Fetal and Neonatal Physiology

A complete discussion of fetal development, functioning of the child immediately after birth, and growth and development through the early years of life lies within the province of formal courses in obstetrics and pediatrics. However, many physiologic principles are peculiar to the infant itself. This chapter discusses the more important of these.

Growth and Functional Development of the Fetus

Initial development of the placenta and fetal membranes occurs far more rapidly than development of the fetus itself. In fact, during the first 2 to 3 weeks after implantation of the blastocyst, the fetus remains almost microscopic, but thereafter, as shown in Figure 83–1, the length of the fetus increases almost in proportion to age. At 12 weeks, the length is about 10 centimeters; at 20 weeks, 25 centimeters; and at term (40 weeks), 53 centimeters (about 21 inches). Because the weight of the fetus is approximately proportional to the cube of length, the weight increases almost in proportion to the cube of the age of the fetus.

Note in Figure 83–1 that the weight remains minuscule during the first 12 weeks and reaches 1 pound only at 23 weeks (5 1/2 months) of gestation. Then, during the last trimester of pregnancy, the fetus gains tremendously, so that 2 months before birth, the weight averages 3 pounds, 1 month before birth 4.5 pounds, and at birth 7 pounds—the final birth weight varying from as low as 4.5 pounds to as high as 11 pounds in normal infants with normal gestational periods.

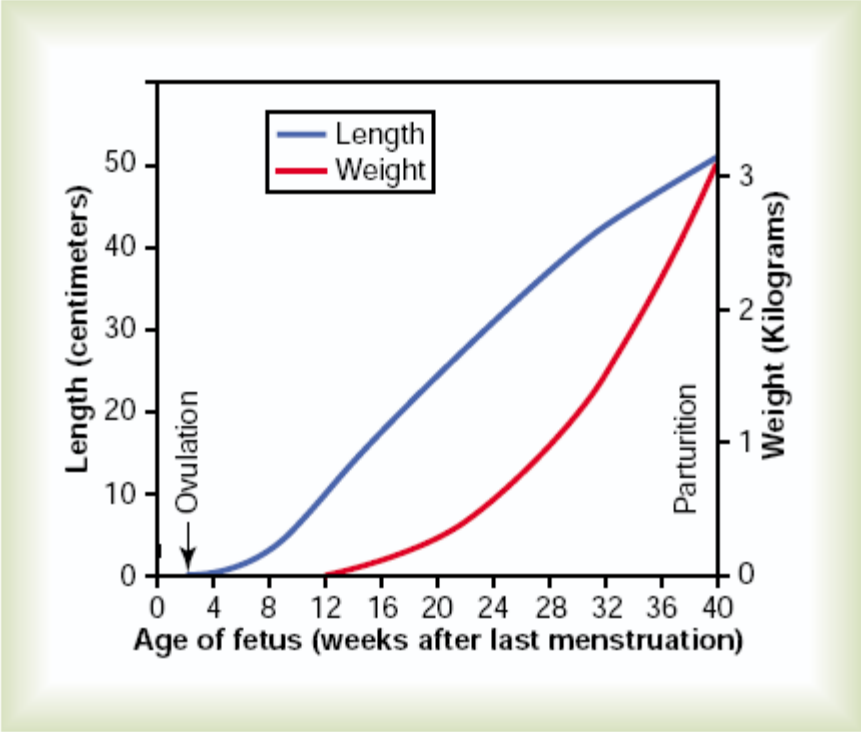


Figure 83–1

Growth of the fetus.

Development of the Organ Systems

Within 1 month after fertilization of the ovum, the gross characteristics of all the different organs of the fetus have already begun to develop, and during the next 2 to 3 months, most of the details of the different organs are established. Beyond month 4, the organs of the fetus are grossly the same as those of the neonate. However, cellular development in each organ is usually far from complete and requires the full remaining 5 months of pregnancy for complete development. Even at birth, certain structures, particularly in the nervous system, the kidneys, and the liver, lack full development.

Circulatory System. The human heart begins beating during the fourth week after fertilization, contracting at a rate of about 65 beats/min. This increases steadily to about 140 beats/min immediately before birth.

Formation of Blood Cells. Nucleated red blood cells begin to be formed in the yolk sac and mesothelial layers of the placenta at about the third week of fetal development. This is followed 1 week later (at 4 to 5 weeks) by formation of non-nucleated red blood cells by the fetal mesenchyme and also by the endothelium of the fetal blood vessels. Then, at 6 weeks, the liver begins to form blood cells, and in the third month, the spleen and other lymphoid tissues of the body begin forming blood cells. Finally, from the third month on, the bone marrow gradually becomes the principal source of the red blood cells as well as most of the white blood cells, except for continued lymphocyte and plasma cell production in lymphoid tissue.

Respiratory System. Respiration cannot occur during fetal life because there is no air to breathe in the amniotic cavity. However, attempted respiratory movements do take place beginning at the end of the first trimester of pregnancy. Tactile stimuli and fetal asphyxia especially cause these attempted respiratory movements.

During the last 3 to 4 months of pregnancy, the respiratory movements of the fetus are mainly inhibited, for reasons unknown, and the lungs remain almost completely deflated. The inhibition of respiration during the later months of fetal life prevents filling of the lungs with fluid and debris from the meconium excreted bythe fetus’s gastrointestinal tract into the amniotic fluid. Also, small amounts of fluid are secreted into the lungs by the alveolar epithelium up until the moment of birth, thus keeping only clean fluid in the lungs.

Nervous System. Most of the reflexes of the fetus that involve the spinal cord and even the brain stem are present by the third to fourth months of pregnancy. However, those nervous system functions that involve the cerebral cortex are still only in the early stages of development even at birth. Indeed, myelinization of some major tracts of the brain itself becomes complete only after about 1 year of postnatal life.

Gastrointestinal. Tract By midpregnancy, the fetus begins to ingest and absorb large quantities of amniotic fluid, and during the last 2 to 3 months, gastrointestinal function approaches that of the normal neonate. By that time, small quantities of *meconium* are continually formed in the gastrointestinal tract and excreted from the anus into the amniotic fluid. Meconium is composed partly of residue from swallowed amniotic fluid and partly of *mucus* and other residues of excretory products from the gastrointestinal mucosa and glands.

Kidneys. The fetal kidneys begin to excrete urine during the second trimester pregnancy, and fetal urine accounts for about 70 to 80 per cent of the amniotic fluid. Abnormal kidney development or severe impairment of kidney function in the fetus greatly reduce the formation of amniotic fluid (*oligohydramnio*s) and can lead to fetal death.

Although the fetal kidneys form urine, the renal control systems for regulating fetal extracellular fluid volume and electrolyte balances, and especially acid base balance, are almost nonexistent until late fetal life and do not reach full development until a few months after birth.

Fetal Metabolism. The fetus uses mainly glucose for energy, and it has a high capability to store fat and protein, much if not most of the fat being synthesized from glucose rather than being absorbed directly from the mother’s

blood. In addition to these generalities, there are special problems of fetal metabolism in relation to calcium, phosphate, iron, and some vitamins.

Metabolism of Calcium and Phosphate.

Figure 83–2 shows the rates of calcium and phosphate accumulation in the fetus, demonstrating that about 22.5 grams of calcium and 13.5 grams of phosphorus are accumulated in the average fetus during gestation. About one half of these accumulate during the last 4 weeks of gestation, which is coincident with the period of rapid ossification of the fetal bones and with the period of rapid weight gain of the fetus.

During the earlier part of fetal life, the bones are relatively unossified and have mainly a cartilaginous matrix. Indeed x-ray films ordinarily do not show any ossification until after the fourth month of pregnancy.

Note especially that the total amounts of calcium and phosphate needed by the fetus during gestation represent only about 2 per cent of the quantities of these substances in the mother’s bones. Therefore, this is a minimal drain from the mother. Much greater drain occurs after birth during lactation.

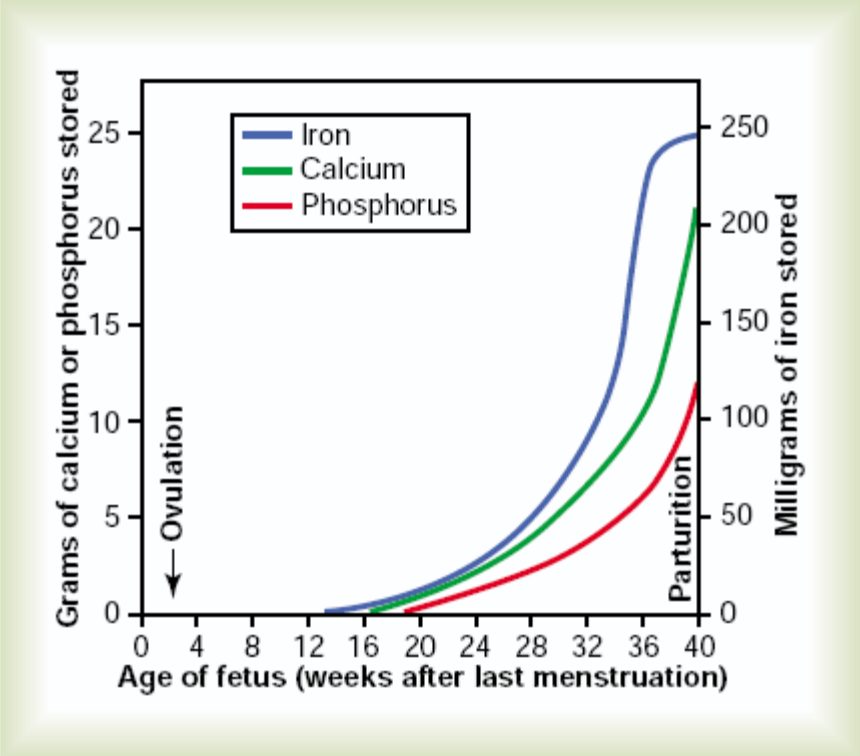


Figure 83–2

Iron, calcium, and phosphorus storage in the fetus at different stages of gestation.

Accumulation of Iron. Figure 83–2 also shows that iron accumulates in the fetus even more rapidly than calcium and phosphate. Most of the iron is in the form of hemoglobin, which begins to be formed as early as the third week after fertilization of the ovum.

Small amounts of iron are concentrated in the mother's uterine progestational endometrium even before implantation of the ovum; this iron is ingested into the embryo by the trophoblastic cells and is used to form the very early red blood cells. About one third of the iron in a fully developed fetus is normally stored in the liver. This iron can then be used for several months after birth by the neonate for formation of additional hemoglobin.

Utilization and Storage of Vitamins. The fetus needs vitamins equally as much as the adult and in some instances to a far greater extent. In general, the vitamins function the same in the fetus as in the adult, Special functions of several vitamins should be mentioned, however.

The B vitamins, especially vitamin B12 and folic acid, are necessary for formation of red blood cells and nervous tissue, as well as for overall growth of the fetus.

Vitamin C is necessary for appropriate formation of intercellular substances, especially the bone matrix and fibers of connective tissue.

Vitamin D is needed for normal bone growth in the fetus, but even more important, the mother needs it for adequate absorption of calcium from her gastrointestinal tract. If the mother has plenty of this vitamin in her body fluids, large quantities of the vitamin will be stored by the fetal liver to be used by the neonate for several months after birth.

Vitamin E, although the mechanisms of its functions are not clear, is necessary for normal development of the early embryo. In its absence in laboratory animals, spontaneous abortion usually occurs at an early stage of pregnancy.

Vitamin K is used by the fetal liver for formation of Factor VII, prothrombin, and several other blood coagulation factors. When vitamin K is insufficient in the mother, Factor VII and prothrombin become deficient in the fetus as well as in the mother. Because most vitamin K is formed by bacterial action in the mother's colon, the neonate has no adequate source of vitamin K for the first week or so of life after birth until normal colonic bacterial flora become established in the newborn infant. Therefore, prenatal storage in the fetal liver of at least small

amounts of vitamin K derived from the mother is helpful in preventing fetal hemorrhage, particularly hemorrhage in the brain when the head is traumatized by squeezing through the birth canal.

Adjustments of the Infant to Extrauterine Life Onset of Breathing

The most obvious effect of birth on the baby is loss of the placental connection with the mother and, therefore, loss of this means of metabolic support. One of the most important immediate adjustments required of the infant is to begin breathing.

Cause of Breathing at Birth. After normal delivery from a mother who has not been depressed by anesthetics, the child ordinarily begins to breathe within seconds and has a normal respiratory rhythm within less than 1 minute after birth. The promptness with which the fetus begins to breathe indicates that breathing is initiated by sudden exposure to the exterior world, probably resulting from **(1)** a slightly asphyxiated state incident to the birth process, but also from **(2)** sensory impulses that originate in the suddenly cooled skin. In an infant who does not breathe immediately, the body becomes progressively more hypoxic and hypercapnic, which provides additional stimulus to the respiratory center and usually causes breathing within an additional minute after birth.

Delayed or Abnormal Breathing at Birth—Danger of Hypoxia. If the mother has been depressed by a general anesthetic during delivery, which at least partially anesthetizes the fetus as well, the onset of respiration is likely to be delayed for several minutes, thus demonstrating the importance of using as little anesthesia as feasible. Also, many infants who have had head trauma during delivery or who undergo prolonged delivery are slow to breathe or sometimes do not breathe at all. This can result from two possible effects: First, in a few infants,

intracranial hemorrhage or brain contusion causes a concussion syndrome with a greatly depressed respiratory center. Second, and probably much more important, prolonged fetal hypoxia during delivery can cause serious depression of the respiratory center.***Hypoxia frequently occurs during delivery because of***

(1) compression of the umbilical cord;

(2) premature separation of the placenta;

(3) excessive contraction of the uterus, which can cut off the mother's blood flow to the placenta;

(4) excessive anesthesia of the mother, which depresses oxygenation even of her blood.

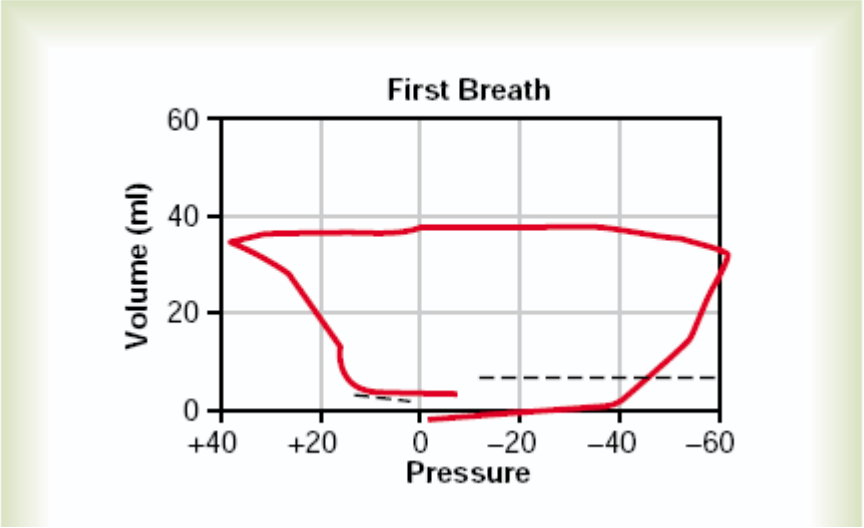
Degree of Hypoxia That an Infant Can Tolerate. In an adult, failure to breathe for only 4 minutes often causes death, but a neonate often survives as long as 10 minutes of failure to breathe after birth. Permanent and very serious brain impairment often ensues if breathing is delayed more than 8 to 10 minutes. Indeed, actual lesions develop mainly in the thalamus, in the inferior colliculi, and in other brain stem areas, thus permanently affecting many of the motor functions of the body.

Expansion of the Lungs at Birth. At birth, the walls of the alveoli are at first collapsed because of the surface tension of the viscid fluid that fills them. More than 25 mm Hg of negative inspiratory pressure in the lungs is usually required to oppose the effects of this surface tension and to open the alveoli for the first time. But once the alveoli do open, further respiration can be effected with relatively weak respiratory movements. Fortunately, the first inspirations of the normal

neonate are extremely powerful, usually capable of creating as much as 60 mm Hg negative pressure in the intrapleural space.

Figure 83–3 shows the tremendous negative intrapleural pressures required to open the lungs at the onset of breathing. At the top is shown the pressure-volume curve ("compliance" curve) for the first breath after birth. Observe, first, the lower part of the curve *beginning at the zero pressure point* and moving to the right.The curve shows that the volume of air in the lungs remains almost exactly zero until the negative pressure has reached -40 centimeters water (-30 mm Hg). Then, as the negative pressure increases to -60 centimeters of water, about 40 milliliters of air enters the lungs. To deflate the lungs, considerable positive pressure, about +40 centimeters of water, is required because of viscous resistance offered by the fluid in the bronchioles.

Note that the second breath is much easier, with far less negative and positive pressures required. Breathing does not become completely normal until about 40 minutes after birth, as shown by the third compliance curve, the shape of which compares favorably with that for the normal adult.



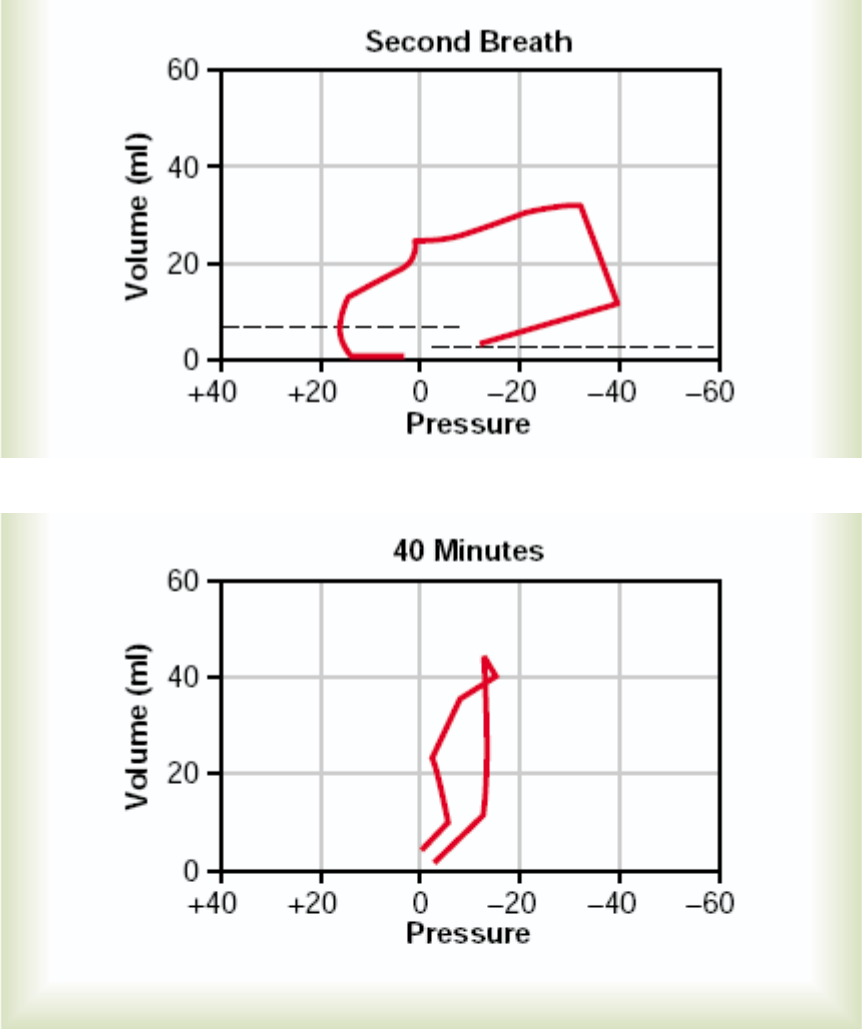


Figure 83–3

Pressure-volume curves of the lungs ("compliance" curves) of a neonate immediately after birth, showing the extreme forces required for breathing during the first two breaths of life and development of a nearly normal compliance curve within 40 minutes after birth. (Redrawn from Smith CA: The first breath. Sci Am 209:32, 1963, © 1963 by Scientific American, Inc. All rights reserved.)

Respiratory Distress Syndrome Caused When Surfactant Secretion Is Deficient. A small number of infants, especially premature infants and infants born of diabetic mothers, develop severe respiratory distress in the early hours to the first several days after birth, and some die within the next day or so. The alveoli of these infants at death contain large quantities of proteinaceous fluid, almost as if pure plasma had leaked out of the capillaries into the alveoli. The fluid also contains desquamated alveolar epithelial cells. This condition is called *hyaline membrane disease* because microscopic slides of the lung show the material filling the alveoli to look like a hyaline membrane.

One of the most characteristic findings in respiratory distress syndrome is failure of the respiratory epithelium to secrete adequate quantities of *surfactant*, a substance normally secreted into the alveoli that decreases the surface tension of the alveolar fluid, therefore allowing the alveoli to open easily during inspiration. The surfactant-secreting cells (type II alveolar epithelial cells) do not begin to secrete surfactant until the last 1 to 3 months of gestation. Therefore, many premature babies and a few full-term babies are born without the capability to secrete sufficient surfactant, which causes both a collapse tendency of the alveoli and development of pulmonary edema.

Circulatory Readjustments at Birth

Equally as essential as the onset of breathing at birth are immediate circulatory adjustments that allow adequate blood flow through the lungs. Also, circulatory adjustments during the first few hours of life cause more and more blood flow through the baby’s liver, which up to this point has had very little blood flow. To describe these readjustments, we must first consider the anatomical structure of the fetal circulation.

Specific Anatomical Structure of the Fetal Circulation. Because the lungs are mainly nonfunctional during fetal life and because the liver is only partially functional, it is not necessary for the fetal heart to pump much blood through either the lungs or the liver. However, the fetal heart must pump large quantities of blood through the placenta. Therefore, special anatomical arrangements cause the fetal circulatory system to operate much differently from that of the newborn baby.

First, as shown in Figure 83–4, blood returning from the placenta through the umbilical vein passes through the *ductus venosus*, mainly bypassing the liver. Then most of the blood entering the right atrium from the inferior vena cava is directed in a straight pathway across the posterior aspect of the right atrium and through the *foramen ovale* directly into the left atrium.

Thus, the well-oxygenated blood from the placenta enters mainly the left side of the heart, rather than the right side, and is pumped by the left ventricle mainly into the arteries of the head and forelimbs.

The blood entering the right atrium from the superior vena cava is directed downward through the tricuspid valve into the right ventricle. This blood is mainly deoxygenated blood from the head region of the fetus, and it is pumped by the right ventricle into the pulmonary artery and then mainly through the *ductus arteriosus* into the descending aorta, then through the two umbilical arteries into the placenta, where the deoxygenated blood becomes oxygenated.

Figure 83–5 gives the relative percentages of the total blood pumped by the heart that pass through the different vascular circuits of the fetus. This figure shows that 55 per cent of all the blood goes through the placenta, leaving only 45 per cent to pass through all the tissues of the fetus. Furthermore, during fetal life,

only 12 per cent of the blood flows through the lungs; immediately after birth, virtually all the blood flows through the lungs.

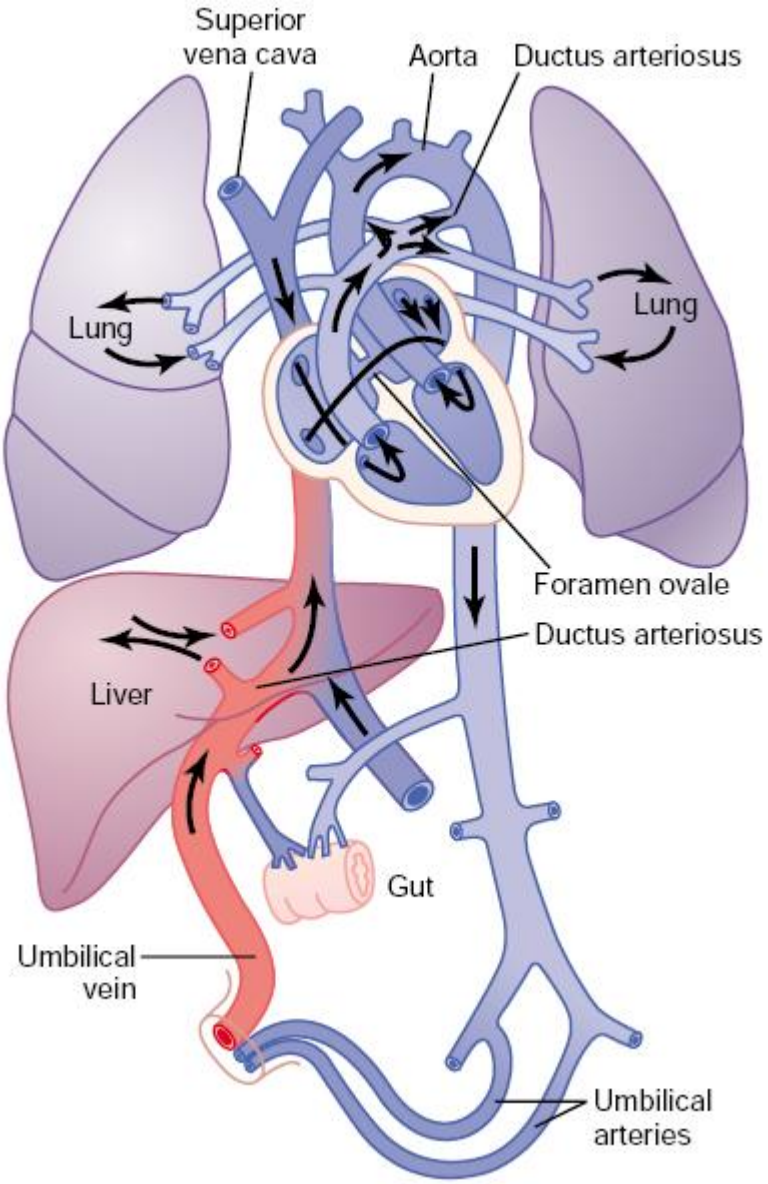


Figure 83–4

Organization of the fetal circulation. (Modified from Arey LB: Developmental Anatomy: A Textbook and Laboratory Manual of Embryology. 7th ed. Philadelphia: WB Saunders Co, 1974.)

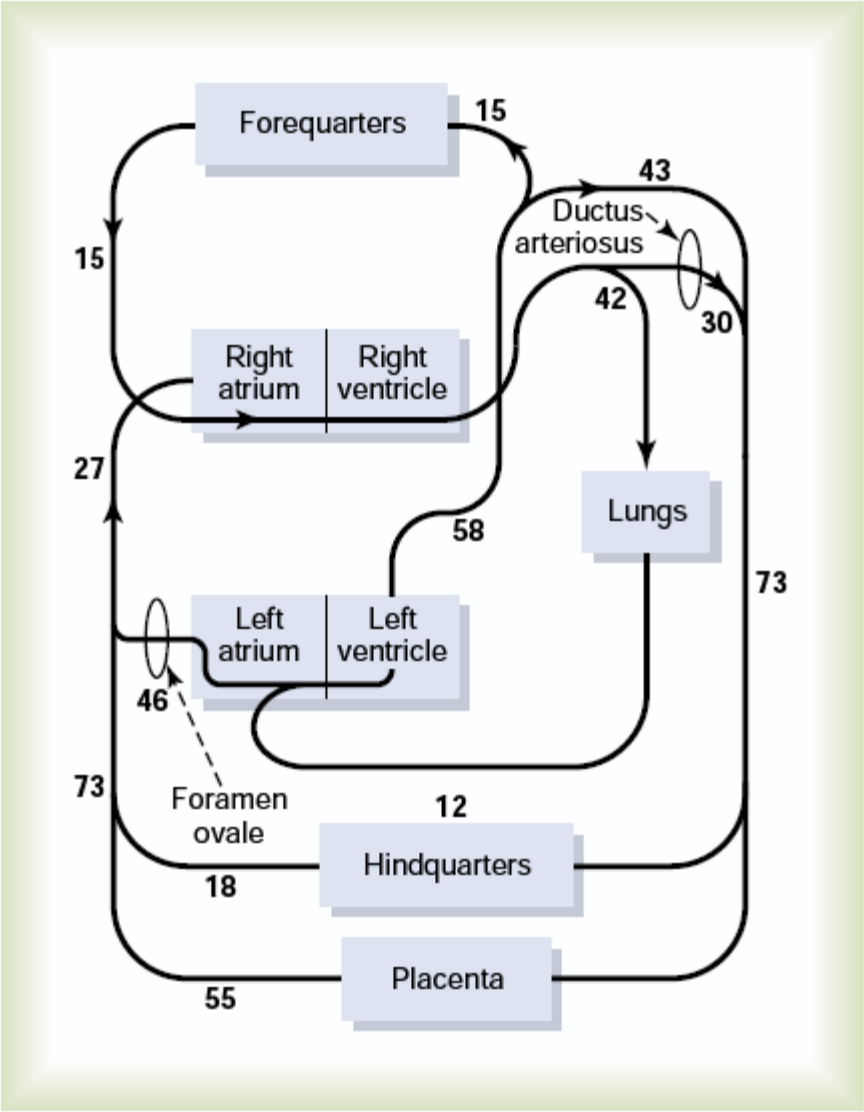


Figure 83–5

Diagram of the fetal circulatory system, showing relative distribution of blood flow to the different vascular areas. The numerals represent the percentage of the total output from both sides of the heart flowing through each particular area.

Changes in the Fetal Circulation at Birth. The basic changes in the fetal circulation at birth are discussed in Chapter 23 in relation to congenital anomalies of the ductus arteriosus and foramen ovale that persist throughout life in a few persons. Briefly, these changes are the following.

Primary Changes in Pulmonary and Systemic Vascular Resistances at Birth

The primary changes in the circulation at birth are, **first,** loss of the tremendous blood flow through the placenta, which approximately doubles the systemic vascular resistance at birth. This increases the aortic pressure as well as the pressures in the left ventricle and left atrium.

Second, the *pulmonary vascular resistance greatly decreases* as a result of expansion of the lungs. In the unexpanded fetal lungs, the blood vessels are compressed because of the small volume of the lungs. Immediately on expansion, these vessels are no longer compressed and the resistance to blood flow decreases several fold. Also, in fetal life, the hypoxia of the lungs causes considerable tonic vasoconstriction of the lung blood vessels, but vasodilation takes place when aeration of the lungs eliminates the hypoxia. All these changes together reduce the resistance to blood flow through the lungs as much as fivefold, which *reduces the pulmonary arterial pressure*, *right ventricular pressure*, and *right atrial pressure.*

Closure of the Foramen Ovale

The *low right atrial pressure* and the *high left atrial pressure* that occur secondarily to the changes in pulmonary and systemic resistances at birth cause blood now to attempt to flow backward through the foramen ovale; that is, from the left atrium into the right atrium, rather than in the other direction, as occurred during fetal life.

Consequently, the small valve that lies over the foramen ovale on the left side of the atrial septum closes over this opening, thereby preventing further flow through the foramen ovale.

In two thirds of all people, the valve becomes adherent over the foramen ovale within a few months to a few years and forms a permanent closure. But even if permanent closure does not occur, the left atrial pressure throughout life normally remains 2 to 4 mm Hg greater than the right atrial pressure, and the backpressure keeps the valve closed.

Closure of the Ductus Arteriosus

The ductus arteriosus also closes, but for differentreasons. First, the increased systemic resistance *elevates the aortic pressure* while the decreased pulmonary resistance *reduces the pulmonary arterial pressure.* As a consequence, after birth, blood begins to flow backward from the aorta into the pulmonary artery through the ductus arteriosus, rather than in the other direction as in fetal life. However, after only a few hours, the muscle wall of the ductus arteriosus constricts markedly, and within 1 to 8 days, the constriction is usually sufficient to stop all blood flow. This is called *functional closure* of the ductus arteriosus. Then, during the next 1 to 4 months, the ductus arteriosus ordinarily becomes anatomically *occluded* by growth of fibrous tissue into its lumen.

The cause of ductus arteriosus closure relates to the increased oxygenation of the blood flowing through the ductus. In fetal life the PO2 of the ductus blood is only 15 to 20 mm Hg, but it increases to about 100 mm Hg within a few hours after birth. Furthermore, many experiments have shown that the degree of contraction of the smooth muscle in the ductus wall is highly related to this availability of oxygen.

In one of several thousand infants, the ductus fails to

close, resulting in a *patent ductus arteriosus*, The failure of closure has been postulated to result from excessive ductus dilation caused by vasodilating prostaglandins in the ductus wall. In fact, administration of the drug *indomethacin*, which blocks synthesis of prostaglandins, often leads to closure.

Closure of the Ductus Venosus In fetal life, the portal blood from the fetus's abdomen joins the blood from the umbilical vein, and these together pass by way of the *ductus venosus* directly into the vena cava immediately below the heart but above the liver, thus bypassing the liver.

Immediately after birth, blood flow through the umbilical vein ceases, but most of the portal blood still flows through the ductus venosus, with only a small amount passing through the channels of the liver.

However, within 1 to 3 hours the muscle wall of the ductus venosus contracts strongly and closes this avenue of flow. As a consequence, the portal venous pressure rises from near 0 to 6 to 10 mm Hg, which is enough to force portal venous blood flow through the liver sinuses. Although the ductus venosus rarely fails to close, we know almost nothing about what causes the closure.

Nutrition of the Neonate

Before birth, the fetus derives almost all its energy from glucose obtained from the mother's blood. After birth, the amount of glucose stored in the infant's body in the form of liver and muscle glycogen is sufficient to supply the infant's needs for only a few hours. The liver of the neonate is still far from functionally adequate at birth, which prevents significant gluconeogenesis. Therefore, the infant's blood glucose concentration frequently falls the first day to as low as 30 to

40 mg/dl of plasma, less than one half the normal value. Fortunately, however, appropriate mechanisms are available for the infant to use its stored fats and proteins for metabolism until mother's milk can be provided 2 to 3 days later.

Special problems are also frequently associated with getting an adequate fluid supply to the neonate because the infant's rate of body fluid turnover averages seven times that of an adult, and the mother's milk supply requires several days to develop. Ordinarily, the infant's weight decreases 5 to 10 per cent and sometimes as much as 20 per cent within the first 2 to 3 days of life. Most of this weight loss is loss of fluid rather than of body solids.

Special Functional Problems in the Neonate

An important characteristic of the neonate is instability of the various hormonal and neurogenic control systems. This results partly from immature development of the different organs of the body and partly from the fact that the control systems simply have not become adjusted to the new way of life.

Respiratory System

The normal rate of respiration in a neonate is about 40 breaths per minute, and tidal air with each breath averages 16 milliliters. This gives a total minute respiratory volume of 640 ml/min, which is about twice as great in relation to the body weight as that of an adult. *The functional residual capacity of the infant's lungs is only one half that of an adult in relation to body weight.* This difference causes excessive cyclical increases and decreases in the newborn baby's blood gas concentrations if the respiratory rate becomes slowed because it is the residual air in the lungs that smooths out the blood gas variations.

Circulation

Blood Volume. The blood volume of a neonate immediately after birth averages about 300 milliliters, but if the infant is left attached to the placenta for a few minutes after birth or if the umbilical cord is stripped to force blood out of its vessels into the baby, an additional 75 milliliters of blood enters the infant, to make a total of 375 milliliters. Then, during the ensuing few hours, fluid is lost into the neonate's tissue spaces from this blood, which increases the hematocrit but returns the blood volume once again to the normal value of about 300 milliliters.

Some pediatricians believe that this extra blood volume caused by stripping the umbilical cord can lead to mild pulmonary edema with some degree of respiratory distress, but the extra red blood cells are often very valuable to the infant.

Cardiac Output. The cardiac output of the neonate averages 500 ml/min, which, like respiration and body metabolism, is about twice as much in relation to body weight as in the adult. Occasionally a child is born with an especially low cardiac output caused by hemorrhage of much of its blood volume from the placenta at birth.

Arterial Pressure. The arterial pressure during the first day after birth averages about 70 mm Hg systolic and 50 mm Hg diastolic; this increases slowly during the next several months to about 90/60. Then there is a much slower rise during the subsequent years until the adult pressure of 115/70 is attained at adolescence.

Blood Characteristics. The red blood cell count in the neonate averages about 4 million per cubic millimeter. If blood is stripped from the cord into the

infant, the red blood cell count rises an additional 0.5 to 0.75 million during the first few hours of life, giving a red blood cell count of about 4.75 million per cubic millimeter, as shown in Figure 83–6. Subsequent to this, however, few new red blood cells are formed in the infant during the first few weeks of life, presumably because the hypoxic stimulus of fetal life is no longer present to stimulate red cell production. Thus, as shown in Figure 83–6, the average red blood cell count falls to less than 4 million per cubic millimeter by about 6 to 8 weeks of age. From that time on, increasing activity by the baby provides the appropriate stimulus for returning the red blood cell count to normal within another 2 to 3 months. Immediately after birth, the white blood cell count of the neonate is about 45,000 per cubic millimeter, which is about five times as great as that of the normal adult.

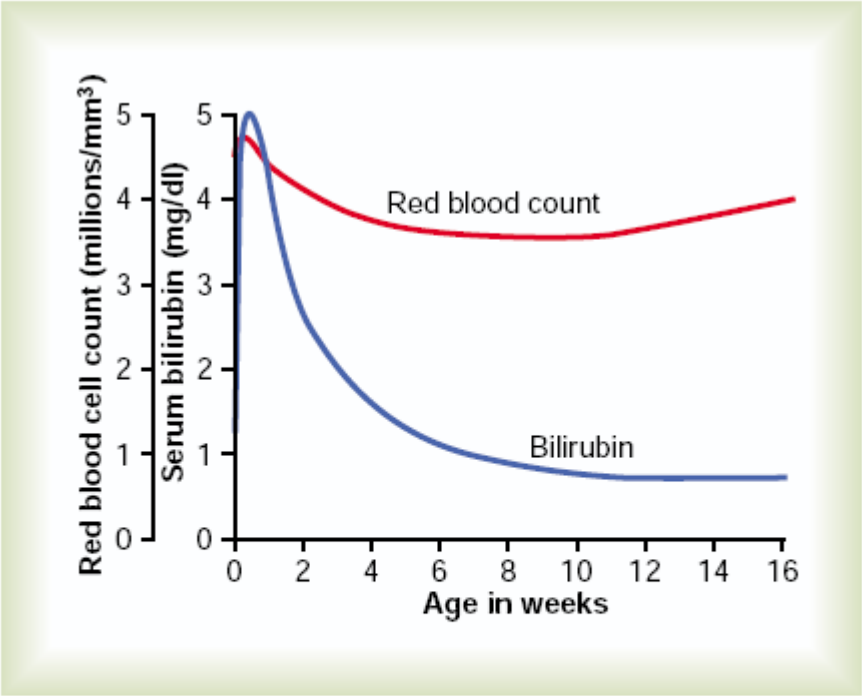


Figure 83–6

Changes in the red blood cell count and in serum bilirubin concentration during the first 16 weeks of life, showing physiologic anemia at 6 to 12 weeks of life and physiologic hyperbilirubinemia during the first 2 weeks of life.

Neonatal Jaundice and Erythroblastosis Fetalis. Bilirubin formed in the fetus can cross the placenta into the mother and be excreted through the liver of the mother, but immediately after birth, the only means for ridding the neonate of bilirubin is through the neonate's own liver, which for the first week or so of life functions poorly and is incapable of conjugating significant quantities of bilirubin with glucuronic acid for excretion into the bile. Consequently, the plasma bilirubin concentration rises from a normal value of less than 1 mg/dl to an average of 5 mg/dl during the first 3 days of life and then gradually falls back to normal as the liver becomes functional. This effect, called *physiologic hyperbilirubinemia,* is shown in Figure 83–6, and it is associated with mild *jaundice* (yellowness) of the infant's skin and especially of the sclerae of its eyes for a week or two.

However, by far the most important abnormal cause of serious neonatal jaundice is *erythroblastosis fetalis,*. Briefly, the *erythroblastotic baby* inherits Rhpositive red cells from the father, while the mother is Rh negative. The mother then becomes immunized against the Rh-positive factor (a protein) in the fetus's blood cells, and her antibodies destroy fetal red cells, releasing extreme quantities of bilirubin into the fetus's plasma and often causing fetal death for lack of adequate red cells. Before the advent of modern obstetrical therapeutics, this condition occurred either mildly or seriously in 1 of every 50 to 100 neonates.

Fluid Balance, Acid-Base Balance, and Renal Function

The rate of fluid intake and fluid excretion in the newborn infant is seven times as great in relation to weight as in the adult, which means that even a slight percentage alteration of fluid intake or fluid output can cause rapidly developing abnormalities.

The rate of metabolism in the infant is also twice as great in relation to body mass as in the adult, which means that twice as much acid is normally formed, which gives a tendency toward acidosis in the infant.

Functional development of the kidneys is not complete until the end of about the first month of life. For instance, the kidneys of the neonate can concentrate urine to only 1.5 times the osmolality of the plasma instead of the adult three to four times. Therefore, considering the immaturity of the kidneys, together with the marked fluid turnover in the infant and rapid formation of acid, one can readily understand that among the most important problems of infancy are acidosis, dehydration, and, more rarely, over hydration.

Liver Function

During the first few days of life, liver function in the neonate may be quite deficient, as evidenced by the following effects:

1. The liver of the neonate conjugates bilirubin with glucuronic acid poorly and therefore excretes bilirubin only slightly during the first few days of life.

2. The liver of the neonate is deficient in forming plasma proteins, so that the plasma protein concentration falls during the first weeks of life to 15 to 20 per cent less than that for older children. Occasionally the protein concentration falls so low that the infant develops hypoproteinemic edema.

3. The gluconeogenesis function of the liver is particularly deficient. As a result, the blood glucose level of the unfed neonate falls to about 30 to 40 mg/dl (about 40 per cent of normal), and the infant must depend mainly on its stored fats for energy until sufficient feeding can occur.

4. The liver of the neonate usually also forms too little of the blood factors needed for normal blood coagulation.

Digestion, Absorption, and Metabolism of Energy Foods; and Nutrition

In general, the ability of the neonate to digest, absorb, and metabolize foods is no different from that of the older child, with the following three exceptions.

First, secretion of pancreatic amylase in the neonate is deficient, so that the neonate uses starches less adequately than do older children.

Second, absorption of fats from the gastrointestinal tract is somewhat less than that in the older child. Consequently, milk with a high fat content, such as cow's milk, is frequently inadequately absorbed.

Third, because the liver functions imperfectly during at least the first week of life, the glucose concentration in the blood is unstable and low.

The neonate is especially capable of synthesizing and storing proteins. Indeed, with an adequate diet, as much as 90 per cent of the ingested amino acids are used for formation of body proteins. This is a much higher percentage than in adults.

Metabolic Rate and Body Temperature. The normal metabolic rate of the neonate in relation to body weight is about twice that of the adult, which accounts also for the twice as great cardiac output and twice as great minute respiratory volume in relation to body weight in the infant.

Because the body surface area is large in relation to body mass, heat is readily lost from the body. As a result, the body temperature of the neonate, particularly of premature infants, falls easily. Figure 83–7 shows that the body temperature of even a normal infant often falls several degrees during the first few hours after

birth but returns to normal in 7 to 10 hours. Still, the body temperature regulatory mechanisms remain poor during the early days of life, allowing marked deviations in temperature, which are also shown in Figure 83–7.

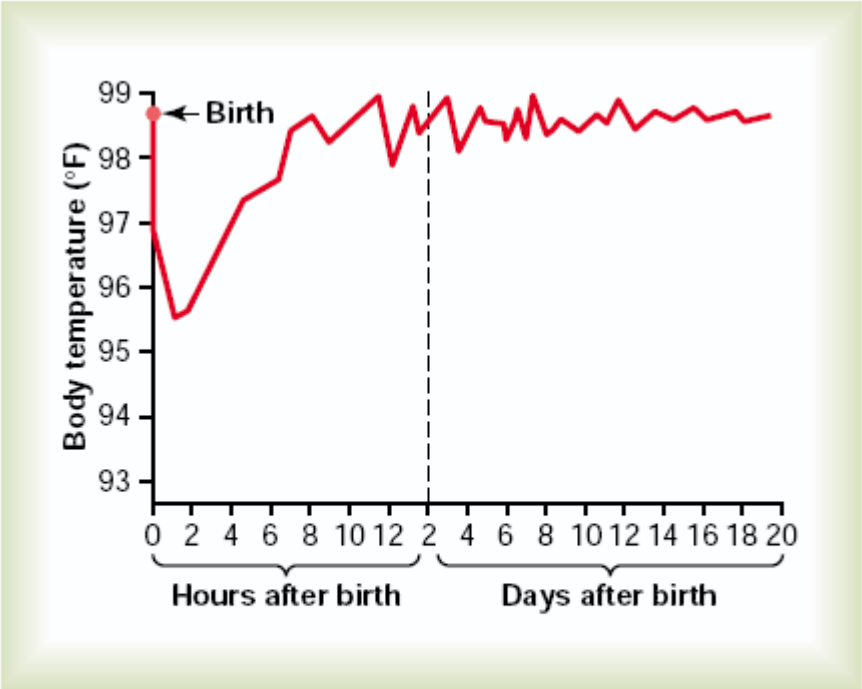


Figure 83–7

Fall in body temperature of the neonate immediately after birth, and instability of body temperature during the first few days of life.

Nutritional Needs During the Early Weeks of Life. At birth, a neonate is usually in complete nutritional balance, provided the mother has had an adequate diet. Furthermore, function of the gastrointestinal system is usually more than adequate to digest and assimilate all the nutritional needs of the infant if appropriate nutrients are provided in the diet. However, three specific problems do occur in the early nutrition of the infant.

Need for Calcium and Vitamin D

The neonate is in a stage of rapid ossification of its bones at birth, so that a ready supply of calcium throughout infancy is needed. This is ordinarily supplied adequately by the usual diet of milk. Yet absorption of calcium by the gastrointestinal tract is poor in the absence of vitamin D. Therefore, the vitamin D–deficient infant can develop severe rickets in only a few weeks. This is particularly true in premature babies because their gastrointestinal tracts absorb calcium even less effectively than those of normal infants.

Necessity for Iron in the Diet

If the mother has had adequate amounts of iron in her diet, the liver of the infant usually has stored enough iron to keep forming blood cells for 4 to 6 months after birth. But if the mother has had insufficient iron in her diet, severe anemia is likely to occur in the infant after about 3 months of life. To prevent this possibility, early feeding of the infant with egg yolk, which contains reasonably large quantities of iron, or the administration of iron in some other form is desirable by the second or third month of life.

Vitamin C Deficiency in Infants

Ascorbic acid (vitamin C) is not stored in significant quantities in the fetal tissues; yet it is required for proper formation of cartilage, bone, and other intercellular structures of the infant. Furthermore, milk has poor supplies of ascorbic acid, especially cow’s milk, which has only one fourth as much as human milk. For this reason, orange juice or other sources of ascorbic acid are often prescribed by the third week of life.

Immunity

The neonate inherits much immunity from the mother because many protein antibodies diffuse from the mother's blood through the placenta into the fetus.

However, the neonate does not form antibodies of its own to a significant extent. By the end of the first month, the baby's gamma globulins, which contain the antibodies, have decreased to less than one half the original level, with a corresponding decrease in immunity. Thereafter, the baby's own immunity system begins to form antibodies, and the gamma globulin concentration returns essentially to normal by the age of 12 to 20 months.

Despite the decrease in gamma globulins soon after birth, the antibodies inherited from the mother protect the infant for about 6 months against most major childhood infectious diseases, including diphtheria, measles, and polio. Therefore, immunization against these diseases before 6 months is usually unnecessary.

Conversely, the inherited antibodies against whooping cough are normally insufficient to protect the neonate; therefore, for full safety, the infant requires immunization against this disease within the first month or so of life.

Allergy. The newborn infant is seldom subject to allergy. Several months later, however, when the infant's own antibodies first begin to form, extreme allergic states can develop, often resulting in serious eczema, gastrointestinal abnormalities, and even anaphylaxis. As the child grows older and still higher degrees of immunity develop, these allergic manifestations usually disappear.

Endocrine Problems

Ordinarily, the endocrine system of the infant is highly developed at birth, and the infant seldom exhibits any immediate endocrine abnormalities. However, there are special instances in which the endocrinology of infancy is important:

1. If a pregnant mother bearing a female child is treated with an androgenic hormone or if an androgenic tumor develops during pregnancy, the child will be born with a high degree of masculinization of her sexual organs, thus resulting in a type of *hermaphroditism.*

2. The sex hormones secreted by the placenta and by the mother's glands during pregnancy occasionally cause the neonate's breasts to form milk during the first days of life. Sometimes the breasts then become inflamed, or infectious mastitis develops.

3. An infant born of an untreated diabetic mother will have considerable hypertrophy and hyper function of the islets of Langerhans in the pancreas.

As a consequence, the infant's blood glucose concentration may fall to lower than 20 mg/dl shortly after birth. Fortunately, however, in the neonate, unlike in the adult, insulin shock or coma from this low level of blood glucose concentration only rarely develops.

Maternal type II diabetes is the most common cause of large babies. Type II diabetes in the mother is associated with resistance to the metabolic effects of insulin and compensatory increases in plasma insulin concentration. The high levels of insulin are believed to stimulate fetal growth factor and contribute to increased birth weight. Increased supply of glucose and other nutrients to the fetus may also contribute to increased fetal growth. However, most of the increased fetal

weight is due to increased body fat; there is usually little increase in body length although the size of some organs may be increased (*organomegaly*).

In the mother with uncontrolled type I diabetes (caused by lack of insulin secretion), fetal growth may be stunted because of metabolic deficits in the mother, and growth and tissue maturation of the neonate are often impaired. Also, there is a high rate of intrauterine mortality, and among those fetuses that do come to term, there is still a high mortality rate. Two thirds of the infants who die succumb to *respiratory distress syndrome*,

4. Occasionally a child is born with hypofunctional adrenal cortices, often resulting from *agenesis* of the adrenal glands or *exhaustion atrophy*, which can occur when the adrenal glands have been vastly overstimulated.

5. If a pregnant woman has hyperthyroidism or is treated with excess thyroid hormone, the infant is likely to be born with a temporarily hyposecreting thyroid gland. Conversely, if before pregnancy a woman had had her thyroid gland removed, her pituitary gland may secrete great quantities of thyrotropin during gestation, and the child might be born with temporary hyperthyroidism.

6. In a fetus lacking thyroid hormone secretion, the bones grow poorly and there is mental retardation.This causes the condition called *cretin dwarfism*,.

Special Problems of Prematurity

All the problems in neonatal life just noted are severely exacerbated in prematurity. They can be categorized under the following two headings: **(1)** immaturity of certain organ systems and **(2)** instability of the different homeostatic

control systems. Because of these effects, a premature baby seldom lives if it is born more than 3 months before term.

Immature Development of the Premature Infant

Almost all the organ systems of the body are immature in the premature infant, but some require particular attention if the life of the premature baby is to be saved.

Respiration. The respiratory system is especially likely to be underdeveloped in the premature infant. The vital capacity and the functional residual capacity of the lungs are especially small in relation to the size of the infant. Also, surfactant secretion is depressed or absent. As a consequence, *respiratory distress syndrome* is a common cause of death. Also, the low functional residual capacity in the premature infant is often associated with periodic breathing of the Cheyne-Stokes type.

Gastrointestinal Function. Another major problem of the premature infant is to ingest and absorb adequate food. If the infant is more than 2 months premature, the digestive and absorptive systems are almost always inadequate. The absorption of fat is so poor that the premature infant must have a low-fat diet. Furthermore, the premature infant has unusual difficulty in absorbing calcium and, therefore, can develop severe rickets before the difficulty is recognized. For this reason, special attention must be paid to adequate calcium and vitamin D intake.

Function of Other Organs. Immaturity of other organ systems that frequently causes serious difficulties in the premature infant includes

(1) immaturity of the liver, which results in poor intermediary metabolism and often a bleeding tendency as a result of poor formation of coagulation factors;

(2) immaturity of the kidneys, which are particularly deficient in their ability to rid the body of acids, thereby predisposing to acidosis as well as to serious fluid balance abnormalities;

(3) immaturity of the blood-forming mechanism of the bone marrow, which allows rapid development of anemia

(4) depressed formation of gamma globulin by the lymphoid system, which often leads to serious infection.

Instability of the Homeostatic Control Systems in the Premature Infant

Immaturity of the different organ systems in the premature infant creates a high degree of instability in the homeostatic mechanisms of the body. For instance, the acid-base balance can vary tremendously, particularly when the rate of food intake varies from time to time. Likewise, the blood protein concentration is usually low because of immature liver development, often leading to *hypoproteinemic edema*. And inability of the infant to regulate its calcium ion concentration frequently brings on hypocalcemic tetany. Also, the blood glucose concentration can vary between the extremely wide limits of 20 to more than 100 mg/dl, depending principally on the regularity of feeding. It is no wonder, then, with these extreme variations in the internal environment of the premature infant, that mortality is high.

Instability of Body Temperature. One of the particular problems of the premature infant is inability to maintain normal body temperature. Its temperature tends to approach that of its surroundings. At normal room temperature, the infant's temperature may stabilize in the low 90°s or even in the 80°s F. Statistical studies show that a body temperature maintained below 96°F (35.5°C) is

associated with a particularly high incidence of death, which explains the almost mandatory use of the incubator in treatment of prematurity.

Danger of Blindness Caused by Excess Oxygen Therapy in the Premature Infant

Because premature infants frequently develop respiratory distress, oxygen therapy has often been used in treating prematurity. However, it has been discovered that use of excess oxygen in treating premature infants, especially in early prematurity, can lead to blindness.

The reason is that too much oxygen stops the growth of new blood vessels in the retina. Then when oxygen therapy is stopped, the blood vessels try to make up for lost time and burst forth with a great mass of vessels growing all through the vitreous humor, blocking light from the pupil to the retina. And still later, the vessels are replaced with a mass of fibrous tissue where the eye's clear vitreous humor should be.

This condition, known as *retrolental fibroplasia*, causes permanent blindness. For this reason, it is particularly important to avoid treatment of premature infants with high concentrations of respiratory oxygen.

Physiologic studies indicate that the premature infant is usually safe with up to 40 per cent oxygen in the air breathed, but some child physiologists believe that complete safety can be achieved only at normal oxygen concentration in the air that is breathed.

Growth and Development of the Child

The major physiologic problems of the child beyond the neonatal period are related to special metabolic needs for growth, which have been fully covered in the sections of this book on metabolism and endocrinology. Figure 83–8 shows the changes in heights of boys and girls from the time of birth until the age of 20 years.

Note especially that these parallel each other almost exactly until the end of the first decade of life. Between the ages of 11 and 13 years, the female estrogens begin to be formed and cause rapid growth in height but early uniting of the epiphyses of the long bones at about the 14th to 16th year of life, so that growth in height then ceases. This contrasts with the effect of testosterone in the male, which causes extra growth at a slightly later age—mainly between ages 13 and 17 years. The male, however, undergoes much more prolonged growth because of much delayed uniting of the epiphyses, so that his final height is considerably greater than that of the female.

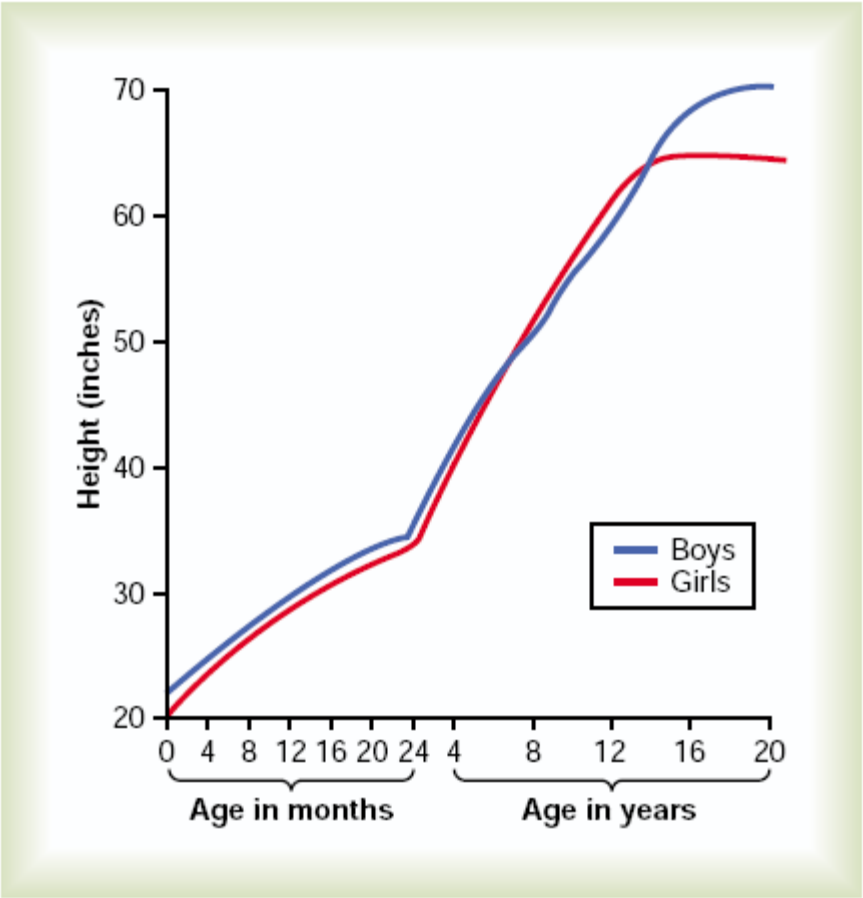


Figure 83–8

Average height of boys and girls from infancy to 20 years of age.

Behavioral Growth

Behavioral growth is principally a problem of maturity of the nervous system. It is extremely difficult to dissociate maturity of the anatomical structures of the nervous system from maturity caused by training.

Anatomical studies show that certain major tracts in the central nervous system are not completely myelinated until the end of the first year of life. For this reason, it is frequently stated that the nervous system is not fully functional at birth. The brain cortex and its associated functions, such as vision, seem to require several months after birth for final functional development to occur.

At birth, the infant brain mass is only 26 per cent of the adult brain mass and 55 per cent at 1 year, but it reaches almost adult proportions by the end of the second year. This is also associated with closure of the fontanels and sutures of the skull, which allows only 20 per cent additional growth of the brain beyond the first 2 years of life. Figure 83–9 shows a normal progress chart for the infant during the first year of life. Comparison of this chart with the baby's actual development is used for clinical assessment of mental and behavioral growth.

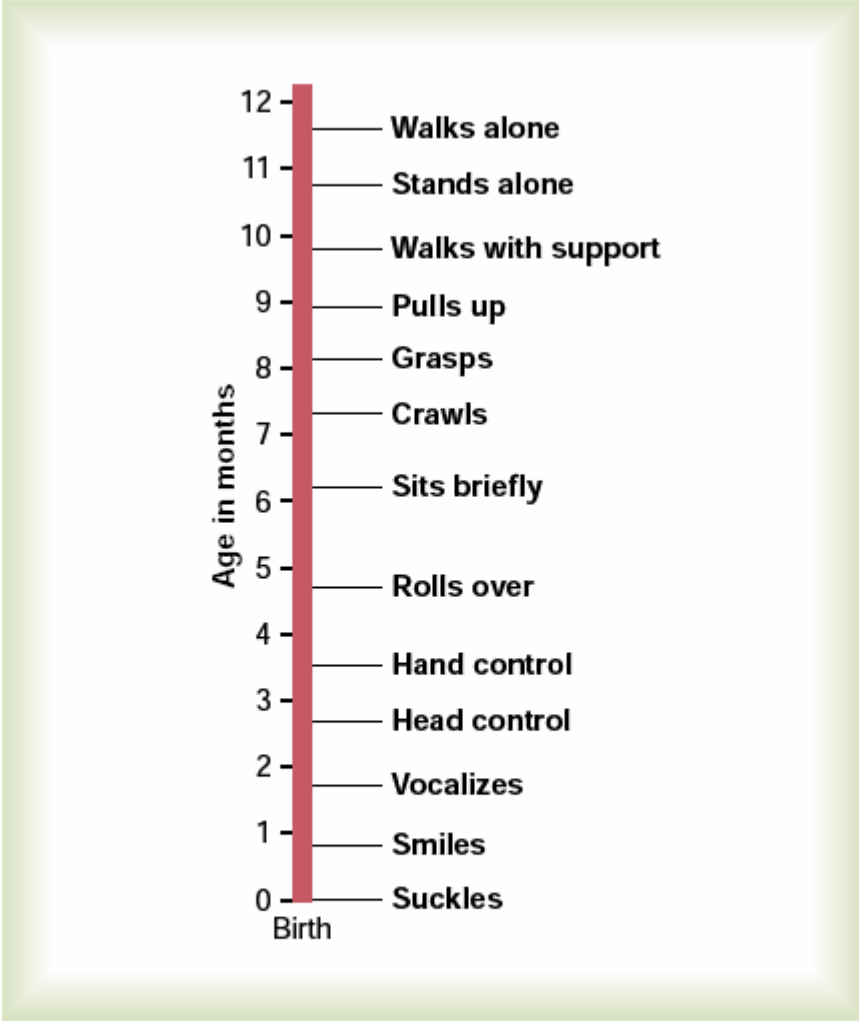


Figure 83–9

Behavioral development of the infant during the first year of life.