Physiology of Pregnancy

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Blastocyst Implantation

- Sperm Surround Ovum
- Fallopian Tube
- Penetration and Fertilization
- Cell Division Begins
- Morula
- Blastocyst
- Embryo
- Uterus
- Ovary
- Embryo at 6 Weeks
  - Embryo
  - Umbilical Cord
  - Amnion
  - Placenta
  - Mother's Blood Vessels
  - Embryo's Blood Vessels
Endometrium and Desidua

3 days to move to uterus  3 -5 days in uterus before implantation
IMPLANTATION

- Implantation has 3 processes:
  1. Adhesion
  2. Penetration
  3. Invasion

- Adequate maternal progesterone level and early paracrine signal from the zygote are necessary for implantation.

- Adhesion is aided by a variety of endometrially produced molecules such as Laminin and fibronectin.
Implantation results from the action of *trophoblast cells* that develop over the surface of the blastocyst.

These cells secrete proteolytic enzymes that digest and liquefy the adjacent cells of the uterine endometrium.

Once implantation has taken place, the trophoblast cells and other adjacent cells (from the blastocyst and the uterine endometrium) proliferate rapidly, forming the placenta and the various membranes of pregnancy.
Implantation

Blastocyst

(a)

(b)

Trophoblast

Inner cell mass

Uterine wall

Invading trophoblast
Implantation

- Following implantation the endometrium is known as the decidua and consists of three regions: the **decidua basalis**, **decidua capsularis**, and **decidua parietalis**.

- The *decidua basalis* lies between the chorion and the stratum basalis of the uterus. It becomes the **maternal** part of the placenta.

- The decidua *capsularis* covers the embryo and is located between the embryo and the uterine cavity.

- The *decidua parietalis* lines the noninvolved areas of the entire pregnant uterus.
When the conceptus implants in the endometrium, the continued secretion of progesterone causes the endometrial cells to swell further and to store even more nutrients.

These cells are now called **decidual cells**, and the total mass of cells is called the **decidua**. As the trophoblast cells invade the decidua, digesting and imbibing it, the stored nutrients in the decidua are used by the embryo for growth and development.

*Figure 82–4* shows this trophoblastic period of nutrition, which gradually gives way to placental nutrition.

*Medical Physiology, Guyton 6 ed, 2006, p.1029*
Decidua

Decidua basalis

Decidua capsularis

Decidua parietalis

Frontal section of uterus

Details of decidua
Implantation

Placental implantation in humans begins with invasion of the uterine epithelium and underlying stroma by extraembryonic trophoblast cells.

Villous cytotrophoblast cells at the tips of some anchoring villi proliferate outwards from the underlying basement membrane to form columns, from which individual cells migrate into the decidual tissue.

These interstitial trophoblast cells invade as far as the superficial layer of the myometrium.
Implantation

Trophoblast cells invade into the uterine wall.

The trophoblast differentiates along two main pathways: Villous and extravillous.

Villous trophoblast includes the villous tree, which is bathed in maternal blood in intervillous space.

Extravillous trophoblast (EVT) encompasses all the invading subpopulation of trophoblast.

EVT cells arise during early development as cyttrophoblast.
Cells from the cytotrophoblast also give arise to endovascular trophoblast.

At the same time, groups of trophoblast cells detach from the columns to invade the lumen of the spiral arteries as endovascular trophoblast.

The dramatic structural alteration of muscular spiral arteries into dilated sac-like vessel, unresponsive to vasoconstrictive agents and capable of high conductance, are essential to accommodate the huge increase in the blood flow required to the intervillous space.
Implantation

This vascular transformation is important to ensure an adequate blood supply to the feto–placental unit. Failure of this process lead to clinical pathological conditions such as miscarriage, intrauterine growth retardation or preeclamptic toxaemia.

Chorionic Villi:
Finger-like growths of the trophoblasts into the endometrium to form the placenta
Implantation

- Viability of the corpus luteum is maintained by human chorionic gonadotropin (hCG) secreted by the trophoblasts.
- hCG prompts the corpus luteum to continue to secrete progesterone and estrogen.
- Chorion – developed from trophoblasts after implantation, continues this hormonal stimulus.
- Between the second and third month, the placenta:
  - Assumes the role of progesterone and estrogen production.
  - Is providing nutrients and removing wastes.
Fetal Membranes

- Called the Bag of Waters
- Consists of two layers
  1) Amnion - inner membrane, next to fetus
  2) Chorion - outer membrane, next to mother
- Function: to house the fetus for the duration of pregnancy, protects from outside world, prevents vertical transmission of infection.
• **Chorion**: Outermost embryonic membrane which forms the placenta & produces human chorionic gonadotropin.
• **Amnion:**
  – Membrane which surrounds embryo to form the amniotic cavity & produces amniotic fluid.
• **Amnioncic Fluid:**
  – Protects fetus from trauma & permits free movement without adhesion.
• **Yolk Sack:**
  - Provides initial nutrients, supplies earliest RBCs and seeds the gonads with primordial germ cells.
Properties of Amniotic Fluid

- Amniotic fluid is the fluid medium that the fetus is surrounded within the amniotic cavity.

- The volume ranges from 400-1,200 ml, depending on the week of pregnancy.

- Mainly composed of water.

- Also composed of ions including sodium, chlorine, and calcium.

- Amniotic fluid contains urea, which comes from the fetus.
## Variations Of Substances In Amniotic Fluid

<table>
<thead>
<tr>
<th>Hemoglobin (%)</th>
<th>Iron (mg/100ml)</th>
<th>Cholesterol (mg/100ml)</th>
<th>Lipids (mg/100ml)</th>
</tr>
</thead>
<tbody>
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</table>

### Graph

- **Hemoglobin (%):** Increases gradually over the months of pregnancy.
- **Iron (mg/100ml):** Remains relatively constant with a slight increase.
- **Cholesterol (mg/100ml):** Increases gradually over the months of pregnancy.
- **Lipids (mg/100ml):** Increases gradually over the months of pregnancy.
1. Amniotic fluid rapidly from an average vol. of 50ml by 12 weeks of pregnancy to 400ml at mid-pregnancy.

2. The 24th week of pregnancy, the vol. of amniotic fluid continues to ↑

3. Maximum of about 1 liter of fluid at 36 to 38 weeks.
Umbilical Cord

- **The lifeline between mother and fetus**
- **Origin**: It develops from the connecting stalk
- 50 cm, diameter 2 cm
- Contains **3 vessels**: 2 arteries and 1 vein,
- If abnormal of vessels present - often associated with fetal anomalies (heart and kidneys).
- The arteries carry “dirty blood” away from fetus. The vein carries “clean” blood to fetus.
- Central insertion into the placenta is normal
- **Contents**
  - 2 arteries that carry blood to the placenta
  - 1 umbilical vein that carries oxygenated blood to the fetus
  - primitive connective tissue
- **Stub** drops off in 2 weeks leaving scar (umbilicus)
The placenta consists of thousands of tiny branched fingers of tissue called **CHORIONIC VILLI** these project into the endometrium. The maternal blood vessels surrounding the chorionic villi break down forming maternal blood sinuses.
The placenta develops from the **chorion frondosum** (foetal origin) and **decidua basalis** (maternal origin).
# The Placenta

## Table showing exchange of materials across the placenta

<table>
<thead>
<tr>
<th>Mother to Foetus</th>
<th>Foetus to Mother</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxygen</td>
<td>Carbon dioxide</td>
</tr>
<tr>
<td>Glucose</td>
<td>Urea</td>
</tr>
<tr>
<td>Amino acids</td>
<td>Other waste products</td>
</tr>
<tr>
<td>Lipids, fatty acids &amp; glycerol</td>
<td></td>
</tr>
<tr>
<td>Vitamins</td>
<td></td>
</tr>
<tr>
<td>Ions : Na, Cl, Ca, Fe</td>
<td></td>
</tr>
<tr>
<td>Alcohol, nicotine + other drugs</td>
<td></td>
</tr>
<tr>
<td>Viruses</td>
<td></td>
</tr>
<tr>
<td>Antibodies</td>
<td></td>
</tr>
</tbody>
</table>
a. Foetal surface

- Smooth, glistening and is covered by the amnion which is reflected on the cord.
- The umbilical cord is inserted near or at the center of this surface and its radiating branches can be seen beneath the amnion.
b. Maternal surface

- Dull greyish red in colour and is divided into 15-20 cotyledons.
- Each cotyledon is formed of the branches of one main villus stem covered by decidua basalis.
Fetal Side of placenta

Maternal side of placenta

Fetal Side of placenta
Functions Of The Placenta

1. Respiratory function
2. Nutritive function
3. Excretory function
4. Production of enzymes
5. Production of pregnancy associated plasma proteins (PAPP)
6. Barrier function
7. Endocrine function
Intervillous space and Chorionic Villi
Umbilical Cord (Tali Pusat)

- The lifeline between mother and fetus
- 20”-22” long, 1” thick.
- Contains 3 vessels: 2 arteries and 1 vein, which are protected by “Wharton’s Jelly”.
- If abnormal of vessels present- often associated with fetal anomalies (heart and kidneys).
- The arteries carry “dirty blood” away from fetus. The vein carries “clean” blood to fetus.
- Central insertion into the placenta is normal
Hormonal Secretion by the Placenta

**Human chorionic gonadotropin (hCG)**
- Rescues corpus luteum from degeneration until the 3rd or 4th month of pregnancy

**Relaxin**
- Increases flexibility of pubic symphysis

**Human chorionic somatomammotropin (hCS)**
- Helps prepare mammary glands for lactation
- Enhances growth by increasing protein synthesis
- Decreases glucose use and increases fatty acid use for ATP production

**Corticotropin-releasing hormone**
- Establishes the timing of birth
- Increases secretion of cortisol

**Progesterone Estrogens**
- Maintain endometrium of uterus during pregnancy
- Help prepare mammary glands for lactation
- Prepare mother’s body for birth of baby

(a) Sources and functions of hormones
Hormones of Pregnancy

• Chorion
  – from day 8 until 4 months secretes hCG
  – keeps **corpus luteum** active
  – corpus luteum produces progesterone & estrogen to maintain lining of uterus

• **Human chorionic gonadotropin (hCG)**
  – mimics LH; its primary role is to stimulate continued production by the corpus luteum of estrogens and progesterone - an activity necessary for the continued attachment of the embryo and fetus to the lining of the uterus (Figure 29.16).
• Placenta
  – by 4th month produces enough progesterone & estrogen that corpus luteum is no longer important
  – relaxin
  – human chorionic somatomammotropoin (hCS) or human placental lactogen (hPL)
  – corticotropin-releasing hormone (CRH)

Relaxin
  – produced by the ovaries, testes, and placenta
  – inhibits secretion of FSH and might regulate secretion of hGH.
Human chorionic somatomammotropin (hCS) (also known as human placental lactogen, or hPL)
- maximum amount by 32 weeks
- produced by the chorion
- role in breast development for lactation, protein anabolism, and catabolism of glucose and fatty acids.

Corticotropin-releasing hormone (CRH)
- increases secretion of fetal cortisol (lung maturation)
- thought to be the “clock” that establishes the timing of birth.
HCG

It is a glycoprotein produced by the syncytiotrophoblast.
- It supports the corpus luteum in the first 10 weeks of pregnancy to produce oestrogen and progesterone until the syncytiotrophoblast can produce progesterone.

HCG molecule is composed of 2 subunits:

a. **Alpha** subunit:
   which is similar to that of FSH, LH and TSH.

b. **Beta** subunit:
   which is specific to hCG.
HCG rises sharply after implantation, reaches a peak of 100,000 mIU/ml about the 60th day of pregnancy. Then it falls sharply by the day 100 to 30,000 mIU/ml and is maintained at this level until term.

Estimation of beta-hCG is used for:

a) Diagnosis of **early** pregnancy.
b) Diagnosis of **ectopic** pregnancy.
c) Diagnosis and **follow-up** of trophoblastic disease.
Hormone Blood Levels

- Human chorionic gonadotropin (hCG) produced by the chorion is less important after 4 months, because the **placenta** takes over the hormonal secretion of the corpus luteum.
Endocrinology of pregnancy

- **Progesterone**
  - Maternal blood supplies cholesterol
  - Placenta converts cholesterol to progesterone
    - Takes over following luteolysis
    - Produces enough to support pregnancy by 5-6 wks in humans
  - Necessary for endometrial support and secretion
    - \( \therefore \) necessary for support of pregnancy
      - “pro” = support ... “gest” = gestation = pregnancy
  - Exerts negative feedback on LH and FSH
    - Ovarian follicles do not grow
    - No stimulation for ovarian steroid production
  - Increases fat deposition
    - Stimulating appetite
    - Diverting energy stores from sugar to fat
Endocrinology of pregnancy

- Feto-Placental Unit - Estrogens
  - Progesterone from placenta to fetal adrenal gland
    - Through umbilical and fetal vasculature
  - Outer layers (cortex)
    - Fetal adrenal zone converts P to DHEA \((\text{dehydroepiandrosterone})\)
  - DHEA circulates to fetal liver \(\rightarrow\) converted to \(16\alpha\text{-OH-DHEA}\) sulfate
  - Converted to estriol in the placenta
    - \(E_3\) is the primary estrogen during pregnancy
  - Fetus and placenta cooperate to produce maternal estrogens
EFFECTS OF PREGNANCY ON THE MOTHER

• Anatomical Changes:
  – The female reproductive organs and breasts become increasingly vascular and engorged with blood
  – The uterus enlarges dramatically, causing a shift in the woman’s center of gravity and an accentuated lumbar curvature (lordosis)
  – Placental production of the hormone relaxin causes pelvic ligaments and the pubic symphysis to soften and relax
    • This increases motility for easier birth passage
  – There is a normal weight gain of around 28 pounds, due to growth of the fetus, maternal reproductive organs, and breasts, and increased blood volume
RELATIVE SIZE OF THE UTERUS BEFORE CONCEPTION AND DURING PREGNANCY

- (a) Before conception
- (b) 4 months
- (c) 7 months
- (d) 9 months
EFFECTS OF PREGNANCY ON THE MOTHER

• Good nutrition is necessary all through pregnancy if the developing fetus is to have all the building materials (especially proteins, calcium, and iron) needed to form its tissues.

• Multivitamins containing *folic acid* seem to reduce the risk of having babies with neurological problems, including such birth defects as spina bifida and anencephaly (absence of brain and cranial vault with cerebral hemisphere missing or reduced in size).
Physiologic changes of pregnancy
Physiological Changes

- Cardiovascular
- Respiratory
- Urinary
- Metabolic
- Thermoregulation
- Digestive
- Skin
- Breasts
- Biomechanical
Cardiovascular Changes

**INCREASE**
- Blood volume
- Cardiac (heart) output
- Stroke volume
- End diastolic volume
- Resting pulse
- % of blood plasma

**DECREASE**
- Hematocrit
- Blood pressure
- Blood supply to uterus
- Cardiac reserve
- Vascular resistance

**HYPERTENSION ???**
About 625 milliliters of blood flows through the maternal circulation of the placenta each minute during the last month of pregnancy. This, plus the general increase in the mother’s metabolism, increases the mother’s cardiac output to 30 to 40 per cent above normal by the 27th week of pregnancy; then, for reasons unexplained, the cardiac output falls to only a little above normal during the last 8 weeks of pregnancy, despite the high uterine blood flow.
Blood Volume During Pregnancy

The maternal blood volume shortly before term is about 30 per cent above normal. This increase occurs mainly during the latter half of pregnancy. The cause of the increased volume is likely due, at least in part, to aldosterone and estrogens, which are greatly increased in pregnancy, and to increased fluid retention by the kidneys. Also, the bone marrow becomes increasingly active and produces extra red blood cells to go with the excess fluid volume. Therefore, at the time of birth of the baby, the mother has about 1 to 2 liters of extra blood in her circulatory system.
Orthostatic Hypotensive Syndromes

- Avoid supine position
- Do strength exercises prior to aerobic exercise
- Limit aerobic exercise to 20 - 45 minutes
- Do thorough cool-down
- Rest daily in the side-lying position
Physiologic anemia of pregnancy

• Physiologic intravascular change
• Plasma volume increases 50-70 %
  – Beginning by the 6\textsuperscript{th} wk
• RBC mass increases 20-35 %
  – Beginning by the 12\textsuperscript{th} wk
• Disproportionate increase in plasma volume over RBC volume----Hemodilution
• Despite erythrocyte production there is a physiologic fall in the hemoglobin and hematocrit readings
Respiratory Changes

- Respiratory capacity increases
- Shortness of breath
- Pulmonary reserve decreases
- Increased risk of muscle soreness
- Tendency to hyperventilate

RESULT: adjust the intensity level and duration of exercise
Respiratory

• Consumption
  – O2 consumption Increases 15-20 %
  – 50 % of this increase is required by the uterus
  – Despite increase in oxygen requirements, with the increase in Cardiac Output and increase in alveolar ventilation oxygen consumption exceeds the requirements.
  – Therefore, arteriovenous oxygen difference falls and arterial PCO2 falls.
Respiratory

• Stimulation
  – Progesterone is known to directly stimulate ventilation
  – Progesterone increases the sensitivity of the respiratory centers to CO2
  – Also, it is thought to reduce total pulmonary resistance
Function of the Maternal Urinary System During Pregnancy

The rate of urine formation is usually slightly increased because of increased fluid intake and increased load or excretory products. But in addition, several special alterations of urinary function occur.

- First, the renal tubules’ reabsorptive capacity for sodium, chloride, and water is increased as much as 50 per cent as a consequence of increased production of steroid hormones by the placenta and adrenal cortex.

- Second, the glomerular filtration rate increases as much as 50 per cent during pregnancy, which tends to increase the rate of water and electrolyte excretion in the urine. When all these effects are considered, the *normal* pregnant woman ordinarily accumulates only about 6 pounds of extra water and salt.
Urinary Changes

• Kidneys grow and filter more blood as the blood volume increases

• Become more susceptible to bladder and kidney infections

• Bladder becomes compressed causing frequent urination and incontinence
Urinary System-Proteinuria

- Normally not evident
- Average is 115 mg/day
- 260 mg/day is in 95 percent confidence limit
- Therefore, our 300 mg screen would exceed most normal variations
As a consequence of the increased secretion of many hormones during pregnancy, including thyroxine, adrenocortical hormones, and the sex hormones, the basal metabolic rate of the pregnant woman increases about 15 per cent during the latter half of pregnancy. As a result, she frequently has sensations of becoming overheated. Also, owing to the extra load that she is carrying, greater amounts of energy than normal must be expended for muscle activity.
Metabolic Changes

**INCREASES IN:**

- Insulin level
- Carbohydrate utilization during exercise as weight increases
- Estrogen
- Progesterone
- Relaxin
- Caloric requirements by ~ 300 calories/day
- Protein and fluid requirements
Thermoregulation

Metabolic storage in body core

Conduction
Contracting muscle works

Evaporation
Sweat & respiration

Convection
Skin & blood
Muscle blood flow

Radiation
Skin & air

Excess body heat is transferred to the environment and body core temperature is regulated.

Adapted from McKarde, Katch, and Katch: Exercise Physiology, Fig. 25.2, P. 503.
Adaptations for Protection

- Core temperature falls
- Perspire more rapidly
- Greater skin area and increased blood vessels allow added evaporation
- Increased ventilation promotes cooling
- Enhanced regulation of internal temperature in consistent exerciser
WATER, WATER, WATER

Hydration is a major concern during maternal exercise.

- Provide a ready source of water
- Encourage frequent water breaks
EFFECTS OF PREGNANCY ON THE MOTHER

• **Metabolic Changes:**
  – As the placenta enlarges, it produces human placental lactogen, which works with estrogen and progesterone to promote maturation of the breasts for lactation
  – Human placental lactogen (hPL) also promotes the growth of the fetus, and exerts a glucose-sparing effect on maternal metabolism
    • Consequently, maternal cells metabolize more fatty acids and less glucose than usual, sparing glucose for use by the fetus
  – Human chorionic thyrotropin from the placenta increases maternal metabolic rate
Digestive Changes

- Digestive system slows
- Intestines are pushed up and to the sides
- Smooth muscle of the stomach relaxes and can cause heartburn

✦ Constipation and hemorrhoids are common during pregnancy
✦ Morning sickness
Urinary Changes

• Kidneys grow and filter more blood as the blood volume increases

• Become more susceptible to bladder and kidney infections

• Bladder becomes compressed causing frequent urination and incontinence
Skin Changes

• Stretch marks
• Dark pigmented line on their abdomen which is called Linea Nigra
• Pigment changes on their face and neck
• Small blood vessels in the face, neck and upper chest

• MOST OF THESE RESOLVE AFTER PREGNANCY
Hyperpigmentation

- Melasma and linea nigra
- Estrogen and progesterone
- Some melanocyte stimulating effect
Striae
Linea nigra
Endocrine

- Normal pregnancy physiology shows
  - “lower lows and higher highs”
- Postprandial hyperglycemia
  - To ensure sustained glucose levels for fetus
- Accelerated starvation
  - Early switch from glucose to lipids for fuels
- Insulin resistance promotes hyperglycemia
  - Resistance-Reduced peripheral uptake of glucose for a given dose of insulin
- Mild fasting hypoglycemia occurs with elevated FFA, triglycerides, and cholesterol
Insulin resistance

- Anti-insulin environment is aided by:
  - placental lactogen
    - Like growth hormone
    - Increases lipolysis and FFA
    - Increases tissue resistance to insulin
  - Increased unbound cortisol
  - Estrogen and Progesterone may also exert some anti-insulin effects
Thyroid

• Estrogen stimulates Increase in TBG
  – Total T3 and T4 are increased
  – However the active hormones remains unchanged

• hCG stimulates thyroid
  – TSH is reduced

• Iodine deficient state
  – Due to Increased renal clearance

• To rule out pathologic changes
  – Early in pregnancy TSH can be used
  – Later free T4 is needed
Breast Changes

- Early in pregnancy, tenderness and tightness is common
- After 8 weeks, breasts grow and blood vessels often are visible

- Nipples become larger and darker
- A thick yellowish fluid can be expressed from the nipple
Biomechanical Changes

• Weight distribution shifts
• Joint movement
• Balance of muscle strength
• Spinal curves increase
• Joint laxity becomes greater
• More structural discomfort
• Increased potential for nerve compression
Changes to Body System

- **First Trimester**
  - Baby begins to grow
  - Increased urination
  - Changes with skin and hair
  - Thickening waistline
  - Nausea/fatigue

- **Second Trimester**
  - Baby’s weight increases
  - Energy level improves
  - Heartburn
  - Leg cramps
  - Pelvis relaxes causing SI discomfort

- **Third Trimester**
  - Baby has more rapid growth & weight gain
  - Backaches
  - Swelling of the hands, legs, and feet
  - Breathlessness
  - More frequent urination
Thank you