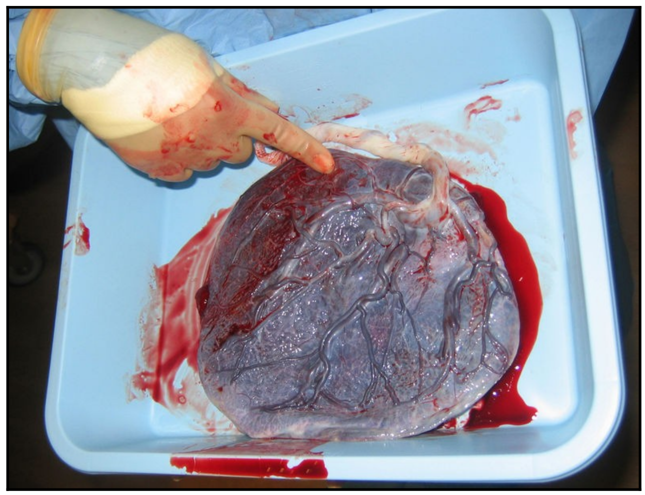
IINTRODUCTION

The embryonic period begins immediately after implantation is completed and will last until the end of the second month, when the fetal phase will commence and last until birth approximately 7 months later. The word "embryo" comes from a Greek word meaning "to swell" (Craig & Dunn, 2007), and quite a lot of swelling goes on in the embryonic period. According to Cherry (1973), during the first month of pregnancy, the embryo's weight will increase by 10,000 times and by another 74 times during the second month.

Embryonic development requires 2 complimentary processes. First, the cells forming the embryo itself (called the embyroblast) begin very quickly to develop and specialize into the hundreds of different cells a human being needs to survive and function. Second, the cells forming the trophoblast also begin to shape themselves into the placenta, the umbilical cord and the amniotic sac to allow for the survival of the embryo. We begin this chapter with a consideration of this amazing process.

EMBRYO SUPPORT STRUCTURES

The Placenta



The placenta has often been called the only throw away organ that human beings will ever have. It is truly an amazing organ and a combination lung-kidney-digestive system-hormone producer. Not bad for a disposable organ!

It is disc-like in shape and grows steadily larger through the early weeks of pregnancy, significantly outpacing the growth of the embryo/fetus early on (Genbacev, 2001). It is fully formed by about 18 weeks. At delivery it will weight a little more than a pound on average. It is a little over an inch thick and almost 8 inches in diameter.

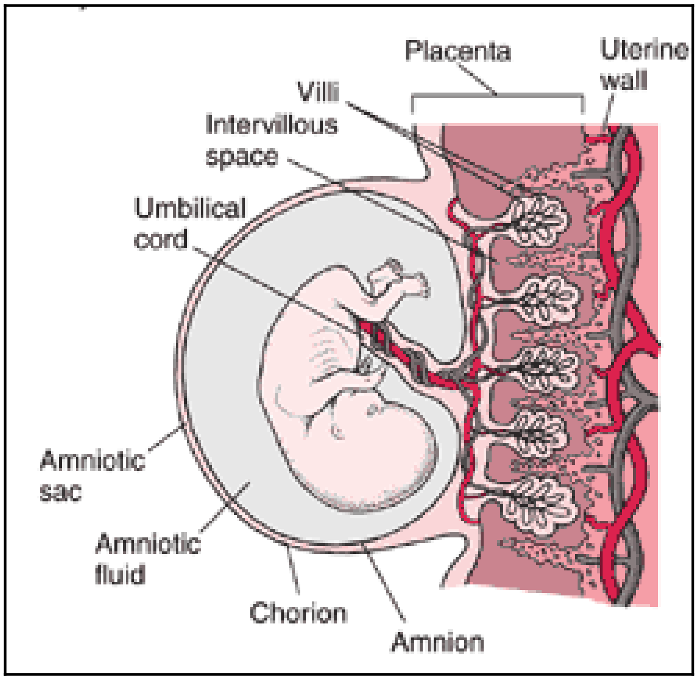
The placenta is actually composed of two complementary parts, one which is part of the embryo/fetus and the other part of his mother. This means that the placenta is a "joint" organ and contains cells from 2 distinct persons. This happens nowhere else in natural biology (Nathanielz, 1996). What makes this amazing is that in just about every other situation, cells from another organism are considered by the body to be pathogens to be killed. Our immune systems protect us constantly from anything "foreign" (like a bacterial infection) to our bodies by marshalling our T and B lymphcytes to get rid of these cells. This is one reason why transplanted organs are so often rejected by the body.

But the placenta does not operate according to these rules (Blaschitz, Hutter, & Dohr, 2001). When things are going "normally", it allows the cells from 2 separate organisms to cooperate and not "kill" each other. But this necessary cooperation does not always occur. It has been theorized that some miscarriages are caused by a mother's immune system "rejecting" the embryo/fetus and attacking the placental fetal cells as pathogens (Nathanielz, 1996; Urban et al, 2001).

The placenta is the mediator between the maternal and fetal systems. It extends itself into the uterine walls on the maternal side by means of the villi, thereby gaining access to oxygen, nutrients, and everything else a baby needs to grow and thrive (water, electrolytes, protein, lipid carbohydrates, vitamins and antibodies). The embryonic blood (in the villi) and the mother's blood (in the intervillous space) are separated by a thin membrane, called the placental barrier. This membrane is several layers of cells thick and is porous enough to allow oxygen and nutrients to be exchanged between the blood of the mother and that of the embryo. The blood vessels in the villi then deliver the oxygen and nutrients from the mother to the baby through the umbilical cord.

But whatever is in the mother's blood stream in addition to oxygen and nutrients is also potentially transferable to the baby, including alcohol, drugs, stress hormones, and some viruses and other infectious diseases. We will discuss some of these teratogens in later chapters.

The extension of the placenta into the mother also allows for the disposal of embryonic "trash", analogous to the post-natal urine and fecal matter. This waste is "picked up" and delivered via the umbilical cord to the villi, and finally passed on to the mother's body to be discarded via her normal excretory processes.



So the placenta is truly an intermediary organ, making deliveries of food and oxygen to the embryo/fetus, and also picking up the "garbage". It is also an organ which multi-tasks constantly, carrying out many different crucial functions.

Placental Functions

The Lung Function

Without oxygen, the embryo/fetus cannot survive. Since the fetus does not have access to the outside world where its lungs (even if they were developed enough) could get oxygen, he must rely on his mother's lungs, and then get it "second-hand" from her blood. Further, unlike glucose and fat, oxygen cannot be stored for later use. Thus, the most crucial task of the placenta is to constantly procure, absorb and deliver oxygen to the growing baby. As the fetus grows, its oxygen needs increase and so does the importance of the placenta's lung function.

Oxygen is delivered in both maternal and fetal system by means of hemoglobin, or red blood cells. Each hemoglobin cell can carry up to 4 molecules of oxygen, but fetal blood has a special type of hemoglobin that is more efficient than maternal blood. But the placenta is still completely dependent on how much oxygen is available in the mother's blood. This oxygen availability is influenced by how much hemoglobin she has in her blood; less hemoglobin will result in lower oxygen availability.

Further, the actual "oxygen load" of maternal hemoglobin is also influenced by the amount of carbon dioxide in her blood, and by the oxygen content in the air she is breathing. A woman that is smoking or breathing in polluted air, or stuck inside a poorly ventilated area will deliver much less oxygen to her baby. If prolonged, this oxygen deficiency can lead to retarded fetal growth and is associated with both pre-maturity and miscarriage.

Hemoglobin cells contain iron. If a pregnant woman does not have adequate amounts of iron, she will be anemic and her ability to transport oxygen to her organs and to her baby will be greatly reduced.

The Kidney Function

After we are born, our kidneys help regulate the concentrations of various ions and water within our bodies so that we can perform all the various functions and activities of our daily lives. Acting like a thermostat, the kidneys release various minerals and remove various toxic byproducts and compounds, insuring the correct chemical composition throughout our bodies and the constancy of the internal environment (Nathanielz, 1996). Due to the immaturity of the fetal kidneys, and their inability to adequately perform these regulatory tasks, the placenta serves as the mineral, compound and fluid regulator for the embryo and fetus throughout the pregnancy.

The Digestive System Function

The basic elements required by the growing embryo/fetus include glucose, various fats, water, amino acids, vitamins and mineral ions. The placenta delivers these elements from the mother to the baby in 2 general ways; an active process and a more passive one. The active process is generally a quicker delivery mode, but requires the placenta to use energy (in the form of glucose). The passive process is slower, but does not tax energy stores nearly as much.

The Passive Process

The passive process of transportation requires that the concentration of whatever substance be higher in the maternal blood than in the fetal blood. When there is a concentration differential, natural diffusion takes place from the area of high concentration to the area of low concentration. This process almost works like gravity. Water on a hill will run down, not up. So passive transportation will occur from high to low concentration areas.

In the case of both glucose and oxygen, maternal blood usually has higher concentrations than fetal blood. This state is maintained because the fetus is removing the glucose and oxygen from his blood constantly to utilize it for growth. In the case of glucose, the fetus may store it for later use.

The Active Process

The passive process does not work for every element that the embryo/fetus needs to grow. Therefore, the placenta also employs an active delivery mechanism. For instance, most of the mineral ions are actively transported because passive diffusion does not work. Glucose can also be conveyed by means of glucose transporters which act as mini-shuttle buses quickly delivering glucose when there is the need. The down-side of the active process is that it increases the placenta's need for fuel, sometimes in direct competition with the baby. When there is a glucose shortage due to a mother's diet, the fetus gets less due to the placenta's needs and must either use whatever reserves it has, or do without (Nathanielz, 1996). As we will see in a later chapter, this may be a significant factor in the long-term health of the baby and a negative fetal programming process begins.

The Endocrine Function

The placenta also functions as a hormone producer and even is powerful enough to alter the various hormones produced by the mother's body. Almost from the very beginning, the placenta and mother's body begin a chemical "conversation" in which hormones serve as the "words" of communication. This chemical "cross-talk" is coordinated and, when all goes well, functions to maximize the embryo/fetal environment, and therefore, the embryo/fetus.

Among the hormones released by the placenta is estrogen, which along with progesterone, is involved in numerous processes necessary to maintain healthy pregnancy. For example, one crucial result of the increased levels of estrogen is the redirection of blood flow in the mother's body to the uterus. As pregnancy proceeds, there is a 50-fold increase in blood volume to the uterine area (Nathanielz, 1996).

Another hormone produced and released by the placenta is somatomammotropin, also called placental lactogen. It functions in several ways, promoting fetal growth by increasing the amount of glucose and fat in the maternal blood. It also "tells" the mother's breasts to start getting larger in readiness for breast-feeding.

An adequate amount of progesterone in the mother's system is crucial to the maintenance of pregnancy. Early on in pregnancy, before the placenta is able produce enough progesterone itself, it gets "help" from the mother by releasing a hormone called human chorionic gonadotropin (hCG). This hormone passes into the mother's body and "instructs" her ovaries to continue producing progesterone for a longer period than usual (Rao, 2001). Every 28 days, one of the ovaries produce an ovum by means of a follicle, which bursts at ovulation and releases the ovum. Following ovulation, this follicle morphs into a structure called the corpus luteum, which routinely produces progesterone for about 2 weeks and then dissolves and dies away during menstruation. But the presence of hCG early in pregnancy causes the corpus luteum to delay its demise and keep working until the placenta can take over its progesterone production duties (Nathanielz, 1996).

Finally, the placenta also plays an endocrine role in the process of labor at the end of the pregnancy. In response to oxytocin, a hormone jointly produced and released by the baby and the mother's pituitary glands, the uterus contracts and the placenta releases prostaglandin hormones. These prostaglandins stimulate the uterus to contract even more and they also incite the greater release of oxytocin in a feedback loop process. This is what makes labor begin with relatively mild and widely-spaced contractions and proceed inexorably to relatively intense and closely-spaced contractions.

Placental Previa

Affecting about 1 out of 200 women, placenta previa is a condition where the placenta is attached and grows in the lower part of the uterus, near or even over the cervix. When the cervix begins to dilate in labor, it may separate from the uterine wall and bleed. It is more common in pregnancies with multiples and in women who have had multiple pregnancies. Interventions may include bed rest, avoidance of travel and sexual intercourse, and in more serious cases, performance of a C-section.

Placental Abruption

Premature separation of the placenta from the wall of the uterus is called placental abruption and occurs in approximately 1 out of 80 deliveries. It is potentially problematic, depending on when it occurs. If it occurs close to delivery, it is not nearly as much of a problem as an earlier abruption may be.

In most cases, the cause of placental abruption is unknown, although certain factors seem to increase its chance of occurring. These factors include maternal hypertension, dietary deficiencies such as a lack of adequate folic acid, smoking, alcohol consumption, uterine scarring, an overly short umbilical cord, and a physical injury to the mother, such as a fall or a car accident. Women who have experienced placental abruption with one pregnancy are at greater risk in subsequent pregnancies, with a rate of reoccurrence estimated as high as 10%.

Separation of the placenta may be partial or complete. A total separation of the placenta from the uterine wall is very serious and will result in premature delivery 20% of the time it occurs, with miscarriage and fetal death occurring in 15% of the cases. Total abruption cuts off the fetus from her mother's blood supply, and thus oxygen and nutrients. Symptoms of placental abruption vary a significantly and may include lower-back pain, uterine sensitivity and tenderness (60% of the time), contractions (35% of the time) and/or bleeding (approximately 75% of the time). A diagnostic ultrasound may be useful in identifying the problem, although the results are often imprecise.

Placental Correlates with Birth Weight

Because the placenta is so important, it should come as no surprise that its weight has been found to be positively correlated with the weight of children at birth (Sanin et al, 2001). Birth weight is an important indicator of health. While the average baby's weight is a little over 6 times as heavy as his or her placenta, research has found that for every ounce heavier the placenta is, the corresponding baby increases her weight by almost 2 ounces. But ethnic differences also affect the placental to birth weight ratio. For unknown reasons, Asian and Hispanic women have the lowest placental weight to birth rate ratio and Caucasian and African American women the highest (Cohn, 2002).

The Umbilical Cord

While the placenta is quite an amazing organ, the umbilical cord is also a marvel of nature. It connects the baby to the placenta and develops from the remnants of the yolk sac and the allantois present early on in embryonic development.

The Yolk Sac and Allantois

The primitive yolk sac comes from cells that have split off from the inner cell mass of the blastocyst. The yolk sac is thus outside the embryo and is filled with vitalline fluid, which help nourish the embryo in the early weeks of life (Hesseldahl & Larsen, 2005). As the embryo grow, so does the volume of the vitalline and thus the yolk sac. This continues until about 10 weeks (Kupesic & Kurjak, 2001). By this time, the placenta and umbilical cord have grown and matured. The yolk sac is no longer needed and gradually "shrivels away" (Macdonald, 2005).

The allantois also emerges from the blastocystic cells and serves as a primitive excretion and waste collection structure. Both the yolk sac and allantois contribute to the structural form of the umbilical cord as it slowly develops.

This rudimentary form of the umbilical cord begins in the 4 to 6 week stage and is initially stalk-like, very short in length and relatively speaking, thick in diameter. It does not have the flexibility it will later have. This umbilical stalk develops from the center of the placenta. By around 10 weeks, it begins to elongate and take on the distinctive flexible cord-like formation. This is facilitated by the emergence of Wharton's jelly.

Wharton's Jelly

Named after the English physician Thomas Wharton who first described it in 1656, Wharton's jelly is a type of specialized tissue which has elastic effects and thus can be stretched, bent, and twisted without harm. Because it is made up of flexible fibers encased in gelatin-like mucus, the umbilical cord can function effectively while allowing for considerable fetal movement and eventually, the process of labor and delivery.

Good maternal nutrition tends to be associated with greater amounts of Wharton's jelly. Low levels of Wharton's jelly are associated with fetal complications and miscarriage. When there are umbilical problems such as twisting, kinking or knotting, these tend to occur at points in the umbilicus where Wharton's jelly is minimal or absent. Finally, for whatever reason, males tend to have more Wharton's jelly than females (Collins, Collins, & Collins, 1990).

Cord Function

The umbilical cord primarily serves as the transit system of oxygen and nutrients from the mother/placenta to the fetus and of waste products from the fetus back to the placenta/mother. By 31 weeks, it has been estimated that the umbilical cord must carry 70 quarts of blood per day, moving at 4 miles an hour (Collins, Collins, & Collins, 1990). In a normal pregnancy, the umbilical cord has 1 vein delivering oxygen and nutrients and 2 arteries returning waste products. Any exception to this pattern (4-vessel or 2-vessel cord) is potentially problematic and associated with fetal malformations and miscarriage. Stressful conditions such as maternal smoking and anoxia (decrease in oxygen availability) are associated with over-branching of the cord vessels, and thus fetal complication, miscarriage and stillbirth (Collins, Collins, & Collins, 1990).

Cord Differences

Apart from the number of vessels (a little less than 99% have 3, 1% have two, with 4 and 5 being very rare), umbilical cords differ from fetus to fetus. Some (about 5%) are straighter (associated with increased complications) and others more twisting and spiraling (about 95%) in formation (Strong, Elliot, &

Radin, 1993; Petrikovsky & Gross, 1996; Dado, Dobrin, & Mrkvicka, 1997). Further, because active fetuses have longer cords than inactive ones, the cord is thought to elongate in response to fetal activity. The elongation occurs up to 36 weeks, but the most rapid changes occur before 28 weeks and then seem to slow (Naeye, 1992). It is not surprising that twins and triplets tend to have shorter umbilical cords than singletons, probably due to the sheer lack of space in the uterus for activity. On average males also seem to have longer cords than females do.

Overly short (less than 13 inches) or overly long (more than 26 inches) cord length has been associated with various complications and neurological abnormalities (Naeye, 1985; 1992; Sornes, 1989), including deficits in IQ (Collins, Collins, & Collins, 1990). The average birth length of the umbilical cord is about 24 inches and first pregnancies tends to result in shorter cords than subsequent one.

A predisposition to rupture and the prevention of fetal descent during labor are associated risks of short umbilical cords. Umbilical cords of less than 10 inches are further associated with cerebral palsy and IQs lower than 80. Long cords are not harmful in and of themselves, but seem to present a greater risk of fetal entanglement at various points in the pregnancy, especially birth (Collins, Collins, & Collins, 1990).

Navel Formation

At birth, the cord is clamped and subsequently cut. Since there are no nerve endings in the cord, this cutting is not painful. There is also ordinarily no significant loss of either maternal or infant blood and the clamp (see below) stops the flow of any blood that is present in the cord at birth. This blood has been discovered to be rich in stem cells and some parents now opt to have it saved and stored in a cord blood bank for potential future use.

The umbilical cord eventually falls off and leaves a scar, which forms the navel or belly button. Because there is only a fewer layers of skin covering the abdominal muscles, this scar does not "heal over", but instead leaves a permanent mark. Like any scar that is semi-randomly caused (the following off of the umbilical cord), they can vary quite significantly in shape, size, depth, and overall look. Generally speaking, they can present as a depression ("innies"; 90% of people) or as a protrusion ("outies"; 10% of people). For those unhappy with their particular belly button, plastic surgeons now offer a procedure called umbilicoplasty.

The Amniotic Sac

The embryo (and later the fetus) is surrounded by fluid and contained within a resilient and very flexible thin 2-layered pouch. The inner layer is called the amnion, and gives its name to both the sac itself and the fluid within the sac. The outer membrane is called the chorion and connects with and is technically part of the placenta. Both membranes are transparent (allowing light to pass through) and very tough, necessary to prevent harm to the baby (Yeh & Rabinowitz**,** 1988).

Amniotic Fluid

Around 2 weeks after fertilization and just a few days of implantation, the amnion begins to grow. As it grows (and the embryo and fetus within), it fills up with a watery fluid containing various electrolytes (ions), carbohydrates, proteins, and fats. At the 10th week, there is just a little over 2 tablespoons present but by week 34 there is over 68 tablespoons (a little more than a quart).

This fluid has several beneficial functions to the growing baby. It serves primarily to protect the fetus by cushioning any pressure or blow from outside the womb. It also acts as a lubricant and facilitates free movement within the amniotic sac, providing buoyancy, and allowing for activity and "exercise" by the growing baby. The fetus also breathes in the amniotic fluid into her lungs, allowing a kind of “practice breathing” to better prepare her lungs for the immediate task of breathing in air as soon as she is born. The fluid also keeps the baby warm. It is slightly higher in temperature (99.7 degrees F) than the mother’s body (98.6 degrees F).

Later on in pregnancy, the fetus will drink the amniotic fluid, getting up to 100 calories per day and allowing her gastrointestinal tract to “practice” digestion. The “taste” of amniotic fluid is affected by a mother’s diet and seems to influence the development of post-natal food preferences as well as odor learning (Mennella, Johnson, & Beauchamp, 1995**;** Schaal, Marlier, & Soussignan, 2000**).** By 15 weeks, a fetus will increase his consumption of sweet-tasting amniotic fluid, and will decrease his drinking of bitter-tasting amniotic fluid (Mennella, Jagnow, & Beauchamp, 2001).

In a normal pregnancy, the amniotic sac will rupture as by-product of the contractions of labor and delivery. The "spontaneous rupture of membranes" (SRM) is commonly referred to as the “water breaking”. In some births, this does not happen, and an amniotomy, or “artificial rupture of membranes” (ARM) is performed by the attending nurse, midwife or obstetrician.

Amniotic Sac Problems

Similar to the placenta and the umbilical cord, at times the amniotic sac can malfunction in a variety of ways.

Premature Rupture

When the amniotic sac leaks prior to 38 weeks or the “water breaks” prematurely, labor and delivery often have to be either induced or a C-section performed. Preterm premature rupture of membranes (PPROM) is a condition associated with either structural defects in the cervix or uterus or a bacterial infection.

Oligohydramnios

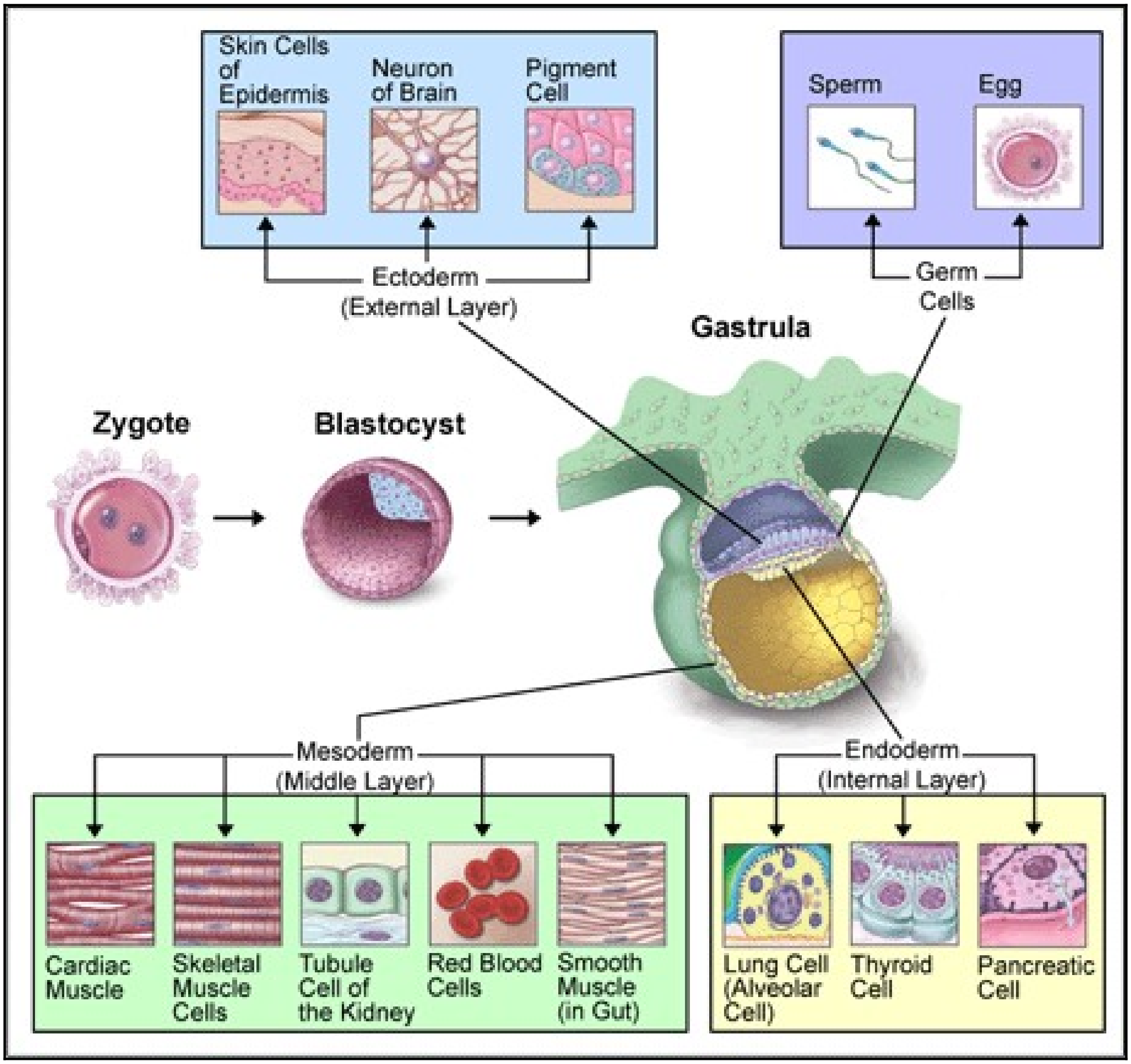
Approximately 8 percent of pregnancies are affected by a condition called oligohydramnios, or too little amniotic fluid in the amniotic sac. It is most commonly seen in pregnancies that are more than 2 weeks overdue or if there is leaking in the amniotic sac. Beyond these 2 situations, oligohydramnios is usually associated with the presence of birth defects (early pregnancy) or poor fetal growth (later pregnancy). This condition is associated with complications, miscarriage and prematurity (Oligohydramnios, 2006).

Polyhydramnios

Too much amniotic fluid, a condition called polyhydramnios, affects about 2 percent of pregnant women. In most cases, complications are minimal or mild and often spontaneously resolve. However, if too much amniotic fluid builds up, polyhydramnios is associated with premature rupture of the amniotic sac, premature delivery and miscarriage. It is also associated with, and perhaps caused by, potential birth defects (Polyhydramnios, 2006).

EMBRYONIC GROWTH

Calculating embryonic and fetal age is done in a variety of ways, and is sometimes confusing. Gestational age is used to calculate a woman’s due date and is calculated from the end of the a woman’s last menstrual cycle. Fertilization age is calculated from fertilization. Thus, gestational age is always 2 weeks over fertilization age. For purposes of clarity, we will use fertilization as the beginning point and so age is calculated as the number of weeks or months since fertilization. A full-term baby is thus 38-40 weeks. Since every baby is a bit different, and development is dynamic, somewhat dependent and influenced by the fetal and maternal environment, each week or month should be understood as being within a range of a couple of days on each side.



The Gastrula

Very soon after implantation, a process called gastrulation (Hamilton, Boyd & Mossman, 1962) begins, whereby the stem cells of the embryoblast differentiate into three “layers” called the endoderm, the mesoderm and the ectoderm. These three eventually differentiate further into the various components of the body.

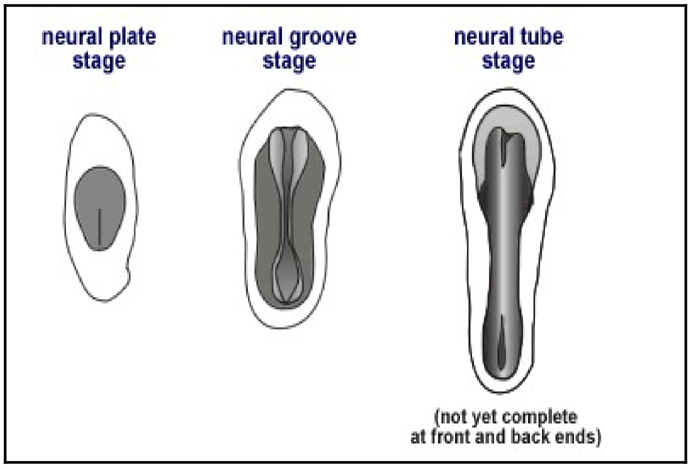
The innermost layer is called the endoderm and will eventually produce most of the internal organs of the body, including the lungs, liver, tongue, pancreas, thyroid, larynx, trachea, digestive tract, and bladder. The middle layer is called the mesoderm and will eventually differentiate into the heart, spleen, skeletal and smooth muscles, kidneys, spleen, blood cells and vessels, connective tissue including bone and cartilage, bone marrow, lymphoid tissue, and gonads. The outermost layer, called the ectoderm, will eventually become the epidermis (including skin, nails, and hair), lenses of the eyes, tooth enamel, pituitary and mammary glands, sense organs, sinuses, mouth, anal canal, and most importantly, the brain and entire nervous system.

Patterns of Development

Once gastrulation has occurred, the embryo quickly begins to develop in 2 overall patterns. Development tends to begin with the head and proceed down the body. This principle, called cephalocaudal development, explains why the top of the embryo (cephalic) containing the brain and the head is so much bigger than the bottom (caudal) of the embryo containing the rest of the body. A second principle influencing development is proximodistal development, whereby organs closest to the center of the body (proximo) such as the spinal cord develop prior to organs further away from the center (distal). This process means that the nervous system and heart develop first, and are thus functional and can support the outer structures when they emerge.

Organogenesis

On about day 9, the embryonic cells begin to arrange themselves in a shield-like form, with a broader top and narrower bottom (Flanagan, 1996). A central streak runs through the center (see the line on neural plate stage to the right).

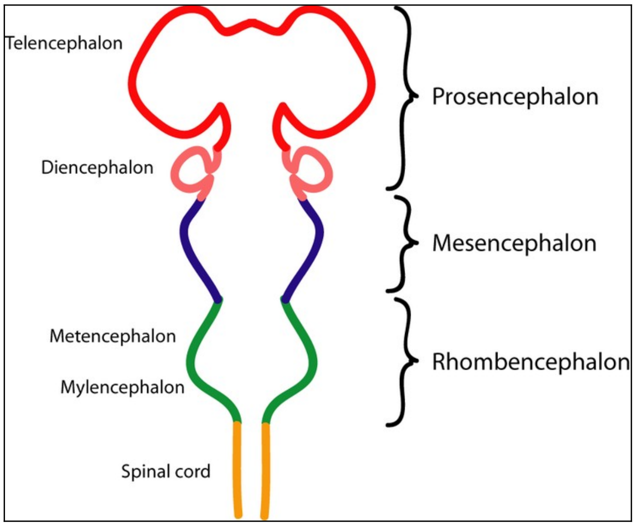


Neurulation

The very first stage of organogenesis is called neurulation, which occurs between the 18th and 26th days. Ectodermal cells first cluster along the central streak into a flat neural "plate", and when enough are present, then folds in on itself to form a "groove". This neural groove begins to elongate and close in the middle, eventually forming the neural tube with open bulges on either end. The top bulge will become the brain and the tube itself is a proto-spinal cord. This neural tube substantially defines the embryonic structure in early pregnancy.

Nervous System Development

During the third week, the nervous system develops rapidly so that by the 18th day after fertilization, primitive nerve cells are present and by the 20th day the brain, spinal cord, and the basic components of the entire nervous system exist.



By 25 days, the embryonic brain has three main vesicles separated along two main grooves, foreshadowing the eventual division of hindbrain, midbrain and forebrain (Lambert, Bramwell, & Lawther, 1982).

By the 5th week right and left hemispheres of the brain are already apparent (Tanner & Taylor, 1965). At around the 32nd day, the spinal nerves begin to sprout from the brain stem (England, 1996) and the final 5 divisions of the brain emerge from the earlier 3.

The prosencephalon divides into 2 parts, the telencephalon (cerebral cortex, amygdale, & hippocampus) and the diencephalon (hypothalamus, thalamus & pituitary gland) .The mesencephalon becomes the midbrain, while the rhombencephalon divides into 2 parts, the metencephalon (pons and cerebellum) and the myelencephalon (medulla)

At 5 weeks, cranial nerves commence sprouting from the brainstem and by the end of the 6th week, the "nervous control system" begins to control the muscles of the developing child. Detectable brain waves emerge at 48 days or so. As development continues into the fetal stage, two large bursts in neural cell proliferation occur at approximately 15-20 weeks and 25 weeks. By 24 weeks, the grooves and ridges called sulci begin to appear in the expanding cerebral cortex.

As the brain develops, the other organs of the body are simultaneously forming and coordinating their functional capacities with the parts of the brain devoted to those areas. While development continues according to the cephalocaudal and proximodistal principles, the speed and process of development differs with each particular organ.

Heart Development

Beginning at day 13, a clump of mesodermic cells move into position where the heart will form. Around days 18-19, these cells begin to form into 2 “tubes” connected at the top into a U-shape (Flanagan, 1996) and by the 22nd day have fused into 1 "cardiac tube" (England, 1996) no bigger than a poppy seed. By day 21, small capillaries begin to appear, and the arrival of the first heart beat, although just an initial twitch and then irregular and weak, occurs at 22 days. Within days, all of the other heart cells are beating in unison, establishing a circulation through the minute blood vessels. These first beats of the heart will be repeated 4 billion more times if the fetus lives to be 100 years old. By the 4th week, the 1-chambered heart is beating a regular 80 beats per minute and gets incrementally faster every day (Macdonald, 2005).

The heart is among the first organs to develop and become functional, because without it, there would be no way to deliver the nutrients and oxygen to the other developing organs. The heart cells continue to grow and differentiate so that by the 49th day, a 4-cavity heart is functional.

Simultaneous to the development of the heart, the cardiovascular system is gradually developing out of the mesoderm. During intra-uterine life, the circulatory system passes through two stages, the first called the vitelline, in which the embryo is living essentially on its own resources, lasts until the beginning of 5th week. The second stage, called the placental, lasts from the 5th week until birth. With the development of the placenta and umbilical cord, the embryo/fetus depends upon his mother for nutrients (Tuchmann-Duplessis & Haegel, 1971).

Other Internal Organ Development

A recognizable liver is clearly apparent by 28 days, with distinct "liver cells" evident one week earlier. Between weeks 6 and 10, the abdominal space in the embryo/fetus is mostly occupied by the liver as it grows. Large carbohydrates reserves are stored in the liver before birth to provide a source of nourishment for the newborn until breast-feeding is well-established. (England, 1996).

The lung buds are evident by the 27th day and the various bronchi slowly emerge and make several divisions, forming the substantial part of the lungs. By the end of the first month the embryo has a windpipe and oral cavity, a primitive kidney, and the beginnings of a stomach (Meredith, 1978). There is a discernible pancreas and intestines, but it will be well into the second month before an anal opening develops.

Sensory Organ Development

Parallel to and interconnected with the development of the central nervous system is the development of the various specialized sense receptors and their neural pathways to the brain. Initially, the sense receptors develop from placodes, where clumps of cells gather and thicken and then form in the organ (Tuchmann-Duplessis & Haegel, 1971).

The Visual System

The visual system begins to develop very early, by the 18th day, and actually originates from two of the three germ layers; the optic nerve and lens emerge from the ectoderm, while the mesoderm contributes the accessory structures of the eye (Tuchmann-Duplessis & Haegel, 1971). The optic primordium develops for approximately 10 days before the lens primordium emerges at 29 days. The complexity of the eye and the various visual structures accompanying it account for the long and gradual development of the visual system. The optic vesicle, the external layer of which forms the retina, begins to differentiate at approximately 40 days and continues until the 7th month. The optic nerve gradually develops out of the axons of differentiated ganglionic cells in each eye, which progress toward the emerging brain, and cross over each other forming the optic chiasma. As with the olfactory sense, these axons correspond to the specialized area of the central nervous system, and particularly the occipital lobe of the brain (Tuchmann-Duplessis & Haegel, 1971). This process starts at about 5 weeks, when eye buds also begin growing from the forebrain (Lambert, Bramwell, Lawther, 1982). The various other visual components, including the cornea, the iris, and the sclera, all gradually emerge and are all present by the 3rd month (Gilbert, 1989). The final event of the visual system is the separation of the eyelids during the 7th month.

The Olfactory System

The olfactory system originates as two placodes which are already apparent at 30 days. These placodal cells gradually differentiate, forming the olfactory epithelium, or nasal cavity. At about 6 weeks, these differentiated cells make contact with the olfactory zones in the emerging brain, which in turn induces the development of olfactory bulbs. The axons of the specialized receptors gradually become more and more interconnected to the cortical area corresponding to the olfactory system. This process occurs from the 46th through the 84th day (Tuchmann-Duplessis & Haegel, 1971).

The Auditory System

The auditory system originates early in the fourth week with the emergence of the otic placode (Gilbert, 1989). The development of the ear, including both the sense of hearing and the sense of balance, is complex and involves all three embryonic germ layers. The endoderm is the source of the inner and outer ear, the ectoderm is the origin of the middle ear, and the mesoderm participates in the formation of all three. Very early on the ganglionic cells from the otic placode form two different clusters, the ganglion of Scarpa and the ganglion of Corti. The axons of these neurons progress towards the metencephalon and eventually bunch together to form the acoustic nerve.

During the fifth and sixth weeks the primordia of the semicircular ducts appear and the cochlear and vestibular ganglion are clearly discernable along with the utricle and sacula (Tuchmann-Duplessis & Haegel, 1971). The development of the semicircular canals, the cochlea, the organ of Corti all gradually differentiate, as do the bones in the middle ear so that the sense of hearing is at least structurally functional from 20 weeks (Chamberlain, 1983).

The Gustatory System

Of the various sense organs, the sense of taste is the last to develop. It is not until the 7th week that the tongue is finished developing and not until the very end of the embryonic period that the taste buds begin to form on the tongue’s surface.

Physical and Structural Growth

For most of the first month of development, the neural tube and the developing nervous system essentially define the shape and structure of the embryo. But starting in the second month, the shape of the embryo begins to be defined by other structural and physical components.

Fourth Week

By day 26, the embryo begins to change shape, curving into a c-shape and the arm buds begin to appear (Carnegie Stage 12, 2006). The arches that give form to the face and neck are slowly becoming apparent and the eye buds and ear buds are just beginning to emerge (Carnegie Stage 13, 2006).

Fifth Week

By day 30, the head goes through a growth spurt to accommodate the huge growth in the brain. The nasal plate (the nose) is discernable and the esophagus forms. The process of ossification begins and the trachea, as well as the Eustachian tubes, thyroid, parathyroid and thymus glands all develop (Meredith, 1978). The leg buds are apparent and the arm buds grow longer and more cylindrical, tapering at the ends into hand plates. Innervation has started in the arms (Carnegie Stage 14, 2006).

During the fifth week, the trunk of the body gets substantially thicker. While the head is still very large relative to the overall body, the enlarging body gives the embryo a more human –like appearance. (Carnegie Stage 15, 2006). Toward the end of the 5^{th} week, the hands become clearly distinct from the arms and shoulder. The leg buds begin the process of elongating and tapering into feet buds and innervation begins in the lower limbs. By the end of the 5^{th} week, the foot is distinguishable from the thigh and leg (Carnegie Stage 16, 2006).

Sixth Week

In the 6th seventh week, the trunk becomes a bit straighter and both the wrist and finger buds are clearly observable, as are the cell buds that have started to specialize into the genitalia. The intestines begin development in the umbilical cord and in the 9th week will migrate into the embryonic abdomen (Grand et al., 1976; Pringle, 1988; Sadler, 2005; Spencer, 1960). The jaws continue to progress and the various plates of tissue growing in from 4 sides over the prior several weeks have formed the embryo's face, which along with the eye buds and eye lids, give the face a more characteristic human-like shape.

By the 6th week, the muscles and now ossifying skeletal structure are both developed enough to allow for the first minute but discernable moves, albeit involuntary (Moss, 1990). The kidneys also produce a very small amount of urine for the first time (Carnegie Stage 18, 2006).

Seventh Week

The 7th week is very eventful, producing the ear buds on the sides of the head and the gonads (testicles and ovaries). The trunk of the body straightens and elongates. Cartilage, muscle and bone continue to grow, solidify and strengthen. The fingers get longer and more distinct and the arms are long enough for the hands to approach each other across the abdomen. (Carnegie Stage 19, 2006). The knees and ankles are distinguishable and proportional and the toes buds are notched (but still webbed) and have the beginnings of toe-nails. Like the hands, the legs are long enough for the fan-shaped feet to approach each other (Carnegie Stage 20, 2006). The nipples and hair follicles begin their formation and by the end of the seventh week all major and essential organ systems have begun to form.

The eyes, though well-developed, are still on the sides of the embryonic head. As development continues into the 8th week and early fetal period, the eyes migrate forward onto the face. The ears are also set low on the head and will migrate up over the next few weeks (Carnegie Stage 21, 2006).

Eighth Week

Brain waves begin in the 8th week and are measurable using an electroencephalogram (EEG) (Hamlin, 1964; Goldering, 1982). Voluntary movement (controlled by the brain) is possible now and the penis and clitoris are also developing. The fingers are clearly and fully separated and both fingers and the feet continue to lengthen, with the toes become more defined. While a stubby tail is still present, it is much smaller than it previously was. While the eyes are closed, the retinas are fully developed (Carnegie Stage 22, 2006). Eye lids begin to come together from the top and bottom about half way. During the last part of the embryonic period, a precursor layer of skin cells replaces the thin ectoderm of the embryo and the tail finally disappears completely (Carnegie Stage 23, 2006).

CONCLUSION

The embryonic period typically concludes at the end of the eighth week and the fetal period begins. This division is somewhat arbitrary because there is no clearly distinct delineation in the activity or development of the emerging child to allow for the division. The signal marker for the end of the embryonic period is perhaps the brain. All the basic brain structures are present prior to the beginning of the fetal stage, as are all of the major organ systems. The final 7 months of pregnancy will be used to expand and grow and this is the topic of our next chapter.

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