hypoplasia
b. asphyxia
c. hyperplasia
d. Chylothorax

23. _____ is the name given to a group of inflammatory diseases that primarily affect infants and children.

a. Croup
b. Pneumonia
c. Aplasia
d. Hypoplasia

24. Acute bronchiolitis is a viral infection that leads to swelling, inflammation, and constriction in the bronchioles. While its consequences are gravest among infants less than six months, it presents potentially serious problems in children up to three years of age. _____ is the primary causative agent, causing about 75% of all cases.

a. RDS
b. RSV
c. SIDS
d. CF

25. _____ is a chronic pulmonary disease that is characterized by tenacious mucus production, which causes obstruction, leading to hyperinflation, an increased chest diameter (barrel-like chest), atelectasis, and infection.

a. RDS
b. ECMO
c. CF
d. RSV

26. _____ attempts to identify and explain the variations in the practice and outcomes which have been observed to occur among regions, among hospitals, and among physicians.

a. JCAHO evaluation

b. Peer review evaluation
c. HMO evaluation
d. Clinical evaluation science

27. The International Neonatal Network has developed the _____ , a scoring system for predicting mortality risk for infants weighing 1,500 grams (3 pounds, 5 ounces) or less. The score is based on birth weight, gestational age, maximum and minimum fraction of inspired oxygen, maximum base excess, and presence of congenital malformations.

a. RSV
b. APGAR
c. SIDS
d. CRIB

28. The multiple barriers to immunization of infants and children include _____.

a. cultural risk factors
b. provider practices
c. inadequate knowledge
d. all the above

29. According to the American Academy of Pediatricians, _____ is the preferred feeding for all infants, including premature and sick newborns, with rare exceptions.

a. cow's milk
b. formula
c. human milk
d. combination of a and b

30. Optimal use of _____ has resulted in a substantial reduction in mortality among critically ill infants.

a. formula feedings
b. parenteral nutrition
c. vitamin supplements
d. all the above

31. Maintaining appropriate _____ in the pediatric patient is essential. Dehydration, hypernatremia and hyperosmolarity may occur if intake is inadequate.

a. fluid balance
b. vitamin A levels
c. FHR
d. surfactant levels

32. Most calories for energy (nonprotein calories) in both infants and adults are supplied as _____, most commonly dextrose, with fat administered to avoid essential fatty acid deficiency.

a. lipids
b. carbohydrates
c. vitamins
d. minerals

33. _____ is most commonly used to supply carbohydrate calories in parenteral nutrition.

a. Mineral water
b. Fruit
c. Dextrose
d. Sucrose

34. Use of _____ in parenteral nutrition will prevent the development of essential fatty acid deficiency, provide a non-carbohydrate source of calories, and provide the pediatric patient with a more physiologic diet.

a. lipids
b. proteins
c. sugars
d. fruits

35. Parenteral nutrition can be delivered either via the peripheral or the central _____.

a. iliac
b. gland
c. vein
d. finger

36. _____ frequently occurs when parenteral nutrition solutions are stopped. For this reason, infusion rates should be tapered down prior to discontinuation of the nutrition solution.

a. Hypoglycemia
b. Hyperglycemia
c. Asphyxia
d. Shock

37. _____ is the most common and serious metabolic complication seen with parenteral nutrition in the neonate.

a. Hyperglycemia
b. Glycoses
c. Cholestasis
d. Homeostasis

38. Healthy term newborns are now routinely discharged _____ after birth.

a. 24 hours
b. less than 48 hours
c. three days
d. one week

39. Jaundice is the most common clinical problem in newborns, observed during the first week of life in approximately _____ of term infants and in _____ of preterm infants.

a. 10%/20%
b. 25%/35%
c. 60%/80%
d. 80%/95%

40. While the ductus venosus and foramen ovale rarely cause problems at birth, if the ductus arteriosus does remain patent or reopens in response to _____, this can lead to problems.

a. asphyxia
b. hypoxia
c. hyperoxia
d. aspiration

41. The difference between fetal circulatory and non-fetal circulatory systems is that, since the fetus _____, very little blood actually perfuses the pulmonary circulation.
a. uses the lungs for gas exchange only
b. usually has only one lung until late in development
c. does not use the lungs for gas exchange
d. has very little blood in circulation

42. _____ is(are) important for changing capillary and interstitial pressures, facilitating removal of fluids from the lungs and lowering pulmonary vascular resistance at birth.

a. Collagen
b. Surfactant
c. Lamellar bodies
d. prostaglandins

43. Reviewing of _____ is an obvious way to identify potentially high-risk neonates.

a. fetal scalp tissue
b. the placenta
c. maternal history
d. FHR

44. _____ is useful only in the presence of abnormal FHR tracings, since normal tracing indicates a healthy infant in most instances.

a. Fetal scalp pH
b. Ultrasound screening
c. Thermoregulation
d. The shake-test

45. The goal in the delivery room is to maintain an environmental temperature such that the neonate's core temperature remains in the normal range of _____.

a. 31.0 to 33.5°C
b. 34.5 to 35.5°C
c. 36.5 to 37.5°C
d. 39.0 to 40.5°C

46. At birth, expansion of the lungs causes _____ to fall dramatically.

a. FHR
b. PVR
c. APGAR
d. BUN

47. In order to assess the degree of respiratory distress in neonates, practitioners often use the _____.

a. FHR test
b. Silverman-Anderson scoring system
c. results of ultrasound screenings
d. shake-test results

48. Most incidences of BPD occur subsequent to the treatment of _____.

a. SIDS
b. RDS
c. pre-natal HIV
d. pneumonia

49. At birth, the rising of $Pa0_2$ levels increases circulating _____levels. This helps constrict the ductus and force more blood through the pulmonary circulation.

a. bradykinin
b. surfactant
c. elastin
d. collagen

50. In comparison to adults, water accounts for a much larger percentage of body weight in neonates, as much as _____, with a greater proportion as extracellular fluid.

a. 20%
b. 35%
c. 50%
d. 80%

MEDEDSYS
PO BOX 81831, San Diego, CA, 92138-3939
TOLL FREE 1-877-295-4719
FAX: 619-295-0252
info@mededsys.com
www.mededsys.com

How to Complete Your Test and Print Your Certificate Online

If you chose to receive your order by postal mail, you have been mailed the printed course material(s) and the printed test(s). To take a test, simply complete the mailed test and send it back. Upon successful completion of a test, a certificate will be mailed or faxed to you. If you don't wish to mail the test back, customers who chose to have the course material(s) mailed may also follow the steps below to complete a test and print a certificate online.

INSTRUCTIONS

1. Go to www.mededsys.com
2. Login and go to "My Account".
3. On the page that opens, select an option from the "My Courses" menu.
4. Select the test you wish to complete.
5. After completion of test, print your certificate online by clicking on the "Continue" button. Alternatively, you may return to the "My Courses" section and select the option to print a certificate.