INTRODUCTION

The fetal stage takes up the last part of the first and all of the second and third trimesters. While the embryonic stage was one of initial development, the fetal stage is more one of consolidation, growth and developing functionality. It is in the fetal stage that the term "psychological" can begin to be tentatively, but legitimately, employed to describe behaviors, emotional states, and cognitive processes not unlike that of the neonate. We will consider this topic in depth in a later chapter, but here we will focus on the physical development of the fetus.

THE THIRD MONTH (Weeks 9-12)

At the beginning of the third month, the fetus is around 2 inches in length and weighs a very slight .3 (8 grams) of an ounce. But by the end of this month, she will be 3 to 4 inches long and weigh almost an ounce (25 grams). Thus, growth is very rapid, with a doubling of length and a tripling of weight. Her head is very big relative to her body (almost ½ of her overall length). Her face, including the nose and lips (Timor-Tritsch et al., 1990), is well-formed and now has a distinctly human look.

Sexual Differentiation

External Genitalia

We noted in the last chapter than the gonads had begun to differentiate and the external organs also have made their "budding" appearance. What causes the genitals to develop into male or female ones is the presence or absence of the Y chromosome, which causes the production and secretion of male hormones collectively called androgens. Female development is the default pathway of development, so the absence of androgens results in female genitalia. The presence of androgens will produce male genitalia.

At 6 weeks, the genitals are undifferentiated (see image at the top to the right) and both males and females appear the same. In males, Leydig cells begin producing testosterone and Sertoli cells begin producing Mullerian inhibiting hormones (MIH), resulting in subtle changes by the beginning of the third month (8 weeks).

As the third and fourth months proceed, the genitals begin to differentiate considerably. In the male, the genital tubule becomes the penis; in females it becomes the clitoris. The urethral folds in males become the urethra and in females become the labia minora. The labioscrotal swelling becomes the labia majora in females and the scrotum in males. The urogenital slit becomes the vaginal opening in females and the seam running the length of the underside of the penis in males. The glans, packed with neural receptors and thus very sensitive, becomes the head of the penis. The undifferentiated gonads become the
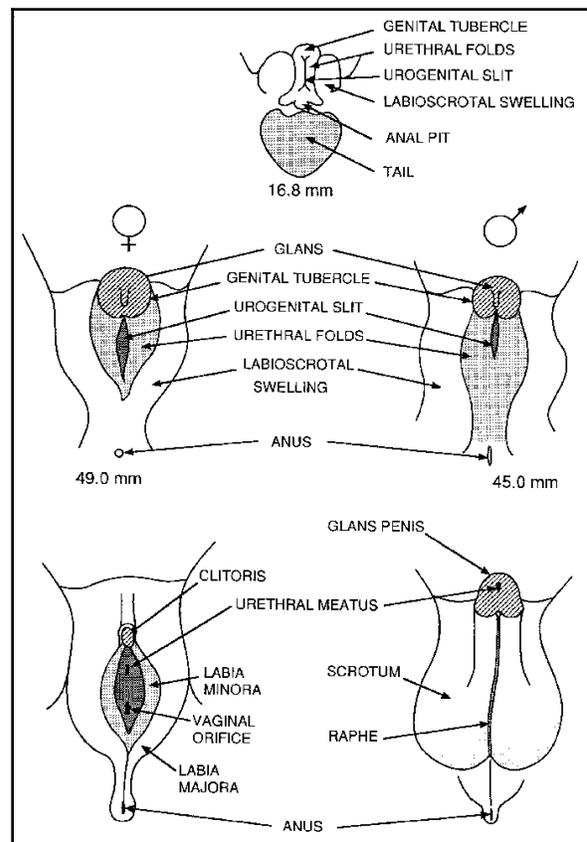
ovaries in females and the testis in males. By 10 or 11 weeks, the external genitalia are clearly identifiable as male or female (O'Rahilly and Müller, 2001).

Internal Genitalia

Both males and females also initially have 2 sets of internal ducts, Mullerian and Wolffian. Boys produce Mullerian inhibiting hormone (MIH), causing the Mullerian ducts to gradually recede and the Wolffian ducts to remain and differentiate into the vas deferens and seminal vesicles. In the absence of MIH, girls retain the Mullerian ducts which differentiate into the uterus and fallopian tubes.

During the third month, the uterus is identifiable in females (O'Rahilly, 1977). The ovaries have developed enough to begin the process (oogonia) of producing all of the immature ova cells (oocytes) that she will release from her ovaries as a mature adult woman in each menstrual cycle (O'Rahilly & Müller, 2001).

Physical Development

The skeletal structure is fully present and will continue to strengthen and develop (Cunningham et al., 2001). These bones, along with the muscles of the fetus continue to strengthen, allowing for slightly more vigorous movement such as flexing of the arms and kicking of the legs, stretching, squinting, and opening her mouth, sighing and yawning (de Vries et al., 1982). The mother cannot feel her baby yet because he is so small. The fetus can turn his head and frown.
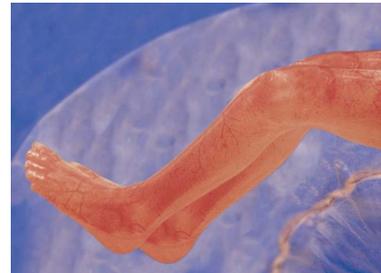
The trunk of the body, legs and arms continue to elongate into a shape more similar to what she will look like at birth. But because the fat a baby puts on does not start until the end of the second trimester, the appearance is of very thin child.

The hands and feet continue to develop. By the end of the third month, the fetus can make a fist with his hand, suck his thumb (Liley, 1972), usually the right one (Hepper et al., 1991) and even grasp an object (Robinson & Tizard, 1966; Valman & Pearson, 1980). Individual fingers and toes can be moved and are sensitive to touch (Humphrey, 1964; Humphrey & Hooker, 1959; Robinson & Tizard, 1966; Valman & Pearson, 1980), and fingernails and toenails are starting their development and can clearly be seen (O'Rahilly and Müller, 2001). The unique fingerprints that identify each and every person appear at about 10 weeks (Babler, 1991; Penrose & Ohara, 1973).

The eyelids are fully developed and fuse together to protect the sensitive and complicated development of the eyes (Andersen et al., 1965; O'Rahilly & Müller, 2001; Pearson, 1980). He will not open them up again for a couple of months, in the 28th week of pregnancy.
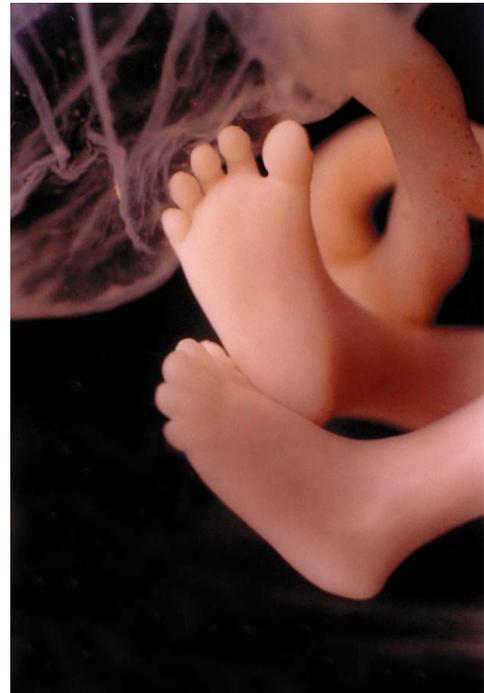
The tooth buds that will produce his 20 baby teeth appear (Pringle, 1988). When these teeth begin to emerge from his gums in the months after birth he will vigorously use his vocal cords, which develop in this month (O'Rahilly & Müller, 1984).

All the organ systems are present and functioning, however minimally, and will continue to grow, develop and increase their functionality. The heartbeat, however faint, can be heard using a Doppler stethoscope, a device which magnifies the sound. Blood circulation increases as the heart pumps and capillaries continue to develop.

The digestive system begins to show activity, now able to absorb small amounts of glucose and water (Koldovský et al., 1965). At 9 weeks the fetus begins to swallow amniotic fluid (de Vries, 1982; Petrikovsky et al., 1995) and the stomach begins to produce its own "juices". The fetus can hiccup and does. Likewise, the kidneys begin limited function, producing very small amounts of urine that seep into the amniotic fluid. Red blood cells begin to be produced by the liver and the pituitary gland begins its production of hormones (Blumenfeld, 2001).

Chorionic Villus Sampling

Chorionic villus sampling (CVS) is a test available since 1983 (Simoni et al, 1983; Smidt-Jensen et al, 1984; Ward et al, 1983) and is given to women between the 10th and 12th weeks of pregnancy (Simpson, 2000). It is designed to obtain genetic and chromosomal information about the growing fetus. Since the cells of the fetus, the placenta, the chorion, the umbilical sac and umbilical fluid all develop from the original zygote, cells from all can be analyzed to produce the same chromosomal and genetic information. A few weeks later in pregnancy, a procedure called amniocentesis can be used to ascertain virtually the same information that CVS will produce. The exception is neural tube defects, which CVS cannot be used to diagnose (CVS, 2006).

CVS is not a test routinely given to pregnant women, nor should it be because it does have some risk of producing complications and even a miscarriage (about ½ to 1% occurrence rate) (Olney et al, 1995). Rather, it is used in situations where there is a moderate to high increased risk of chromosomal or genetic defects or other anomalies. Some of these risk factors include maternal (and in some cases paternal) age, the presence in a previous pregnancy or child of a birth defect, and/or a family history of genetic disorders or defects (Jenkins & Wapner, 1999).

The chorion is the outermost layer which emerges from trophoblast and contributes to the development of the placenta. On the chorionic surface are wispy finger-like projections called villi that attach to the uterine wall and function to help supply the placenta and thus the fetus with nutrients and oxygen from the mother's blood. CVS is thus a procedure to get a small sample of these villi and remove it from the mother and analyze it's genetic and chromosomal content.

Types of CVS

There are two types of CVS.

Transcervical CVS

The first type of CVS is called transcervical CVS and it is the most commonly utilized. In this type of CVS, the villi sample is obtained by inserting a thin tube through the vagina and the cervix into the uterus and using suction to remove a small sample of villi. The process is aided by the simultaneous use of ultrasound to guide the

Chorionic villi

Pubic bone

Speculum

Catheter

Catheter   Uterus   Vagina

Wendolyn Hill

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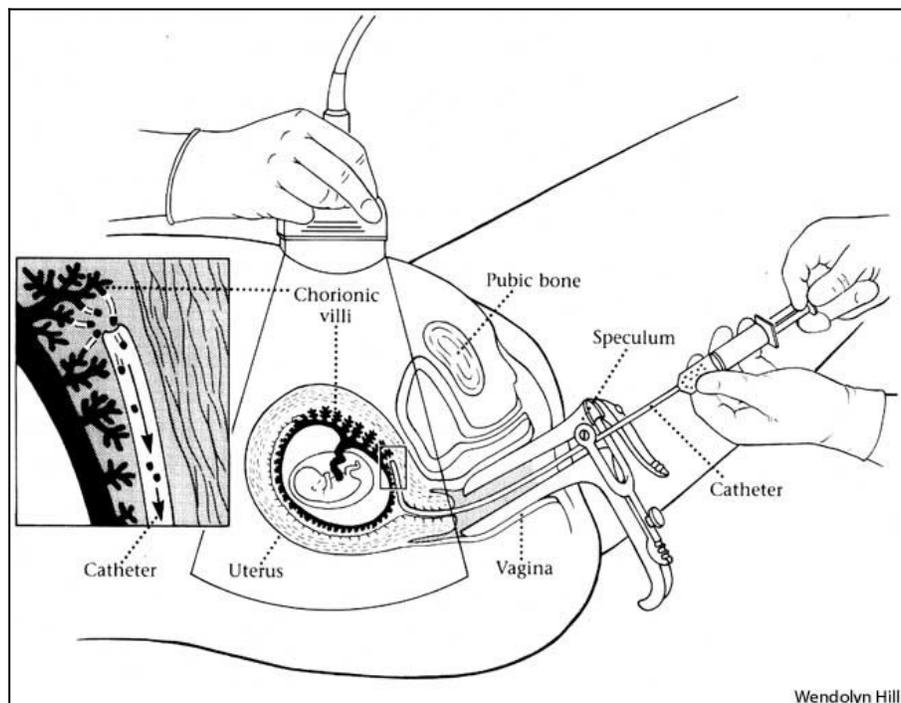
positioning of the tube. Generally, no anesthetic is required, the process is painless, and the procedure takes less than 10 minutes to perform.

Transabdominal CVS

The second type of CVS is much less commonly used. Called transabdominal CVS, it is most often used in cases where a woman has a tipped (or retroverted) uterus, which makes the transcervical CVS problematic and increases the likelihood of complications and miscarriage (about 5%). The process is similar except the tube is inserted directly through the woman's abdominal wall and as such, a local anesthetic is often used. Risk factors for complications and miscarriage are about the same as for transcervical CVS (1/2 to 1%) (Olney et al, 1995).

Following the procedure, it is routine to monitor the fetus' heartbeat using ultrasound to insure a positive fetal response. A few hours of rest are recommended. About 20% of women report cramping following the procedure and about one-third of women have a few days of limited bleeding or spotting (CVS, 2006).

Depending on what genetic or chromosomal risk factors are suspected, results are may be available within a few days or may require as long as 2 weeks to be fully analyzed. CVS can produce information on all chromosomal disorders, but not all genetic ones. Further, using CVS to diagnose metabolic disorders is very difficult and usually must be confirmed later by an amniocentesis (Zaret, Jatlow, & Katz, 1997).

In slightly more than 19 out of 20 cases, CVS results confirm that the baby is healthy, while in 3 or 4 cases out of 100, the results confirm the existence of a genetic or chromosomal problem. Most of these cannot be treated and so parents are presented with often wrenching ethical choices regarding what to do with the information. In some cases, selective abortion is chosen. Other parents will use the information to prepare psychologically for a baby with the challenges characteristic of the specific diagnosed chromosomal or genetic syndrome.

In some cases, however, the CVS results can allow for treatment in utero, and thus can help mitigate and even prevent problems from developing. A good example of this is a disorder called CAH (congenital adrenal hyperplasia), a birth defect that is inherited and causes female fetuses to develop male-like external genitalia. CAH girls are lacking an enzyme, which can be treating prenatally (in the 10th to 16th weeks) by hormone treatments, effectively preventing the necessity for surgery after birth (CVS, 2006).
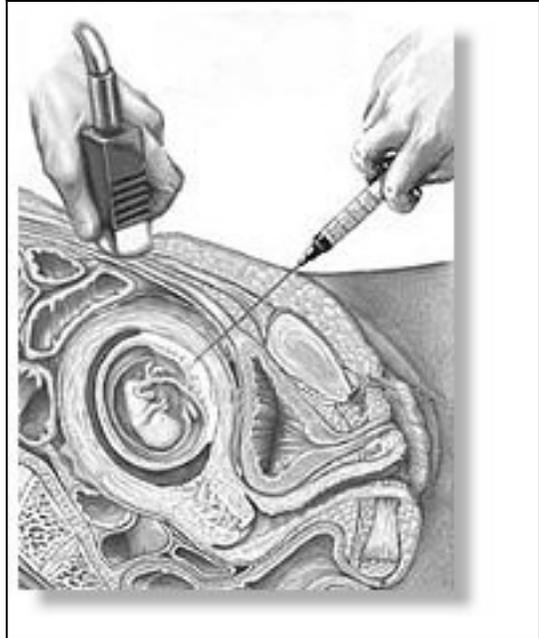
CVS vs. Amniocentesis

While the overall risk of complications and miscarriage for CVS is slightly higher than for amniocentesis (which is about ¼ to ½ %), CVS seems to be safer earlier in pregnancy (Philip et al, 2004) and amniocentesis much safer after 14 weeks (ACOG, 2001). But CVS done prior to 10 weeks also carries higher risks of causing birth defects such as abnormal development of the tongue and lower jaw and missing or shortened fingers or toes (Zaret, Jatlow, & Katz, 1997). But research has found that this risk essentially disappears after 10 weeks. Thus, CVS is only rarely done prior to 10 weeks (Olney et al, 1995).

While CVS test results are more than 99% accurate, they are slightly less accurate than amniocentesis results, and are a bit more likely to give inconclusive results due to the presence of some of the mother's cells in the sample (in about 1-3% of the time) and, in rare cases, discrepancies between chorionic villi cells and fetal cells (Zaret, Jatlow, & Katz, 1997). If this happens, an amniocentesis procedure is often recommended after waiting for a few weeks.

THE FOURTH MONTH (Weeks 13-16)

At the beginning of the fourth month, the fetus is between 3 and 4 inches long and weighs a little more than an ounce (about 30 grams). By the end of the fourth month, she will be about 4/1/2 inches long and will weigh 3.5 ounces (about 100 grams). Thus, she will have tripled her weight during this crucial month.

Fetal Breathing

Toward the end of the third month, indeed as early as 10 weeks (Connors et al, 1989) and in the early fourth month, the fetal lungs begin a process of breathing amniotic fluid in and out of the lungs. This process allows for "practice" (using amniotic fluid instead of air) for the necessary task done immediately after birth. The fetus will not "drown" because getting oxygen is not the point. He gets that from his mother's blood stream by way of the placenta and umbilical cord. Initially, this breathing is rather irregular and erratic, but as he goes into the fourth month and beyond, the breathing patterns regularize and gradually become quicker and more vigorous (Dawes, 1976).

Even after these breathing patterns are regularized, distinct patterns of breathing continue. One occurs only when the fetus is in REM sleep and occurs most often (about 90% of fetal breathing activity). It is rapid and somewhat irregular and episodic, interspersed with periods of apnea. Periodic "sighs" accompany this type of breathing. The second type of breathing is much slower (about 1 to 4 breathes per minute) and deeper and seems to be accompanied by gasps that resemble coughing or grunting. The first pattern (but not the second) is accompanied by increased blood pressure and fetal heart rate (Cosmi, La Torre, & Cosmi, 2001).

There are normal variations in fetal breathing, but various outside factors can also influence breathing (Kaplan, 1983). Any drug that is a central nervous system depressant (alcohol, general anesthetics, & barbiturates) slows down fetal breathing while the opposite occurs with nervous system stimulants such as caffeine (Devoe, Murray, Youssif, & Arnaud, 1993), nicotine, cocaine. Smoking tobacco tends to cause a decrease (by up to 20%) in fetal breathing because of the hypoxia (lack of oxygen), even though it contains nicotine (Manning, 1976). Maternal exercise also tends to result in a decrease in fetal breathing (Jakobovits, 1983).

Lanugo

Babies in the fourth month are still relatively thin and very slowly begin to put on fat, starting with the cheeks first and only later and gradually in the shoulders, back, and abdominal area (15 weeks), and arms and legs (16 weeks) (Poissonnet et al., 1983; Poissonnet et al., 1984). But adding fat is a slow and very gradual process and the big additions do not occur until the third trimester.

Perhaps because of this relative slenderness, babies grow a type of fine hair called lanugo that functions as a type of insulation to keep the baby warm. Adolescent and adult anorexics will also grow lunugo hair to keep them warm in

the absence of the normal presence of fat in the human body. The lanugo, along with the amniotic fluid, also reduces friction within the womb similar to the way adult underarm hair minimizes chafing as we move and use our arms.

Lanugo hair will last until around the 7th or 8th month, when it will gradually all drop out and be replaced by the normal vellus hair, a kind of fine "peach fuzz". The lanugo covers most of the body, with the exception of the palms of the hands and sides of the fingers, the soles of the feet and the sides of the toes, the lips, and in boys, the penis. It tends to be thickest in the trunk, limbs, and face. The photo to the left is of a premature baby's back.

Mecomium

The late 3rd and early fourth months also bring the first appearance of mecomium, a kind of fetal feces (Abramovich & Gray, 1982; O'Rahilly & Müller, 2001; Ramón y Cajal & Martinez, 2003). It is not surprising that the appearance of mecomium and lanugo happen simultaneously, because the mecomium is actually partially composed of lanugo hair that has been shed and swallowed by the fetus. Other dead cells, along with digestive enzymes and proteins, constitute the remainder of the mecomium content (Grand et al., 1976).

"Quickening"

Although movement begins as early as 6 weeks, most women cannot feel it. The first sensation of fetal movement usually occurs some time in the fourth month and usually between 14 and 18 weeks (Sorokin & Dierker, 1982). But some women report feeling a fluttering movement as early as 12 weeks (Leader, 1995) and generally speaking, women tend to identify movement earlier in their subsequent pregnancies and later in their first. This perception of movement, traditionally called quickening (Spraycar, 1995; Timor-Tritsch et al., 1976) is often a psychologically significant moment for pregnant women.

Physical Development

The existence of the mecomium implies that the baby has something to digest, process and excrete. Amniotic fluid is part of this "food", and its taste is discernibly different depending upon the mother's diet. In the fourth month, the fetus has taste buds covering the inside of the mouth, but by the 9th month they will only remain on the roof of the mouth and tongue (Lecanuet & Schaal, 1996; Miller, 1982; Mistretta & Bradley, 1975).

During the fourth month, the internal and external genitalia continue to develop. But gender-specific behavioral differences seem to appear for the first time. For instance, research has found that as early as the fourth month, female fetuses seem to move their jaws more frequently than males do (Hepper, Shannon, & Dornan, 1997).

Due to cephalocaudal development, the upper limbs of the body first reach their final proportions at the beginning of the 4th month. The lower body is a bit delayed and takes a few weeks longer to reach its appropriate proportions (Moore & Persaud, 2003). Due to the increases in body growth, the proportion of the head to the overall body is a little more than 1/3.

During this month, the heart goes from pumping several quarts of blood through the body every day to about 25 quarts per day. Bone marrow also begins to form and the liver and pancreas produce their appropriate fluid secretions.

The baby's skin appears a dark red, owing to blood flow beneath his near transparent skin. This is due partially to the relative absence of fat we noted earlier. The eyebrow and scalp hair may make their appearance and for

babies that will eventually have darker hair, the hair follicles will commence the production of melanin, which gives hair (and skin) its pigmentation.

The fourth month sees the baby's eyes and ears in an almost neonatal-like appearance, due to the fact that both have almost reached their final position on the head. The muscles in the face have developed, allowing for a much greater range of facial expressions, including frowning and squinting.

Prior to the fourth month, a withdrawal response to stimulation occurs. But in this month, the fetus will respond to gentle stimulation positively (Lecanuet & Schaal, 1996; Reinis & Goldman, 1980) and even exhibits an early version of the rooting reflex (Bates, 1987) whereby light stimulation on his cheeks will cause him to turn toward what he expects to be the nipple, a source of food (Mancia, 1981).
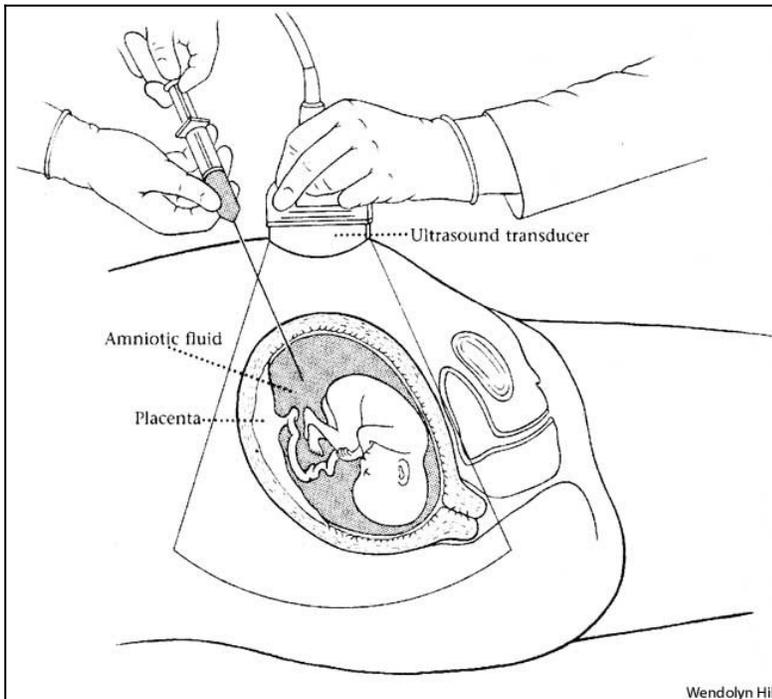
Amniocentesis

Amniocentesis is a relatively common test first used in 1882 (Woo, 2006) to remove excessive amniotic fluid and used for diagnostic purposes beginning in the 1930s (Fuchs & Riis, 1956; Menees, Millar, & Holly, 1930). It is given to women between the 15th and 20th weeks of pregnancy and is used to obtain a sample of amniotic fluid for the purposes of either diagnosing (or ruling out) various genetic and chromosomal factors that may be present in the growing fetus. Because the amniotic fluid contains actual cells from the skin and digestive tract of the fetus (along with proteins and fetal urine), amniocentesis provides more accurate information than CVS because there is almost no risk of maternal cells interfering with the results (Amniocentesis, 2005).

As we noted earlier, amniocentesis provides much of the same information that CVS does, but is used at a later point in the pregnancy when CVS (usually the 10th to the 12th weeks) becomes a bit more risky. Amniocentesis is also more accurate than CVS and provides a more complete and comprehensive genetic and chromosomal profile of the fetus. But it cannot identify some possible problems such as cleft palate or congenital heart disease.

Similar to CVS, amniocentesis is not routinely performed on pregnant women, partially due to the slightly elevated risk of miscarriage in approximately ¼ to ½ % of the time (Olney et al, 1995). Thus, amniocentesis is recommended only in particular situations: when the mother is over age 35 (ACOG, 2005a); when there is a family history of genetic disorders or defects (Jenkins & Wapner, 1999); when there has been a previous pregnancy or birth of a child with some genetic or chromosomal disorder; when there has been a previous pregnancy or birth of a child with a neurological problem (such as a neural tube defect); and when a previous blood test, ultrasound or CVS has indicated the need for further information and clarification.

Amniocentesis is also occasionally employed in the third trimester to determine if a baby's lungs are developed enough for delivery (in situations where an early delivery may be advisable or even necessary). It may also be employed to diagnose any uterine infections or to determine how severe fetal anemia may be in situations of Rh disease (when the baby and mother have different blood types that are incompatible) (Amniocentesis, 2005).

Using an ultrasound to guide the process and prevent harm to the fetus, a thin needle is inserted through the abdominal wall, uterus and amniotic sac and a small sample (1-2 tablespoons) of the clear

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amber-colored amniotic fluid (resembling urine in color) is removed. The procedure takes less than an hour and while some women report no discomfort, others relate feelings of cramping when the needle is inserted and/or pressure when the sample is withdrawn. Sometimes a local anesthetic is used, but it is often not necessary.

Following the procedure, it is routine to monitor the fetus' heartbeat using ultrasound to insure a positive fetal response. A day or so of rest is recommended, as is the avoidance of any strenuous activity (Amniocentesis, 2005). About 1-2% of women report cramping, leakage of amniotic fluid, and/or spotting following the procedure (ACOG, 2001).

The fetal cells in the amniotic fluid are separated, removed and grown in a laboratory for 10-12 days. This cell culture is then tested and analyzed for genetic and chromosomal anomalies (ACAG, 2005b). Results are available within 3 weeks (ACOG, 2005a). Levels of AFP (alpha-fetoprotein) are also contained in the amniotic fluid and can be measured in just a few days. Elevated levels are associated with neural tube defects (Amniocentesis, 2005).

As with CVS, amniocentesis provides positive news to most women. In cases where the results indicate some genetic or chromosomal defect, prospective parents have difficult choices to make regarding future actions (Kocun et al, 2000). This may or may not include selective abortion or it may result in a preparation process to meet the challenges of a differently-abled child. While most birth defects diagnosed by amniocentesis cannot be treated, some can. Inherited metabolic disorders such as biotin deficiency and methylmalonic acidemia can be successfully treated and result in perfectly healthy children (Harrison, Golbus & Fillylife, 1981). Amniocentesis can also be a very effective diagnostic tool in identifying disorders and congenital problems which are amenable to fetal surgery (Adzick et al. 1993; Flake & Harrison, 1995; Harrison et al. 1982; Meuli et al, 1997; Sydorak & Harrison, 2003).

While the risk of miscarriage from an amniocentesis in the second trimester is very small, it may be three times higher if done in the first trimester (CEMAT, 1998) and thus CVS is recommended and safer in this period (Philip at al, 2004). Several other complications, also very rare, must be noted, including infection, injury to the fetus from the needle (Olney et al, 1995), and an increase in clubfoot, a fetal deformity (Farrell et al, 1999). Maternal factors have also been found to increase complications from an amniocentesis procedure. These include maternal hypertension and being significantly overweight (Johnson et al, 1999).

THE FIFTH MONTH (Weeks 17-20)

At the beginning of the fifth month, the fetus is about 4 ½ inches long and weighs less than 4 ounces (about 125 grams). By the end of the fifth month, she will be a little over 7 inches long and will weigh 10.5 ounces (about 300 grams). She is about the size of a large banana. Thus, in this month, she will almost double in length and almost triple in weight.

Vernix

During the fifth month, the fetus's sebaceous glands begin to produce a waxy white substance called vernix caseosa. It is composed of a combination of sebum (oil produced by sebaceous glans) and sloughed-off dead skin cells. Along with the lanugo discussed earlier, the vernix works as a lubricant, protecting the skin of the fetus as it moves around in the now-somewhat crowded uterus (Campbell, 2004; Moore & Persaud, 2003).
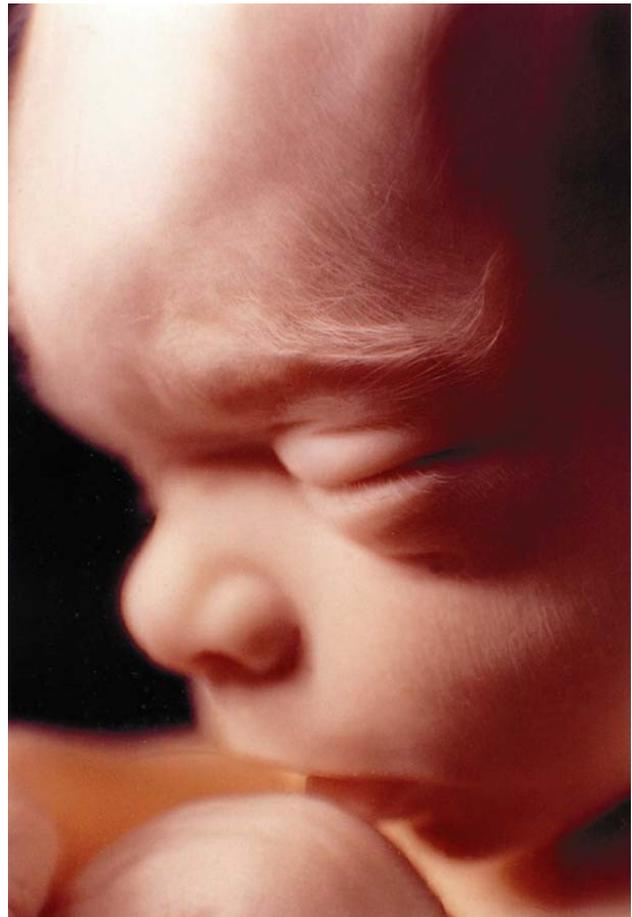
REM Sleep

During the fifth month, rapid eye movement sleep (REM) can be measured. This is the type of sleep that in children and adults we are most likely to dream and there is no reason to believe that dreams are not also part of fetal sleep. The question of what the fetus is dreaming about is one that will probably never be answered. Apart from the dreaming aspect of REM sleep, it seems crucial for brain development and function. In fact, the fetus spends about 80% of their time in REM sleep, with the remaining 20% devoted to non-REM sleep and wakefulness.

Why so much REM sleep? Much is still unknown about REM sleep and so definitive answers to this question are not answerable at this point. But researchers believe that the brain activity occurring in REM sleep contributes directly to the maturation of the brain structures by providing stimulation to the brain (Mirmiran, 1986). Similar to what we have seen with fetal breathing as a type of practice preparing the fetus for later life, so REM sleep provides active "practice" for the brain as it grows. One example of this seems to involve the eye and parts of the brain governing vision. Activity in these neural cells in necessary to prepare for later vision and REM sleeps appears to do this. It is speculated that REM sleep does this for multiple other brain functions as well.

Underlying this speculation are studies that show negative outcomes when REM sleep is disturbed. Much of this research has been done on animals. For instance, when rats are deprived of REM sleep early in life, numerous negative consequences occur in adulthood. It is thought that such REM disturbances may be associated with later apnea, cardiovascular and respiratory problems and result in increased vulnerability to various diseases later in life (NIH, 2006).

Physical Development

With the brain and nervous system development that REM sleep promotes and pain awareness allows for, neural function is at a relatively high level. From the 19th week on breathing activity, movement, and heart rate begin to follow daily cycles called circadian rhythms (de Vries et al., 1987; Goodlin & Lowe, 1974; Okai et al., 1992; Romanini & Rizzo, 1995). The heartbeat can now be heard with a just a stethoscope and the lungs continue to develop significantly (DiFiore & Wilson, 1994; Pringle, 1988).

Fetoscopy

Fetoscopy is a general term used to refer to various procedures that evaluate and treat a fetus. Two different types of fetoscopy are used, one being non-invasive and external, while the other is invasive and is known as endoscopic fetoscopy. This second type of fetoscopy was first pioneered in 1954 (Westin, 1954).

Types of Fetoscopy

External Fetoscopy

External fetoscopy employs a device very similar to a stethoscope (but with a headpiece) in order to listen to the fetal heartbeat. It is used after about 18 weeks, because prior to this time, the fetal heartbeat is too faint to hear without the use of a Doppler stethoscope, a device which amplifies the sound of the heartbeat. The fetoscope is placed on the mother's abdomen and moved around until the heartbeat is discernable. Ideal fetal heart rate is 120 to 160 beats per minute. Anything significantly higher or lower than this may require further interventions.

Endoscopic Fetoscopy

The second type of fetoscopy is invasive and uses a device called an endoscope, which is tipped with a fiber-optic camera. Similar to the process used with CVS, it is inserted either through the vagina or through the abdominal wall (Deprest & Gratacos, 1999). It is used to "see" the fetus for either diagnostic or surgical purposes.

As with external fetoscopy, endoscopic fetoscopy is usually done during or after the 18th week of a pregnancy. By this time, the placental, amniotic and fetal structures are developed enough to provide useful diagnostic data. Because endoscopic fetoscopy does have risks to both mother and baby, it is not routinely given. Rather, it is used when there are significant indications of a possible problem and/or if there is a strong family history of birth defects. Risks include infection, bleeding, excessive leakage of amniotic fluid, premature rupture of the amniotic sac requiring
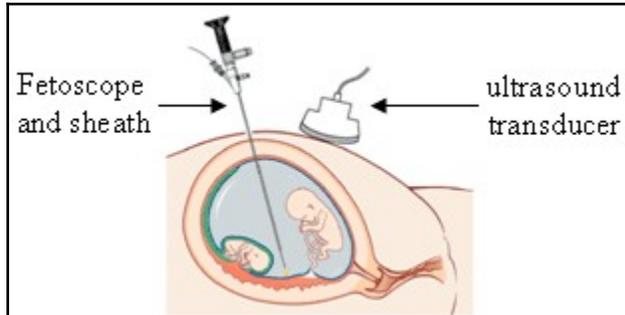
early delivery, and miscarriage rates of 3-5% (Fetoscopy, 2006) or as high as 12% when fetoscopy is done in conjunction with surgery (Youngerman-Cole, 2006).

The procedure itself takes between 1 to 2 hours and usually includes administration of a sedative (both to relax the mother and to prevent the baby from moving excessively) and a local anesthetic. Often used in conjunction with ultrasound, the endoscope is inserted and the procedure is done. If surgery is being done, the procedure takes longer and is more complicated. An ultrasound is often repeated the next day to ensure a positive fetal response (Gratacos & Deprest, 2000).

Women report that they often feel some discomfort in the form of pain or pressure as the procedure is occurring, with feelings of nausea and/or mild cramping following the fetoscopy. Women are encouraged to avoid strenuous activity for several weeks (Yang & Adzick, 1999).

When used in conjunction with ultrasound and other devices, endoscopic fetoscopy can be used to ascertain a wide variety of types of information. These include samples of fetal or umbilical cord blood which can be used to diagnose hemophilia (Firscheim, 1979), sickle-cell disease (Alter et al, 1976; Fairweather, Ward & Modell, 1980; Hobbins & Mahoney, 1977), CGD (chronic granulomatous disease), an type of immune disorder disease (Newberger et al, 1979), galactosaemia (Fensom et al, 1979), and Tay-Sachs disease (Perry, 1979).

A fetoscopy can also be used to procure a sample of fetal skin tissue, which can be used to diagnose Duchenne muscular dystrophy (Golbus et al, 1979a; 1979b) and Weber-Cockayne Syndrome (Rodeck, Eadi & Godsden, 1980) Fetal liver tissue samples are used to diagnose OTC (ornithine transcarbamylase) deficiency (Rodeck, Patrick, & Pembrey, 1982). Finally, the clear images of a fetoscope can identify physical malformations which can be

fetoscopic image of foot, 17 weeks

sued to diagnose spina bifida and neural tube defects (Rodeck & Campbell, 1978a; 1978b; 1979).

Results involving images are immediately available. Those involving tissue or blood samples may take a few days or up to a week. An overly active fetus, hydramnios (excessive amniotic fluid), very cloudy amniotic fluid or a mother who is excessively overweight may all be factors limiting the usefulness of endoscopic fetoscopy.

THE SIXTH MONTH (Weeks 21-24)

At the beginning of the sixth month, the fetus is about 7 – 7 ½ inches long and weighs around 11-12 ounces (325-350 grams or so). By the end of the sixth month, she will be almost 8 ½ inches long and will weigh 1.2 pounds (about 550 grams).

Sensory Capabilities

While all of the sense organs are functioning somewhat prior to the sixth month, their development reaches a level where their sensory capabilities are approximating their post-natal level. Here we discuss the physical development of each (we will discuss the various psychological aspects in a later chapter).

Vision

As noted earlier, the eyelids have been closed since the 9th week in order to protect the developing eyes. But by the end of the 6th month (about 24 weeks), they re-open (Campbell 2002; O'Rahilly & Müller, 2001). While there would appear to be very little to see in utero, light can pass through the mother's abdominal wall and the fetus will respond behaviorally to bright flashing lights (Fulford et al, 2003; Robinson & Tizard, 1966). Fetal exposure and response to light may influence long-term vision (Noback et al., 1996).

Hearing

As early as 20 weeks, the cochlea, necessary for hearing, has reached full maturity (Lecanuet & Schaal, 1996) and thus allows the fetus to hear and respond to many different sounds (Hepper & Shahidullah, 1994; Querleu et al., 1989). Just like newborns or even adults, fetuses will exhibit a blink-startle reflex in response to loud noises **(**Birnholz and Benacerraf, 1983; Campbell, 2002). Apparently, this reaction can be seen in females earlier than in males (Lecanuet & Schaal, 1996). And just like newborns or adults, a fetus will respond somewhat negatively to loud sudden noises with a prolonged increase in heart rate and abrupt behavioral changes such as excessive swallowing of amniotic fluid (Visser et al., 1989). Prolonged loud noises may negatively affect hearing long-term (Gerhardt, 1990; Petrikovsky et al., 1993; Pierson, 1996).

Taste

As we noted earlier, amniotic fluid subtly changes in flavor depending upon the mother's diet. Functioning fetal taste buds have been present for over a month and a fetus will alter his intake of amniotic fluid, increasing it in response to a pleasant taste and decreasing it in response to a bitter taste. Sometimes, the fetus will change his facial expression in response to the taste (Lecanuet & Schaal, 1996; Liley, 1972; Mennella, Jagnow, & Beauchamp, 2001; Moore & Persaud, 2003; Reinis & Goldman, 1980). These early gustatory experiences seem to predict some post-natal food preferences (Beauchamp, 1995**).**

Smell

The sense of smell is operational by 26 weeks (Bradley & Misretta) and has been documented in premature babies (Lecanuet and Schaal, 1996). As with the sense of taste, variations in amniotic fluid as a function of a mother's diet seem to predispose the fetus for postnatal preferences in smell (Mennella, Johnson, & Beauchamp, 1995; Schaal, Marlier, & Soussignan, 2000).

Touch

Fetal sensitivity to touch is seen as early as the third month. In the fourth month, a fetus that is gently stroked will respond positively (Lecanuet

& Schaal, 1996; Reinis & Goldman, 1980). There is a large body of research showing the positive benefits of therapeutic massage on premature and mature babies (Agarwal et al, 2000; Barnard & Bee, 1983; Hasselmeyer, 1964; Mathai et al, 2001; Rose et al, 1980; Scafidi, Field, & Schanberg, 1993; White-Traut et al, 1993). Much more controversial has been the debate regarding fetal pain, especially in the light of some abortion techniques such as D&X (also known as partial-birth abortion) which are done in the second and third trimesters without fetal anesthetics. A recent review of the evidence (Lee et al, 2005), stated that there was no way to prove that fetuses can feel pain prior to the third trimester, and therefore the question remains somewhat open. But the exact same argument has been used in previous years to argue that infants do not feel pain when circumcised or operated on. Subsequent research has indicated that this was (and is) untrue.

Numerous other studies indicate evidence to the contrary. Since one cannot ask a fetus (or a newborn) whether they are experiencing pain, one infers its existence by neural capability and behavioral responses. Thus, as Anand (2006) and others (Anand & Hickey, 1987; Glover & Fisk, 1999; Smith, Gitau, Glove, & Fisk, 2000; Valman & Pearson, 1980) have argued, the evidence is strong that pain can be experienced very early on in pregnancy. The structural and hormonal mechanisms are present which would allow for pain sensation. Fetal behavioral responses to painful stimuli are also plentiful. For instance, at 16 weeks, the insertion of a needle into the fetus will trigger a hormonal stress responses (norepinephrin and cortisol) as well as avoidance behavior such as pulling away from needle (Giannakoulopoulos et al., 1994; Giannakoulopoulos et al., 1999; Glover & Fisk, 1999; Smith et al., 2000).

Fetal Viability

The sixth month is also considered the absolute cut-off for survival outside the mother's womb. While most infants born in the 6th month will still not survive, there are a few that will if intensive medical care is available.

Even though the lungs have started to develop at 4 weeks after fertilization, and the fetus as been practicing fetal breathing for months, the lungs continue to develop even in the third trimester. Thus, for premature babies, their lungs are often too immature to function adequately outside the womb. What makes survival even theoretically possible at this point is the baby's lungs begin to produce surfactant, a slick substance that allows the alveoli, (the air sacs) in the lungs to inflate and also keeps them from collapsing and sticking to each other when they deflate.

Gestation (weeks)	Survival to discharge (%)
21	0
22	1
23	11
24	26
25	44

But fetuses at this stage only have about 5% of the total surfactant they actually need and will eventually produce. While replacement surfactant can help, along with corticosteroid treatments and respirators (Draper, Manktelow, Field, & James, 1999), survival is still unlikely. Even if the fetus does survive, they are at serious risk for developing respiratory distress syndrome (RDS), brain damage, cerebral palsy, learning disabilities, developmental disabilities, blindness, and various lung diseases (Marlow et al, 2005; Wood et al, 2000).

A large on-going study being done in the UK (called EPICure) has followed over 2000 babies born very early and has found that the survivor rate of 22 week-old fetuses is about 1% (see table above). By just three weeks later (at 25 weeks), this number has jumped to 44% (Costeloe, Gibson, Marlow, & Wilkinson, 2000). Two follow-up studies were done at 2 ½ years (Wood et al, 2000) and at 6 years of age (Marlow et al, 2005). As you can see from the table to the above, outcomes were serious, even for survivors.

Summary of outcomes among extremely preterm children				
Outcome	22 wk	23 wk	24 wk	25 wk
At 6 years of age survived with:	Per cent			
Severe disability	0.7	2	5	6
Moderate disability	0	4	4	8
Mild disability	0.7	2	7	12
No impairment	0	1	3	8

One factor that several studies have found is that the weight of the fetus is a more important factor than the actual gestational age as far as survival and outcome goes (Williams et al, 1982; Costeloe, Gibson, Marlow, & Wilkinson, 2000).

Ultrasound

Initially developed and used in World War II as a means of locating submarines and other objects underwater, ultrasound is now primarily used as a medical test. Also called a sonogram, because it uses sound waves, it is most prominently associated with obstetrical testing. It can be used at any point in pregnancy, but is most often utilized in the second and third trimesters when the fetus is large enough and developed enough to be able to provide an "image" to evaluate.

Because it is noninvasive, it cannot give genetic or hormonal information, but is instead used to indicate the size, age (often by the size of the head; see image at right of baby at 14 weeks), gender, level of development, and the position of the baby. Sonograms are also utilized to determine the presence of observable physical birth defects such as hydroencephaly, microencephaly or the distinct physical characteristics associated with Down syndrome. It can likewise indicate abnormalities in bone structure, kidneys, bladder or heart.

Ultrasound is additionally used to reveal the existence of multiple babies (twins, triplets or quadruplets), and to observe fetal heartbeat (as early as the 5th week), breathing and movement (as early as the 7th week). It can provide information on the amount of amniotic fluid, the location and size of the placenta, and the presence of any uterine abnormalities or tumors. Finally, as we have previously indicated, ultrasound is often used in conjunction with CVS, fetoscopy and amniocentesis to minimize the risks of these procedures.

Ultrasound imaging uses high-frequency sound waves to produce images of the baby or placenta. A device called a transducer sends the sound waves through body tissues, which are reflected back by the various internal body structures. These "echoes" are then picked up by the transducer, and transmitted electronically onto a viewing screen (see image of a 23-week old baby above). These images can be videotaped or printed out as a "photograph".

Since the transducer is placed directly onto the skin of the abdomen, and moved around and positioned to get the best image, a lubricant gel is applied to the skin to decrease the friction caused by the transducer. This gel is merely wiped off after the procedure.

Women are asked to drink a lot of water (4 to 6 full glasses of water) prior to an ultrasound because a full bladder tends to enhance the resulting images. The bladder is in front of the uterus and when empty tends to cause the uterus to be positioned in between the pelvic bones. Since bones obscure the sound waves

from the transducer, this interferes with the clear imaging of the baby. A full bladder, however, pushes the uterus up from the pelvis, maximizing the chances of a clearer image. The full bladder almost serves as a "window" into the uterus and thus the baby.

Ultrasound does not utilize the radiation found in other procedures (x-ray and CT scans), but rather uses sound waves. It is generally considered to be completely safe and because of this, its use has become more and more routine. There are, however, several studies that have connected exposure to ultrasound and left-handedness, especially in boys (Kieler et al, 2001; Kieler et al, 2002). A recent study found that mice exposed to ultrasound

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experienced some cerebral cortex damage (Ang et al, 2006). But so far, human studies have not found such effects (Kieler et al, 2005; Stark et al, 1984).

There is some debate about the potential negative effects of multiple ultrasounds. One study found that repeated ultrasound exposure produced slightly smaller birth weights (Newnham et al, 1993) but other studies have not found this result (Bellieni et al, 2005).

Recent developments in sonography have made the images much more sophisticated and thus much more useful. The addition of 3-D (still images like the one on the right) and 4-D (video images) scans have also produced a market for prenatal pictures as keepsakes. When produced in non-medical facilities with names such as Fetal Fotos, Peek-a-Boo, Womb with a View, and Baby Insight, the FDA has warned against such keepsakes, primarily due to the still unknown long-term effects of exposure and repeated exposure to sonography. These facilities may use sound levels that are stressful and potentially harmful to the baby (Rados, 2004).

Ultrasound has also been somewhat controversial when used to determine sex for the purposes of gender selection. In cultures such as China and India where male children are highly prized, ultrasound has been used to identify female fetuses, who are then subsequently aborted. While this is illegal in both countries, a recent study estimated that over the past 20 years, up to 10 million female fetuses have been aborted in India alone (Sheth, 2006).

THE SEVENTH MONTH (Weeks 25-28)

Fetal Development

At the beginning of the seventh month, the fetus is about 8 ¾ inches long (crown to rump) and weighs around 1.5 pounds. By the end of the seventh month, she will weight around 2.5 pounds and will have an overall length of 15 ½ inches (about 10 inches or so from crown to rump).

The seventh month begins the third and final trimester. During the final three months or so of pregnancy, there is vigorous brain development, particularly myelination of the 100 billion neurons that are already present. Thus, brain weight increases dramatically (Mancuso & Palla, 1996). The thin appearance of the fetus begins to change and fat deposits begin to appear beneath the skin all over the body (England, 1983). As the lanugo hairs begin to fall out, these fat deposits serve to insulate the child and serve as energy storage deposits to be drawn on immediately after birth. The combination of brain growth and fetal fat storage results in increasing calorie needs.

The fetus also continues to develop physically and movement is more common and vigorous. Although room in the uterus is limited, babies will perform "somersaults", "walking" up the side of the uterus and flipping over (Liley, 1972).

Fetal Surgery

Advances in technology combined with greater levels of knowledge over the past 50 years have created a new subfield in surgery. The earliest attempts at therapeutic operations on fetuses came in the 1960s (Nihoul-Fekete, 1990). The problem at hand during this time was Rh incompatibility, and the first successful intrauterine fetal blood transfusion occurred in 1965 (Menon & Rao, 2005). Since that time, many more fetal problems have been addressed and numerous other partially successful procedures devised (Brunner, 2003; Cortes & Farmer, 2004; Pringle, 1986).

Types of Fetal Surgery

Obstructive Uropathy

Progress was initially slow, but in 1981 the first successful surgery was performed to correct a urinary blockage in an unborn baby (Lanzetta, 1992). Since this time, surgery to treat various urinary tract obstructions has become more common because these abnormalities are among the most common birth defects. If the urethra becomes obstructed or does not develop properly, urine has no way to leave the body and backs up, causing an enlarged bladder and contributing to kidney damage. The level of amniotic fluid may consequently decrease relative to fetal urine. This in turn hampers fetal lung development. If the condition is serious enough, it can even result in fetal death. A prenatal surgical intervention, in which a shunt is inserted to open up the urethra (Clark et al, 2003), is often life-saving and the long-term prognosis for such interventions is good (Baird et al, 2005; Freedman et al, 1999; Holmes, Harrison & Baskin, 2001; Shimada, 1998).

Congenital Diaphragmatic Hernia (CDH)

The first successful prenatal surgery to repair a diaphragmatic hernia occurred in 1989. CDH is a condition in which the diaphragm forms incompletely. The result is inadequate and hampered lung development, because the inadequate diaphragm allows the lower organs (stomach, spleen, liver, and intestines) to enter into the chest cavity. This can occur on both sides, or on either the right or the left. If left untreated, numerous long-term problems can result, including asthma, scoliosis, hearing problems, brain damage and even fetal death (Conforti & Losty, 2006). Because CDH occurs in 1 out of 2500 babies, this type of fetal surgical intervention has been among the most common.

The surgical intervention techniques involve repairing the herniated diaphragm (Grethel & Nobuhara, 2006; Harrison et al, 1997; Wilson, DiFiore & Peters,1993) or using a procedure called fetal tracheal occlusion (FETO). The trachea is temporarily blocked (occluded) by means of a small balloon. This traps fluid in the lungs and stimulates lung growth, displacing and pushing the abdominal organs back into their normal cavities. The balloon is removed immediately after birth of the baby (Chiba, 2000). But outcomes for this type of surgery are still being evaluated with some studies finding little or no benefit to the prenatal intervention (Harrison et al, 2003; Smith et al, 2005) and others reporting better results (Deprest, Gratacos, & Nicolaides, 2004; Deprest et al 2005; Deprest et al, 2006).

Regardless of the type of intervention for CDH, it may or may not be the best option due to less than ideal outcomes. The decision to surgically intervene depends upon numerous factors, the most important being how severe lung development is being hampered by the CDH (Cass, 2005; Colvin et al, 2005; Cortez et al, 2005).

Congenital Cystic Adenomatoid Malformation (CCAM)

Surgery for another congenital disorder was first successfully achieved in 1990. CCAM (congenital cystic adenomatoid malformation) is an abnormal growth of a cystic mass in the lungs. Most of the time these masses either disappear over time or are too small to cause problems. But they may grow large enough to interfere with lung normal development and cause pulmonary hyperplasia. They may also grow large enough to put enough pressure on the heart to cause heart failure. Occasionally, they may become infected or cancerous or cause pneumonia. Surgery to remove these masses has been somewhat successful (Davenport et al, 2004), depending on how localized and contiguous the mass is (Adzick et al, 1998; Adzick & Kitano, 2003; Choi, 2001; Kitano & Adzick, 1999; Kitano et al, 1999).

Sacrococcygeal Teratoma (SCT)

The first successful surgery to remove a tumor called sacrococcygeal teratoma (SCT) occurred in 1992. Occurring in 1 out of 30,000 babies (Makin et al, 2006), this tumor is usually benign (90% of the time) and develops and grows at the base of the spine in the coccyx area. They can grow quite large (at time as large as the fetus) and have extensive blood vessel development, effectively robbing the growing fetus of oxygen and nutrients. This can result in significant stress on the fetal heart and delayed fetal development. If the tumor is large enough, surgery may be done to remove the tumor. Results have been somewhat mixed due to the presence of other complicating factors (Chan et al, 2002; Hedrick et al, 2004; Hirose & Farmer, 2003), but one study found overall survival rates of over 75% (Makin et al, 2006).

Spina Bifida (Myelomeningocele)

Spina bifida, also called myelomeningocele, was successfully treated in utero by surgery for the first time in 1998 (Menom & Rao). Spina bifida is a disorder in which the spinal vertebrae do not close and form properly around some point on the spinal cord. Affecting 1 out of 1000 babies, spina bifida has numerous consequences as the baby grows prenatally. Left untreated, the spinal cord is exposed and the result may be neurological problems, partial or full paralysis, bowel and bladder problems, and fluid buildup in the brain (hydrocephalus).

Surgery for spina bifida includes repair to the spinal column (Brunner & Tilipan, 2005; Kohl et al, 2006) or the insertion of a shunt (Moise, 2003). While the treatment of spina bifida prenatally is thought to improve long-term outcomes (Brunner et al, 2004), it is not yet clear how beneficial this treatment is will be (Walsh & Adzick, 2003).

Risks of Fetal Surgery

What makes fetal surgery possible are the various other techniques which are used to diagnose any problem in the first place. Ultrasound, amniocentesis, fetoscopy, CVS, and other tests both identify the problem, and in some cases, assist in the surgical intervention.

Once an abnormality has been identified, all possible non-surgical interventions are usually considered before surgery. Due to the relative novelty of this field, many risks and complications continue to remain for both babies and mothers. All surgical procedures noted above are associated with much higher risk of premature delivery, often before 30 weeks. Thus, babies who survive the procedure often must also struggle with the consequences of prematurity and low birthweight. This prematurity is a direct consequence of breeching the uterus, whether by means of incision or puncture (Menon & Rao, 2005). Blood loss, amniotic fluid loss, placental difficulties, premature rupture of the amniotic sac, and other complications (Longaker et al, 1991; Sydorak et al, 2004) are all associated with fetal surgical procedures. Long-term studies have also shown a 21% incidence of neurological damage (Menon & Rao, 2005). It is important to note, however, that all of the risks above must be balanced with the risks of outcome in the absence of fetal surgical interventions. In some cases this would be close to a 0% survival rate.

THE EIGHTH MONTH (Weeks 29-32)

At the beginning of the eighth month, the fetus is about 10 inches long from the crown of the head to the rump and almost 16 inches overall. She weighs around 2.5 pounds or so. By the end of the eighth month, she will weigh around 4.5 pounds and will have an overall length of about 19 inches.

In many ways the eighth month is functionally a continuation of the seventh month. The baby continues her physical activities in preparation for her life outside the womb. She alternates between time periods of activity and rest (DiPietro et al., 2002). These patterns function to coordinate the various parts of the body with the brain, and represent the process of integration so important to post-birth functioning.

She continues to add body fat to her body and also accelerates the storage of iron, calcium and phosphorus, all important for the burst of growth that she will experience in the weeks after she is born. The fetus continues to practice breathing, spending up to third of her time breathing the amniotic fluid in and out of her lungs, even while sleeping (Connors et al., 1989: de Vries et al., 1985; Patrick et al., 1980; Visser et al., 1992). The alveoli in the lungs continue development in preparation for life after birth and will do so until about 8 years of age (Lauria et al., 1995).

THE NINTH MONTH (Weeks 33 to Birth)

The final month in utero includes the addition of a couple of inches in length and an almost doubling of weight. The heart is now pumping approximately 300 gallons of blood per day. The baby continues to store fat, exercise, practice and build up antibodies.

Most babies spend the bulk of pregnancy in the head up position. But approximately 6 or 7 days prior to birth, the baby usually drops her head down into the pelvic cavity. At some point in time, the fetus initiates the process of labor (Liley, 1972) by releasing large amounts of estrogen (Moore & Persaud, 2003) into the mother's blood stream. This has a cascading effect, causing the increased release of several other hormones, resulting in the muscular contractions in the abdomen (Cunningham et al., 2001), and finally concluding with birth.

CONCLUSION

We will discuss birth in much greater detail in a later chapter, but the end of the fetal stage marks a huge milestone in development. In seven months, the fetus has gone from approximately 8 grams to 3400 grams and has grown from 2 inches to an average at birth of 21.5 inches. This is quite an amazing transformation! But if the physical growth is impressive, how much more impressive are the functional capabilities. At the end of this relatively short period of time, the fetus officially becomes a baby. But the only real difference is whether she is still inside her mother or has made the profound transition into the world at large.

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