Chapter 28
Pregnancy
Definitions

• **Pregnancy**
  – from time of fertilization to birth.

• **Conceptus**
  – the developing offspring.

• **Gestation Period**
  – from 1st day of Last Menstrual Period to birth.
  – is about 280 days or about 40 weeks.

• **Embryo**
  – what conceptus is called from week 0 to 8.

• **Fetus**
  – what conceptus is called from week 9 to birth.
Maternal Physiologic Changes

- elevated progesterone and estrogen levels can cause nausea in first trimester. Most adjust.
  - same thing happens to those who take BCPs.
- Stomach and Esophagus are crowed so there is heartburn later in pregnancy.
- Constipation occurs with decreased GI motility.
- More urine due to extra wastes to remove.
  - frequency and urgency are seen in last trimester.
- Blood volume increases by 25 to 40%
“The almost 3 Day Window”

- Oocyte is viable for 12 to 24 hours once it is ovulated.
- Sperm is viable for 24 to 48 hours after ejaculation.
- For successful fertilization these two viability times need to overlap briefly.
  - sex can result in a baby if it occurs no more than 2 days before ovulation and no later than 24 hours after.
  - egg viability is virtually zero 24 hours after ovulation.
“Less than 2000 Survive the Trip out of Millions, but only 1 Fertilizes”

1. millions leak out of the vagina.
2. millions more are destroyed by the vagina’s acidic environment.
3. the trip comes to a complete stop unless the cervical mucus is less viscous.
4. in the uterus, thousands more are destroyed by resident phagocytes.
5. about 200 to 2000 make it into the fallopian tubes to meet the oocyte.
6. 1 sperm gets there first and fertilizes.
Random Odds per average 28-day Cycle of Getting Pregnant

• best case scenario for highest odds:
  – 24 hour viable egg and 48 hour viable sperm.
  – have sex day before and day of ovulation.
    – either of these two days could result in a pregnancy.
    – 2 days capable of getting pregnant ÷ 28 day cycle = 7.1% chance a pregnancy could result from having sex if each day of a 28-day cycle is treated equally likely to result in an episode of intercourse.
  – actual odds are likely to be higher because:
    – less couples have intercourse during menses.
    – some evidence that sex is more frequent during ovulation.
    – increased intercourse frequency with less protection in those still in prime reproductive years.
Capacitation

• Sperm, freshly deposited in the vagina are incapable of penetrating an oocyte.

• over the next 6 to 8 hours, as they swim to the egg, their mobility is enhanced and their membranes become fragile so that the hydrolytic enzymes in their acrosomes can be released.

  – the difficulty of the trip not only ensures the most viable sperm reach the egg but also strips away some of the membrane proteins on the sperm.

  – some sperm can reach the egg in minutes but have to wait for capacitation to occur.
Acrosomal Reaction & Sperm Penetration

• oocyte has 2 barriers the sperm must cross:
  – Corona Radiata
    • the sperm has hyaluronidase that digests this cement between the granulosa cells in the immediate area
    • after breaching the corona radiata, the sperm head binds to the ZP3 glycoprotein of the zona pellucida.
      – sperm receptor on the egg
      – functions to trigger the acrosomal enzymes
  – Zona Pellucida
    • Acrosomal Reaction, on the sperm, breaks down the membrane and releases enzymes.
    • enzymes from any sperm that releases its enzymes helps to digest hundreds of holes in the zona pellucida.
Acrosomal Reaction & Sperm Penetration

• once a path has been cleared and a single sperm fuses with the oocyte’s membrane receptors, its nucleus is pulled into the oocyte cytoplasm.

• the region where the sperm enters determines the future right and left axes of the embryo’s body.

• **Polyspermy**
  – entry of several sperm into an egg.

• **Monospermy**
  – entry of one sperm into the egg.
Blocks to Polyspermy

- once the sperm has entered the oocyte, waves of Ca$^{2+}$ are released by the oocyte’s endoplasmic reticulum.
- this Ca$^{2+}$ wave causes the cortical reaction in which granules located just inside the plasma membrane quickly dump zonal inhibiting proteins (ZIPs).
  - the ZIPs destroy any remaining sperm ZP3 receptors, preventing further sperm entry.
  - this also attracts water, causing the oocyte membrane to “swell and push back other sperm”.
Sperm Penetration of the Egg and the Cortical Reaction (Slow Block to Polyspermy)

1. Aided by surface hyaluronidase enzymes, a sperm cell weaves its way past granulosa cells of the corona radiata.

2. Binding of the sperm to ZP3 molecules in the zona pellucida causes a rise in Ca^{2+} level within the sperm, triggering the acrosomal reaction.

3. Acrosomal enzymes digest holes through the zona pellucida, clearing a path to the oocyte membrane.

4. The sperm forms an acrosomal process, which binds to the oocyte’s sperm-binding receptors.

5. The sperm and oocyte plasma membranes fuse, allowing sperm contents to enter the oocyte.

6. Entry of sperm contents causes a rise in the Ca^{2+} level in the oocyte’s cytoplasm, triggering the cortical reaction (exocytosis of cortical granules). The result is hardening of the zona pellucida and clipping off of sperm receptors (slow block to polyspermy).
Events of Fertilization: Step 1

1 After the sperm penetrates the secondary oocyte, the oocyte completes meiosis II, forming the ovum and second polar body.
Events of Fertilization: Step 2

- Male pronucleus
- Female pronucleus (swollen ovum nucleus)
- Polar bodies

Sperm and ovum nuclei swell, forming pronuclei.
Events of Fertilization: Step 3

Male pronucleus
Mitotic spindle
Centriole
Female pronucleus

③ Pronuclei approach each other and mitotic spindle forms between them.
Events of Fertilization: Step 4

4 Chromosomes of the pronuclei intermix. Fertilization is accomplished. Then, the DNA replicates in preparation for the first cleavage division.
Cleavage from Zygote to Blastocyst

• the zygote (fertilized egg) begins to divide about 24 hours after fertilization.

• rapid mitotic division continues as the egg travels down the fallopian (uterine) tube.

• 3 to 4 days after ovulation, the embryo reaches the uterus and floats freely for 2-3 days—nourished by the secretions of endometrial glands.

• at the late blastocyst stage, the embryo is implanting into the endometrium about 7 days after ovulation.
Cleavage from Zygote to Blastocyst

- **Zygote** (fertilized egg) 2 days
- **4-cell stage** 2 days
- **Morula** (a solid ball of blastomeres) 3 days
- **Early blastocyst** (Morula hollows out, fills with fluid, and "hatches" from the zona pellucida) 4 days
- **Implanting blastocyst** (Consists of a sphere of trophoblast cells and an eccentric cell cluster called the inner cell mass) 7 days

- **Fertilization** (sperm meets and enters egg)
- **Oocyte** (egg)
- **Ovulation**
- **Uterine tube**
- **Uterus**
- **Endometrium**
- **Cavity of uterus**
- **Blastocyst cavity**
- **Troplhoblast**
- **Inner cell mass**
Implantation

• estrogen and progesterone levels are surging at this time, preparing the endometrium to receive and sustain the embryo.
  – if the endometrium is not ready, the blastocyst can detach and migrate to another area.
  – the endometrium quickly thickens at the point of contact
    • blood vessels become leaky and permeable.
    • lymphocytes, NK cells, macrophages enter the area.
  – the trophoblast proliferates into 2 layers
    • syncytiotrophoblast which invades the endometrium
    • cytotrophoblast
Implantation of the Blastocyst

- Endometrium
- Uterine endometrial epithelium
- Inner cell mass
- Trophoblast
- Blastocyst cavity
- Lumen of uterus

- Endometrial stroma with blood vessels and glands
- Syncytiotrophoblast
- Cytotrophoblast
- Inner cell mass (future embryo)
- Lumen of uterus
Surviving the Odds

• 66% of all zygotes formed will fail to implant by the end of the first week or spontaneously abort.

• of the 33% that do implant, 30% of those embryos will later miscarry.

• this means that even if one can successfully get to the stage of fertilization only 24% of all zygotes will make it to term.

• also implantation takes about 5 days, finishing just before a period would occur.
Hormonal Changes

• The trophoblast cells secrete the hormone human chorionic gonadotropin (hCG).
• hCG bypasses the pituitary-ovarian controls at this critical time and prompts the corpus luteum to continue to secrete progesterone and estrogen.
• the chorion which develops from the trophoblasts cells maintains hCG secretion
  – hCG levels rise and become detectable in the mother’s blood at about 1 week after fertilization.
  – at month 3 (end of the 1st Trimester) the placenta takes over progesterone and estrogen secretion.
Hormonal Changes During Pregnancy

![Graph showing changes in blood levels of Hormone, Estrogens, and Progesterone during pregnancy](image)

- **Human chorionic gonadotropin**
- **Estrogens**
- **Progesterone**

**Axes:**
- Y-axis: Relative blood levels
- X-axis: Gestation (weeks)

**Key Events:**
- Ovulation and fertilization
- Birth

**Legend:**
- Orange line: Human chorionic gonadotropin
- Blue line: Estrogens
- Green line: Progesterone
Placenta Formation

• Implanting blastocyst at conceptus age 7 days
  – endometrial erosion by the syncytiotrophoblast is ongoing and cells of the embryonic disc are now separated by a fluid-filled space from the amnion.

• Implantation is completed by conceptus age 12 days.
  – extra-embryonic mesoderm is forming a separate or discrete layer beneath the cytotrophoblast.

• at conceptus age 16 days
  – the cytotrophoblast and and mesoderm have become the chorion.
  – embryo has all 3 germ layers and a yolk sac.
(a) Implanting 7 1/2-day blastocyst. The syncytiotrophoblast is eroding the endometrium. Cells of the embryonic disc are now separated from the amnion by a fluid-filled space.

(b) 12-day blastocyst. Implantation is complete. Extraembryonic mesoderm is forming a discrete layer beneath the cytotrophoblast.

(c) 16-day embryo. Cytotrophoblast and associated mesoderm have become the chorion, and chorionic villi are elaborating. The embryo exhibits all three germ layers, a yolk sac and an allantois, which forms the basis of the umbilical cord.
Placenta Formation

• 4 to 5 week embryo
  – the decidua capsularis and decidua basalis are well formed.
  – the chorionic villi lie in blood-filled intervillus spaces within the endometrium.
  – organs are forming in the embryo
  – umbilical cord formed

  – many women have taken their first pregnancy test as they have missed their period by 2 to 3 weeks at this point.
  – by the end of the first trimester (3 months), the placenta is fully formed.
**Placenta Formation**

4½-week embryo. The decidua capsularis, decidua basalis, amnion, and yolk sac are well formed. The chorionic villi lie in blood-filled intervillous spaces within the endometrium. The embryo is now receiving its nutrition via the umbilical vessels that connect it (through the umbilical cord) to the placenta.
7 Week Embryo (17 mm long)
3 Month Fetus (6 cm Long)
5 Month Fetus (19 cm long)
13 Week Fetus

- Placenta
- Decidua basalis
- Chorionic villi
- Yolk sac
- Amnion
- Amniotic cavity
- Umbilical cord
- Decidua capsularis
- Extraembryonic coelom
- Lumen of uterus
- Uterus
Vasculature of the Mature Decidua Basalis

- Placenta
- Chorionic villi
- Decidua basalis
- Umbilical cord
- Uterus
- Lumen of uterus
- Decidua capsularis
- Maternal arteries
- Maternal veins
- Myometrium
- Stratum basalis of endometrium
- Maternal portion of placenta (decidua basalis)
- Fetal portion of placenta (chorion)
- Fetal arteriole
- Fetal venule
- Amnion
- Umbilical cord
- Umbilical arteries
- Umbilical vein
- Connection to yolk sac
- Chorionic villus containing fetal capillaries
- Maternal blood in lacuna (intervillous space)
Newborn Circulation

- Aortic arch
- Superior vena cava
- Ductus arteriosus
- Ligamentum arteriosum
- Pulmonary artery
- Pulmonary veins
- Heart
- Lung
- Foramen ovale
  - Fossa ovalis
  - Liver
- Ductus venosus
  - Ligamentum venosum
  - Hepatic portal vein
- Umbilical vein
  - Ligamentum teres
  - Inferior vena cava
  - Umbilicus
  - Abdominal aorta
  - Common iliac artery
- Umbilical arteries
  - Medial umbilical ligaments
- Urinary bladder

Legend:
- High oxygenation
- Moderate oxygenation
- Low oxygenation
- Very low oxygenation
Uterus Growth During Pregnancy

(a) Before conception
(Uterus the size of a fist and resides in the pelvis.)

(b) 4 months
(Fundus of the uterus is halfway between the pubic symphysis and the umbilicus.)

(c) 7 months
(Fundus is well above the umbilicus.)

(d) 9 months
(Fundus reaches the xiphoid process.)
Several triggers interlock to bring on labor.

New studies indicate the fetus has rising levels of adrenocortical hormones (mostly cortisol) late in pregnancy.
Early Dilation

Baby head is engaged in the “true pelvis”. Cervix is dilating (opening) & effacing (thinning).
Late Dilation

The baby’s head rotates so that its greatest dimension is in the mom’s anteroposterior axis. “baby comes out looking at the floor”.

Pubic symphysis

Sacrum
Expulsion

Baby’s head extends as it reaches mom’s perineum & is delivered.
Within 30 minutes after the baby is delivered, strong uterine contractions push the placenta out and clamp down on any bleeding vessels.
Milk Production & the Let-Down Reflex

Start

Stimulation of mechanoreceptors in nipples by suckling infant sends afferent impulses to the hypothalamus.

Positive feedback

Inhibits hypothalamic neurons that release dopamine. Hypothalamus releases prolactin releasing factors (PRFs) to portal circulation.

Hypothalamus sends efferent impulses to the posterior pituitary where oxytocin is stored.

Oxytocin is released from the posterior pituitary and stimulates myoepithelial cells of breasts to contract.

Alveolar glands respond by releasing milk through ducts of nipples.

Anterior pituitary secretes prolactin to blood.

Prolactin targets mammary glands.

↑ Milk production
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<thead>
<tr>
<th>TIME</th>
<th>CHANGES AND ACCOMPLISHMENTS</th>
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| 8 weeks (end of embryonic period) | Head nearly as large as body; all major brain regions present; first brain waves in brain stem  
Liver disproportionately large and begins to form blood cells  
Limbs present; digits are initially webbed, but fingers and toes are free by the end of this interval  
Ossification just begun; weak, spontaneous muscle contractions occur  
**Cardiovascular system fully functional (heart has been pumping blood since the fourth week)**  
All body systems present in at least rudimentary form  
Approximate crown-to-rump length: 22 mm (0.9 inches); weight: 2 grams (0.06 ounce) |
| 9–12 weeks (month 3) | Head still dominant, but body elongating; brain continues to enlarge, shows its general structural features; cervical and lumbar enlargements apparent in spinal cord; retina of eye is present  
Skin epidermis and dermis obvious; facial features present in crude form  
Liver prominent and bile being secreted; palate is fusing; most glands of endodermal origin are developed; walls of hollow visceral organs gaining smooth muscle  
Blood cell formation begins in bone marrow  
Notochord degenerating and ossification accelerating; limbs well molded  
**Sex readily detected from the genitals**  
Approximate crown-to-rump length at end of interval: 90 mm |
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<tr>
<th>TIME</th>
<th>CHANGES AND ACCOMPLISHMENTS</th>
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<tbody>
<tr>
<td>13–16 weeks (month 4)</td>
<td>Cerebellum becoming prominent; general sensory organs differentiated; eyes and ears assume characteristic position and shape; <strong>blinking of eyes and sucking motions of lips occur</strong></td>
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<td>16 weeks</td>
<td>Face looks human and growth of the body beginning to outpace that of the head</td>
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<td>Glands developed in GI tract; meconium is collecting</td>
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<td>Kidneys attain typical structure</td>
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<td>Most bones are now distinct and joint cavities are apparent</td>
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<td>Approximate crown-to-rump length at end of interval: 140 mm</td>
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<td>17–20 weeks (month 5)</td>
<td>Vernix caseosa (fatty secretions of sebaceous glands) covers body; lanugo (silkylike hair) covers skin</td>
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<td>Fetal position (body flexed anteriorly) assumed because of space restrictions</td>
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<td>Limbs reach near-final proportions</td>
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<td><strong>Quickening occurs</strong> (mother feels spontaneous muscular activity of fetus)</td>
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<td>Approximate crown-to-rump length at end of interval: 190 mm</td>
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| 21–30 weeks (months 6 and 7) | Period of substantial increase in weight (may survive if born prematurely at 27–28 weeks, but hypothalamic temperature regulation and lung production of surfactant are still inadequate)  
Myelination of cord begins; eyes are open  
Distal limb bones are beginning to ossify  
Skin is wrinkled and red; fingernails and toenails are present; tooth enamel is forming on deciduous teeth  
Body is lean and well proportioned  
Bone marrow becomes sole site of blood cell formation  
**Testes reach scrotum in seventh month (in males)** |
|                      | Approximate crown-to-rump length at end of interval: 280 mm                                                                                                                                                  |
| 30–40 weeks (term) (months 8 and 9) | Skin whitish pink; fat laid down in subcutaneous tissue (hypodermis)  
Approximate crown-to-rump length at end of interval: 360 mm (14 inches); weight: 3.2 kg (7 lb)                                            |
| At birth             |                                                                                                                                                                                                          |
Contraception Options

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<th>Male</th>
<th>Female</th>
<th>Technique</th>
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<tr>
<td>Technique</td>
<td>Event</td>
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<tr>
<td>Vasectomy</td>
<td>Production of viable sperm</td>
<td>Production of primary oocytes</td>
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<tr>
<td>Abstinence</td>
<td>Transport down the male duct system</td>
<td>Ovulation</td>
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<tr>
<td>Condom</td>
<td>Sperm deposited in the vagina</td>
<td>Capture of the oocyte by the uterine tube</td>
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<tr>
<td>Coitus interruptus (high failure rate)</td>
<td>Sperm move through the female’s reproductive tract</td>
<td>Transport down the uterine tube</td>
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<tr>
<td></td>
<td>Meeting of sperm and oocyte in uterine tube</td>
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