AN ODE TO FEARLESS WOMEN

Defined by no man, you are your own story, blazing through the world, turning history into herstory.

And when they dare to tell you about all the things you cannot be, you smile and tell them, "I am both war and woman and you cannot stop me"

Nikita Gill



William Golding British Novelist, Playwright & Poet 1911 -- 1993

I think women are foolish to pretend they are equal to men. They are far superior and always have been. Whatever you give a woman, she will make greater. If you give her sperm, she will give you a baby. If you give her a house, she will give you a home. If you give her groceries, she will give you a meal. If you give her a smile, she will give you her heart. She multiplies and enlarges what is given to her. So, if you give her any crap, be ready to receive a ton of shit!



PHYSIOLOGY OF PREGNANCY

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LEARNING OBJECTIVES

By the end of this lecture the students should be able to:

- Describe the Transport of the Fertilized Ovum in the Fallopian Tube
- Explain the Function of Human Chorionic Gonadotropin in causing persistence of the corpus luteum
- Describe the Secretion of Estrogens and Progesterone by the Placenta
- Describe the functions of Human Chorionic Somatomammotropin
- Describe the Response of the Mother's Body to Pregnancy
- Explain the Changes in the Maternal Circulatory System During Pregnancy
- Describe the development of the Breasts in pregnancy

RECALL OF PREVIOUS KNOWLEDGE...



FERTILIZATION

Fertilization is the process by which male and female gametes are fused together, initiating the development of a new organism.

the ovum becomes fertilized by a sperm, a new sequence of events called gestation or pregnancy takes place

the fertilized ovum eventually develops into a full-term fetus.



After ejaculation, sperms reach *ampulla* of fallopian tube within 30-60 min (PG and OT actions)



The fertilizing sporm penetrates the corona radiata via membrane-bound enzymes in the plasma membrane of its head and binds to ZP3 receptors on the zona pellucida.

Binding of sperm to these receptors triggers the acrosor reaction, in which hydrolytic enzymes in the acrosome are released onto the zona pelluco

The acrosomal enzymes digest the zona pellucida, creating a pathway to the plasma membrane of the ovu When the sperm reaches the ovum, the plasma membrane of the two cells fuse.

The sperm nucleus enten the ovum cytoplasm.

The sperm stimulates rele of Ca²⁺ stored in cortical granules in the ovum, which i...



MATURATION AND FERTILIZATION OF THE OVUM

- While still in the ovary, the ovum is in the *primary oocyte* stage.
- Shortly before it is released from the ovarian follicle, its nucleus divides by meiosis and a *first polar body* is expelled from the nucleus of the oocyte.
- The primary oocyte then becomes the *secondary oocyte*.
- In this process, each of the 23 pairs of chromosomes loses one of its partners, which becomes incorporated in a *polar body* that is expelled.
- This leaves 23 *unpaired* chromosomes in the secondary oocyte.
- It is at this time that the ovum, still in the secondary oocyte stage, is ovulated into the abdominal cavity.
- Then, almost immediately, it enters the fimbriated end of one of the fallopian tubes.

ENTRY OF THE OVUM INTO THE FALLOPIAN TUBE (UTERINE TUBE)

- When ovulation occurs, the ovum, along with a hundred or more attached granulosa cells that constitute the *corona radiata*, is expelled directly into the peritoneal cavity and must then enter one of the fallopian tubes (also called uterine tubes) to reach the cavity of the uterus.
- The fimbriated ends of each fallopian tube fall naturally around the ovaries.
- The inner surfaces of the fimbriated tentacles are lined with ciliated epithelium, and the *cilia* are activated by estrogen from the ovaries, which causes the cilia to beat toward the opening, or *ostium*, of the involved fallopian tube.
- One can actually see a slow fluid current flowing toward the ostium

 \bullet

FERTILIZATION OF THE OVUM

- after the male ejaculates semen into the vagina during intercourse, a few sperm are transported within 5 to 10 minutes upward from the vagina and through the uterus and fallopian tubes to the *ampullae* of the fallopian tubes near the ovarian ends of the tubes.
- This transport of the sperm is aided by contractions of the uterus and fallopian tubes stimulated by prostaglandins in the male seminal fluid and also by oxytocin released from the posterior pituitary gland of the female during her orgasm.
- Of the almost half a billion sperm deposited in the vagina, a few thousand succeed in reaching each ampulla.





Transport of the Fertilized Ovum in the Fallopian Tube

 After fertilization, 3 to 5 days is required for transport of the fertilized ovum through the remainder of the fallopian tube into the cavity of the uterus

- Transport is effected by
 - 1. A weak **fluid current** in the tube resulting from epithelial secretion.
 - 2. Beating of **the ciliated epithelium** that lines the tube toward the uterus.
 - **3.** Weak contractions of the fallopian tube.





From Fertilization to Implantation



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TRANSPORT OF THE FERTILIZED OVUM IN THE FALLOPIAN TUBE

- During fallopian transport, several stages of <u>cell division</u> occur forming the **blastocyst**
 - Fallopian tube secretory cells produce large quantities of secretions used for the **nutrition** of the developing blastocyst.





TRANSPORT OF THE FERTILIZED OVUM IN THE FALLOPIAN TUBE

 The isthmus of the fallopian tube remains spastically contracted for about the first 3 days after ovulation.

• <u>Progesterone</u> secreted by the ovarian corpus luteum increases and activates progesterone receptors, leading to isthmus <u>relaxation</u> allowing entry of the ovum into the uterus.





IMPLANTATION OF THE BLASTOCYST IN THE UTERUS

- Blastocyst remains in the uterine cavity an additional 1 to 3 days before it implants in the endometrium
- the blastocyst obtains its nutrition from the uterine endometrial secretions, called "uterine milk"
- Implantation normally occurs on about the 5th 7th day after ovulation.



: Guyton and Hall Textbook of Medical Physiology, 12th Edition yright © 2011 by Saunders, an imprint of Elsevier, Inc. All rights rese Implantation results from the invasion of **trophoblast cells** over the surface of the blastocyst.

- These cells <u>secrete proteolytic enzymes</u> that digest and liquefy uterine endometrium cells.
- Some of the fluid and nutrients released are utilized for blastocyst growth.
- Trophoblast cells , uterine endometrium cells, & other blastocyct cells form the **placenta** and the various membranes of pregnancy.



Implanted human embryo at 7¹/₂, 13, and 23 days

71/2 days



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FUNCTION OF THE PLACENTA

- Trophoblastic cords from blastocyst attach to endometrium (form placental villi)
- Fetal <u>blood capillaries grow into the trophoblastic cords</u>
- Maternal blood sinuses develop around the outsides of the trophoblastic cords (villi)
- placenta is composed of fetal components & maternal components
- Nutrients and other substances pass through this placental membrane mainly by diffusion





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PLACENTAL PERMEABILITY AND MEMBRANE DIFFUSION CONDUCTANCE

- The major function of the placenta is to provide for diffusion of foodstuffs and oxygen from the mother's blood into the fetus's blood and diffusion of excretory products from the fetus back into the mother.
- In the early months of pregnancy, the placental membrane is still thick because it is not fully developed. Therefore, its permeability is low.
- the surface area is small because the placenta has not grown significantly. Therefore, the total diffusion conductance is minuscule at first.
- in later pregnancy, the permeability increases because of thinning of the membrane diffusion layers and because the surface area expands many times over, thus giving the tremendous increase in placental diffusion

DIFFUSION OF OXYGEN THROUGH THE PLACENTAL MEMBRANE

- Almost the same principles for diffusion of oxygen through the pulmonary membrane are applicable for diffusion of oxygen through the placental membrane.
- The dissolved oxygen in the blood of the large maternal sinuses passes into the fetal blood by *simple diffusion*, driven by an oxygen pressure gradient from the mother's blood to the fetus's blood.
- Near the end of pregnancy, the mean PO₂ of the mother's blood in the placental sinuses is about 50 mm Hg, and the mean PO₂ in the fetal blood after it becomes oxygenated in the placenta is about 30 mm Hg.
- Therefore, the mean pressure gradient for diffusion of oxygen through the placental membrane is about 20 mm Hg.

HOW IT IS POSSIBLE FOR A FETUS TO OBTAIN SUFFICIENT OXYGEN WHEN THE FETAL BLOOD LEAVING THE PLACENTA HAS A PO₂ OF ONLY 30 MM HG.

There are three reasons why even this low PO_2 is capable of allowing the fetal blood to transport almost as much oxygen to the fetal tissues as is transported by the mother's blood to her tissues.

- First, the hemoglobin of the fetus is mainly *fetal hemoglobin*, a type of hemoglobin synthesized in the fetus before birth.
- This means that at the low PO₂ levels in fetal blood, the fetal hemoglobin can carry 20 to 50 percent more oxygen than maternal hemoglobin can.



- Second, the *hemoglobin concentration of fetal blood is about 50 percent greater than that of the mother;*
- this is an even more important factor in enhancing the amount of oxygen transported to the fetal tissues.

THE BOHR EFFECT



- The fetal blood entering the placenta carries large amounts of carbon dioxide, but much of this carbon dioxide diffuses from the fetal blood into the maternal blood.
- Loss of the carbon dioxide makes the fetal blood more alkaline, whereas the increased carbon dioxide in the maternal blood makes it more acidic.
- These changes cause the capacity of fetal blood to combine with oxygen to increase and that of maternal blood to decrease.
- This forces still more oxygen from the maternal blood, while enhancing oxygen uptake by the fetal blood.

Thus, the Bohr shift operates in one direction in the maternal blood and in the other direction in the fetal blood.

These two effects make the Bohr shift twice as important here as it is for oxygen exchange in the lungs; therefore, it is called the *double Bohr effect*.

The Bohr Effect



DIFFUSION OF FOODSTUFFS THROUGH THE PLACENTAL MEMBRANE

- Fetus uses mainly glucose for nutrition so the trophoblast cells in placental villi transport glucose by carrier molecules; GLUT (facilitated diffusion)
- Fatty acids diffuse due to high solubility in cell membrane (more slowly than glucose)
- The placenta actively transports all amino acids, with fetal concentrations exceeding maternal levels.
- K+, Na+ and Cl- diffuse from maternal to fetal blood

EXCRETION OF WASTE PRODUCTS THROUGH THE PLACENTAL MEMBRANE

- Excretion from the fetus depends mainly, if not entirely, on the diffusion gradients across the placental membrane and its permeability
- 🗸 Urea
- ✓ Uric acid
- ✓ Creatinine
- Because there are higher concentrations of the excretory products in the fetal blood than in the maternal blood, there is continual diffusion of these substances from the fetal blood to the maternal blood.

HORMONES OF PREGNANCY

HUMAN CHORIONIC GONADOTROPIN - HCG

- Secreted by the syncytial trophoblast cells into the fluids of the mother, <u>8 to 9 days after ovulation</u> (shortly after implantation)
- Rate of secretion <u>rises</u> rapidly to reach a <u>maximum</u> at about **10** to **12** weeks of pregnancy
- Secretion then <u>decreases</u> back to a lower value by **16** to **20** weeks & <u>continues</u> at this elevated level for the remainder of pregnancy.



FUNCTIONS OF HUMAN CHORIONIC GONADOTROPIN

Causes persistence of the corpus luteum and prevents menstruation

- Continued secretion of estrogens and progesterone by Corpus Luteum maintains the decidual nature of the uterine endometrium, which is necessary for the early development of the fetus.
- The corpus luteum involutes slowly after the 13th to 17th week of gestation.

Exerts an interstitial cell-stimulating effect on the testes of the male fetus, resulting in the production of testosterone in male fetuses until the time of birth.

- Fetal testosterone causes the fetus to grow male sex organs instead of female organs.
- Fetal testosterone causes the testes to descend into the scrotum.
SECRETION OF ESTROGENS BY THE PLACENTA

 Estrogens are formed <u>from androgenic compounds</u> which are formed in the <u>adrenal glands</u> of the mother & the fetus & converted by the trophoblast cells into Estradiol, Estrone, & Estriol

□ Functions of Estrogen in Pregnancy

- enlargement of the mother's uterus
- enlargement of the mother's breasts and growth of the breast ductal structure
- enlargement of the mother's external genitalia.
- relaxation of the pelvic ligaments of the mother (sacroiliac joints & symphysis pubis) which allow easier passage of the fetus through the birth canal



SECRETION OF PROGESTERONE BY THE PLACENTA

- Progesterone is secreted in moderate quantities by the corpus luteum at the beginning of pregnancy, & later on in tremendous quantities by the placenta
- Functions of Progesterone in Pregnancy
 - causes the decidual cells to develop in the uterine <u>endometrium</u> which play an important role in the nutrition of the early embryo
 - decreases the <u>contractility</u> of the pregnant uterus, thus preventing abortion
 - Contributes to the development of the ovum prior to implantation
 - helps to prepare the mother's <u>breasts</u> for lactation along with estrogen



HUMAN CHORIONIC SOMATOMAMMOTROPIN

- Secreted by the placenta at about the **5**th week of pregnancy.
- Secretion increases progressively throughout pregnancy in direct proportion to the weight of the placenta.
- Exact role is uncertain but appears to be a general metabolic hormone that helps in nutrition of fetus

• Possible important effects:

causes decreased insulin sensitivity and decreased utilization of glucose in the mother, (making larger quantities of glucose available to the fetus).

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- promotes the release and utilization of free fatty acids for energy in the mother
- Increases protein formation like Growth hormone

SECRETION OF "RELAXIN" BY THE OVARIES AND PLACENTA

- secretion is increased by a stimulating effect of human chorionic gonadotropin at the same time that the corpus luteum and the placenta secrete large quantities of estrogens and progesterone.
- Relaxin is a 48-amino acid polypeptide having a molecular weight of about 9000.
- This hormone, when injected, causes relaxation of the ligaments of the symphysis pubis in the estrous rat and guinea pig.
- This effect is weak or possibly even absent in pregnant women.
- Instead, this role is probably played mainly by the estrogens, which also cause relaxation of the pelvic ligaments. It has also been claimed that relaxin softens the cervix of the pregnant woman at the time of delivery.

Pituitary Secretion

Anterior Pitutary enlarges 50% during pregnancy increases its production of :

- <u>Corticotropin</u>
- <u>Thyrotropin</u>
- Prolactin

secretion of FSH and LH is suppressed
 (feedback inhibition of placental estrogen and progesterone).

Increased Corticosteroid Secretion

- Increased secretion <u>Glucocorticoids</u>
- help mobilize amino acids from the mother's tissues to be used for synthesis of tissues in the fetus
- Increased secretion of <u>Aldosterone</u>
- reabsorbs excess sodium from her renal tubules leading to fluid retention that might cause <u>pregnancy-induced hypertension</u>

- Increased Thyroid Gland Secretion
 - Thyroid gland enlarges to 50%
 - increases its production of Thyroxine
 Due to thyrotropic effect of
 - placental hCG
 - > & secretion of placental human chorionic thyrotropin



- Increased Parathyroid Gland Secretion
 - Enlarges & causes <u>calcium absorption from the mother's</u> <u>bones</u>
 - maintains normal calcium ion concentration in the mother's extracellular fluid even while the fetus removes calcium to ossify its own bones
 - (more intensified during lactation)

- Secretion of "Relaxin" by the Ovaries and Placenta
 - secreted by the corpus luteum of the ovary and by placenta.
 - causes relaxation of the ligaments of the symphysis pubis
 - softens the cervix of the pregnant woman at the time of delivery.





PHYSIOLOGICAL CHANGES OF PREGNANCY

"How can you ever say anything negative about your body after you have felt the dancing of life from inside your womb?"

AMETHYST JOY

PHYSIOLOGICAL CHANGES OF PREGNANCY



METABOLIC
CARDIOVASCULAR
HEMATOLOGICAL
RESPIRATORY
RENAL
NERVOUS
GASTROINTESTINAL
ENDOCRINE

MOTHER'S RESPONSE TO PREGNANCY

Hormones can cause changes in physical appearance and sexual organs of pregnant woman
uterus increases from 50 to 1100gms
breasts double in size
Vagina enlarges
Introitus opens widely



UTERUS IN PREGNANCY

With pregnancy progression, the uterus leaves the pelvic and ascends to the abdominal cavity

The abdominal content displaced in response to the increased size of the uterus which is five times more than normal

This increases in the size of uterus associated with an increase of blood supply to the uterus and uterine muscle activity

Uterus increases in size till the 38 weeks after that the funds level starts to descend preparing for delivery.



MOTHER'S RESPONSE TO PREGNANCY

Hormones can cause changes in appearance of pregnant woman
Development of edema
Acne, Melasma
Masculine features
Acromegalic feature





PHYSIOLOGICAL CHANGES OF PREGNANCY

Weight gain in Pregnancy

Average wt gain during normal pregnancy about 25-35 lb (10.9 kg) Foetus=8 lb (3.2 kg) Amniotic fluid, placenta, membranes = 4 lb (1.8kg) Uterus=2 lb (0.9 kg) Breasts = 2lb (0.9 kg) ECF n blood = 5 lb (2.7 kg) Fats = 3 lb (1.4 kg)





PHYSIOLOGICAL CHANGES OF PREGNANCY

Metabolism During Pregnancy

 The basal metabolic rate of the pregnant woman increases about 15 percent during the latter half of pregnancy (sensations of overheated)

Effects of:

- > Thyroid hormones
- Adrenocortical hormones

Sex hormones

▶ hCS (causes ↓glucose utilization by mother ↓glucose utilization by mother
 ↑ fat metabolism ↑ fat metabolism ↑ protein metabolism ↑ protein
 metabolism)

NUTRITION DURING PREGNANCY

- By far the greatest growth of the fetus occurs during the last trimester of pregnancy;
- its weight almost doubles during the last 2 months of pregnancy.
- Ordinarily, the mother does not absorb sufficient protein, calcium, phosphates, and iron from her diet during the last months of pregnancy to supply these extra needs of the fetus.
- However, anticipating these extra needs, the mother's body has already been storing these substances—some in the placenta, but most in the normal storage depots of the mother.



MATERNAL DEFICIENCIES

- If appropriate nutritional elements are not present in a pregnant woman's diet, a number of maternal deficiencies can occur, especially in calcium, phosphates, iron, and the vitamins.
- For example, the fetus needs about 375 milligrams of iron to form its blood, and the mother needs an additional 600 milligrams to form her own extra blood.
- The normal store of nonhemoglobin iron in the mother at the outset of pregnancy is often only 100 milligrams and almost never more than 700 milligrams.
- Therefore, without sufficient iron in her food, a pregnant woman usually develops hypochromic anemia.
- Also, it is especially important that she receive vitamin D, because although the total quantity of calcium used by the fetus is small, calcium is normally poorly absorbed by the mother's gastrointestinal tract without vitamin D.
- Finally, shortly before birth of the baby, vitamin K is often added to the mother's diet so that the baby will have sufficient prothrombin to prevent hemorrhage, particularly brain hemorrhage, caused by the birth process.

CHANGES IN THE MATERNAL CIRCULATORY SYSTEM DURING PREGNANCY

- Blood flow through the placenta, and maternal cardiac output increases during pregnancy
- Maternal blood volume increases during pregnancy
 - Due to aldosterone and estrogens, and to increased fluid retention by the kidneys.
 - Also, the bone marrow becomes increasingly active and produces extra red blood cells



MATERNAL BLOOD VOLUME INCREASES DURING PREGNANCY

- The maternal blood volume shortly before term is about 30 percent above normal.
- This increase occurs mainly during the latter half of pregnancy
- Therefore, at the time of birth of the baby, the mother has about 1 to 2 liters of extra blood in her circulatory system.
- Only about one fourth of this amount is normally lost through bleeding during delivery of the baby, thereby allowing a considerable safety factor for the mother.



Effect of pregnancy to increase the mother's blood volume

CADDIOVACCI II AD CHANCEC



Hemodynamic changes in normal pregnancy Normal pregnancy is characterized by an increase in cardiac output, a reduction in systemic vascular resistance, and a modest decline in mean blood pressure. These changes are associated with a 10 to 15 beat/min increase in heart rate.



Parameter	Percentage of change	
Cardiac output	40-50%	Increase
Stroke volume	30%	Increase
Heart rate	15-25%	Increase
Intravascular volume	45%	Increase
Systemic vascular resistance	20%	Decrease
Systolic BP		Minimal
Diastolic BP	20%	Decrease at mid-pregnancy Pre-pregnant values at term
CVP		Unchanged
O ₂ consumption	30-40%	Increase

HEMATOLOGICAL CHANGES

Blood volume +30%
Plasma volume +40%
Red blood cell volume +20%
Dilutional anemia
Decrease blood viscosity
Vasodilatation
Serum iron concentration falls
absorption from gut and iron-binding capacity rise

MATERNAL RESPIRATION DURING PREGNANCY

□ Increase in O2 consumption (20%)

- ↑ in BMR
- ↑ in weight

\Box \uparrow in CO 2 production

□ Minute ventilation increases (50%)

- Due to effect of progesterone on Respiratory centre
- growing uterus presses upward against the abdominal contents, which press upward against the diaphragm (total excursion of the diaphragm is decreased & respiratory rate is increased to ⁵⁵ maintain the extra ventilation)

GASTROINTESTINAL CHANGES

Increased salivation (ptyalism)

Taste is often altered very early in pregnancy

□ Increase appetite & thirst

Heart burn (reflux oesophagitis) due to relaxation of the cardiac sphincter due to progesterone and relaxin

Emesis gravidarum, morning sickness in 50 %

Decreased gastric acidity, which interfere with iron absorption

- Constipation reduced gut motility due to progesterone increased water and salt absorption
- Hemorrhoids due to elevated venous pressure due compression by gravid uterus.



OTHER MATERNAL CHANGES DURING PREGNANCY Maternal kidney function during pregnancy

- rate of urine formation by a pregnant woman is usually slightly increased because of
- increased fluid intake
- increased load of excretory products.

- renal tubules' reabsorptive capacity for sodium, chloride, and water is increased
- renal blood flow and glomerular filtration rate increase due to renal vasodilation. (NO or relaxin effect ???)
- Normal pregnant woman accumulates only about 5 pounds (2. 27 Kg) of extra water and salt.









Changes in Endocrine Gland

Gland	Morphological	Physiological
Pituitary	Increase in weight by 30- 50%. Twice in size	★GH, Prolactin, ACTH, CRH Normal – TSH ↓Gonadotrophin
Thyroid	Hyperplasia	♠BMR, TBG, Total T ₃ , T ₄ Normal – fT ₃ , fT ₄ , TSH♦Maternal Serum Iodine
Adrenal Cortex	Minimal enlargement	▲Aldosterone, DOC(deoxycorticosterone), CBG, Corisol, Free Cortisol
Parathyroid	Hyperplasia	Normal PTH – does not cross placenta
Pancreas		Hyperinsulinism in 3 rd Trimester. Anti insulin factors and insulin resistance modify action of insulin during pregnancy



DEVELOPMENT OF THE BREASTS

- Begin to develop (the glandular tissue) at puberty, but it is only during pregnancy that the development of the glandular tissue is complete and has the ability to produce milk.
- Development is stimulated by the <u>estrogens</u> of the monthly female sexual cycle

 Estrogens stimulate growth of the breasts' mammary glands plus the deposition of fat to give the breasts mass. Before pregnancy Milk glands and ducts are present, but undeveloped Toward the end of pregnancy: Milk glands and ducts are larger and more in number; breast is noticeably larger


DEVELOPMENT OF THE BREASTS

- Estrogens stimulate the growth of the ductal system
- Estrogen
- Growth hormone
- Prolactin
- □ Adrenal glucocorticoids
- Insulin
- Progesterone is required for full development of the lobule- alveolar system





FOR FEEDBACK

contact me at: dr_sarah@yahoo.com



RECOMMENDED BOOKS

- Text book of Medical Physiology-Guyton and Hall
- Principles of human Physiology-Lauralee Sherwood





That's all Folks!

AMNIOTIC FLUID AND ITS FORMATION

Normally, the volume of *amniotic fluid* (the fluid inside the uterus in which the fetus floats) is between 500 milliliters and 1 liter, but it can be only a few milliliters or as much as several liters. Isotope studies of the rate of formation of amniotic fluid show that, on average, the water in amniotic fluid is replaced once every 3 hours and the electrolytes sodium and potassium are replaced an average of once every 15 hours. A large portion of the fluid is derived from renal excretion by the fetus. Likewise, a certain amount of absorption occurs by way of the gastrointestinal tract and lungs of the fetus. However, even after in utero death of a fetus, some turnover of the amniotic fluid is still present, which indicates that some of the fluid is formed and absorbed directly through the amniotic membranes.

About 5 percent of all pregnant women experience a rapid rise in arterial blood pressure to hypertensive levels during the last few months of pregnancy. This is also associated with leakage of large amounts of protein into the urine. This condition is called preeclampsia or toxemia of pregnancy. It is often characterized by excess salt and water retention by the mother's kidneys and by weight gain and development of edema and hypertension in the mother. In addition, there is impaired function of the vascular endothelium and arterial spasm occurs in many parts of the mother's body, most significantly in the kidneys, brain, and liver. Both the renal blood flow and the glomerular filtration rate are decreased, which is exactly opposite to the changes that occur in the normal pregnant woman. The renal effects also include thickened glomerular tufts that contain a protein deposit in the basement membranes.

Various attempts have been made to prove that preeclampsia is caused by excessive secretion of placental or adrenal hormones, but proof of a hormonal basis is still lacking. Another theory is that preeclampsia results from some type of autoimmunity or allergy in the mother caused by the presence of the fetus. In support of this, the acute symptoms usually disappear within a few days after birth of the baby.

There is also evidence that preeclampsia is initiated by insufficient blood supply to the placenta, resulting in the placenta's release of substances that cause widespread dysfunction of the maternal vascular endothelium. During normal placental development, the trophoblasts invade the arterioles of the uterine endometrium and completely remodel the maternal arterioles into large blood vessels with low resistance to blood flow. In patients with preeclampsia, the maternal arterioles fail to undergo these adaptive changes, for reasons that are still unclear, and there is insufficient blood supply to the placenta. This, in turn, causes the placenta to release various substances that enter the mother's circulation and cause impaired vascular endothelial function, decreased blood flow to the kidneys, excess salt and water retention, and increased blood pressure.

Although the factors that link reduced placental blood supply with maternal endothelial dysfunction are still uncertain, some experimental studies suggest a role for increased levels of inflammatory cytokinessuch as tumor necrosis factor-α and interleukin-6. Placental factors that impede angiogenesis (blood vessel growth) have also been shown to contribute to increased inflammatory cytokines and preeclampsia. For example, the antiangiogenic proteins soluble fms-related tyrosine kinase 1 (s-Flt1) and soluble endoglin are increased in the blood of women with preeclampsia. These substances are released by the placenta into the maternal circulation in response to ischemia and hypoxia of the placenta. Soluble endoglin and s-Flt1 have multiple effects that may impair function of the maternal vascular endothelium and result in hypertension, proteinuria, and the other systemic manifestations of preeclampsia. However, the precise role of the various factors released from the ischemic placenta in causing the multiple cardiovascular and renal abnormalities in women with preeclampsia is still uncertain.

Eclampsia is an extreme degree of preeclampsia, characterized by vascular spasm throughout the body; clonic seizures in the mother, sometimes followed by coma; greatly decreased kidney output; malfunction of the liver; often extreme hypertension; and a generalized toxic condition of the body. It usually occurs shortly before birth of the baby. Without treatment, a high percentage of eclamptic mothers die. However, with optimal and immediate use of rapidly acting vasodilating drugs to reduce the arterial pressure to normal, followed by immediate termination of pregnancy—by cesarean section if necessary—the mortality even in eclamptic mothers has been reduced to 1 percent or less.

- Human chorionic gonadotropin is a glycoprotein having a molecular weight of about 39,000 and much the same molecular structure and function as luteinizing hormone secreted by the pituitary gland. By far, its most important function is to prevent involution of the corpus luteum at the end of the monthly female sexual cycle. Instead, it causes the corpus luteum to secrete even larger quantities of its sex hormones—progesterone and estrogens—for the next few months. These sex hormones prevent menstruation and cause the endometrium to continue to grow and store large amounts of nutrients rather than being shed in the menstruum. As a result, the *decidua-like cells* that develop in the endometrium during the normal female sexual cycle become actual *decidual cells*—greatly swollen and nutritious—at about the time that the blastocyst implants.
- Under the influence of human chorionic gonadotropin, the corpus luteum in the mother's ovary grows to about twice its initial size by a month or so after pregnancy begins. Its continued secretion of estrogens and progesterone maintains the decidual nature of the uterine endometrium, which is necessary for the early development of the fetus.
- If the corpus luteum is removed before approximately the seventh week of pregnancy, spontaneous abortion almost always occurs, sometimes even up to the 12th week. After that time, the placenta secretes sufficient quantities of progesterone and estrogens to maintain pregnancy for the remainder of the gestation period. The corpus luteum involutes slowly after the 13th to 17th week of gestation.