Chapter 28

Pregnancy & Human Development
Pregnancy

- Pregnancy: events that occur from fertilization until the infant is born
- Conceptus: the developing offspring
- Gestation period: time from the last menstrual period until birth (~280 days)
- Embryo: conceptus from fertilization through week 8
- Fetus: conceptus from week 9 through birth
Figure 28.1

Fertilization → 1-week conceptus → Embryo → 3-week embryo (3 mm) → 5-week embryo (10 mm) → 8-week embryo (22 mm) → 12-week fetus (90 mm)
From Egg to Zygote

- The oocyte is viable for 12 to 24 hours
- Sperm is viable 24 to 48 hours after ejaculation
From Egg to Zygote

• For fertilization to occur, coitus must occur no more than
  – Two days before ovulation
  – 24 hours after ovulation

• Fertilization: when the sperm’s chromosomes combine with those of a secondary oocyte to form a fertilized egg (zygote)
Accomplishing Fertilization

• Ejaculated sperm
  – Leak out of the vagina immediately after deposition
  – Are destroyed by the acidic vaginal environment
  – Fail to make it through the cervix
  – Are dispersed in the uterine cavity or destroyed by phagocytes
  – Few (100 to a few thousand) reach the uterine tubes
Accomplishing Fertilization

• Sperm must become motile
• Sperm must be activated before they can penetrate the oocyte
  – Secretions of the female tract weaken acrosome membrane
Acrosomal Reaction and Sperm Penetration

• Sperm must breach oocyte coverings
  – Corona radiata and zona pellucida

• Sperm binds to the zona pellucida and undergoes the acrosomal reaction
  – Enzymes are released to digest holes in the zona pellucida
  – Hundreds of acrosomes release their enzymes to digest the zona pellucida
Acrosomal Reaction and Sperm Penetration

- Sperm head approaches the oocyte
- An acrosomal process forms and binds to receptors
- Oocyte and sperm membranes fuse
- Only one sperm is allowed to penetrate the oocyte (monospermy)
Blocks to Polyspermy

• Upon entry of a sperm, $\text{Ca}^{2+}$ surge from the ER causes the cortical reaction
  – Cortical granules release enzymes (zonal inhibiting proteins, or ZIPs)
  – ZIPs destroy sperm receptors
  – Spilled fluid binds water and swells, detaching other sperm (slow block to polyspermy)
Aided by surface hyaluronidase enzymes, a sperm cell weaves its way past granulosa cells of the corona radiata.

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.

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

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

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

Entry of sperm contents (tail and plasma membrane remain behind) 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).
Completion of Meiosis II and Fertilization

• As sperm nucleus moves toward the oocyte nucleus it swells to form the male pronucleus
• The Ca$^{2+}$ surge triggers completion of meiosis II → ovum + second polar body
• Ovum nucleus swells to become a female pronucleus
• Membranes of the two pronuclei rupture and the chromosomes combine
1. After the sperm penetrates the secondary oocyte, the oocyte completes meiosis II, forming the ovum and second polar body.

2. Sperm and ovum nuclei swell, forming pronuclei.

3. Pronuclei approach each other and mitotic spindle forms between them.

4. Chromosomes of the pronuclei intermix. Fertilization is accomplished. Then, the DNA replicates in preparation for the first cleavage division.
Embryonic Development

• Cleavage
  – Mitotic divisions of zygote
  – First cleavage at 36 hours → two daughter cells (blastomeres)
    – At 72 hours → morula (16 or more cells)
• At day 3 or 4, the embryo of ∼100 cells (blastocyst) has reached the uterus
Embryonic Development

• Blastocyst: fluid-filled hollow sphere
• Trophoblast cells
  – Display factors that are immunosuppressive
  – Participate in placenta formation
• Inner cell mass
  – Becomes the embryonic disc (→ embryo and three of the embryonic membranes)
Figure 28.4

(a) Zygote (fertilized egg)

(b) 4-cell stage 2 days

(c) Morula (a solid ball of blastomeres). 3 days

(d) Early blastocyst (Morula hollows out, fills with fluid, and “hatches” from the zona pellucida). 4 days

(e) Implanting blastocyst (Consists of a sphere of trophoblast cells and an eccentric cell cluster called the inner cell mass). 7 days

- Zona pellucida
- Morula
- Blastocyst cavity
- Degenerating zona pellucida
- Trophoblast
- Inner cell mass
- Uterus
- Endometrium
- Ovary
- Oocyte (egg)
- Uterine tube
- Fertilization (sperm meets and enters egg)
- Ovulation
- Sperm

Fertilization (sperm meets and enters egg)
Implantation

- Blastocyst floats for 2–3 days
- Implantation begins 6–7 days after ovulation
  - Trophoblast adheres to a site with the proper receptors and chemical signals
  - Inflammatory-like response occurs in the endometrium
Figure 28.5a

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

• Trophoblasts proliferate and form two distinct layers
  1. Cytotrophoblast (cellular trophoblast): inner layer of cells
  2. Syncytiotrophoblast: cells in the outer layer lose their plasma membranes, invade and digest the endometrium
Endometrial stroma with blood vessels and glands
Syncytiotrophoblast
Cytotrophoblast
Inner cell mass (future embryo)
Lumen of uterus
Implantation

• The implanted blastocyst is covered over by endometrial cells
• Implantation is completed by the twelfth day after ovulation
Endometrial stroma with blood vessels and glands
Syncytiotrophoblast
Cytotrophoblast
Lumen of uterus
Hormonal Changes During Pregnancy

- **Human chorionic gonadotropin (hCG)**
  - Secreted by trophoblast cells, later the chorion
  - Prompts corpus luteum to continue secretion of progesterone and estrogen
  - hCG levels rise until the end of the second month, then decline as the placenta begins to secrete progesterone and estrogen
Figure 28.6

- **Relative blood levels**
- **Gestation (weeks)**
- **Human chorionic gonadotropin**
- **Estrogens**
- **Progesterone**

- **Ovulation and fertilization**
- **Birth**
Placentation

• Formation of the placenta from embryonic and maternal tissues
  1. Embryonic tissues
    • Mesoderm cells develop from the inner cell mass and line the trophoblast
    • Together these form the chorion and chorionic villi
(a) Implanting 7½-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.
Placentation

• Development of the placenta
• Forms from both embryonic cells and maternal cells
(d) 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.
(e) 13-week fetus.
Placenta

• Maternal and embryonic blood supplies do not intermix
• Embryonic and maternal blood vessels lie side-by-side.
• However, some embryonic cells may cross into mother's blood stream
• Embryonic placental barriers include:
  – Membranes of the chorionic villi
  – Endothelium of embryonic capillaries
Embryonic Development: Gastrula to Fetus

• Germ Layers
  – During implantation, the blastocyst starts to convert to a gastrula
  – Inner cell mass develops into the embryonic disc (subdivides into epiblast and hypoblast)
  – The three primary germ layers and the extraembryonic membranes develop
Extraembryonic Membranes

1. Amnion: epiblast cells form a transparent sac filled with amniotic fluid
   – Provides a buoyant environment that protects the embryo
   – Helps maintain a constant homeostatic temperature
   – Allows freedom of movement and prevents parts from fusing together
   – Amniotic fluid comes from maternal blood, and later, fetal urine
Extraembryonic Membranes

2. Yolk sac: a sac that hangs from the ventral surface of the embryo
   – Forms part of the digestive tube
   – Source of the earliest blood cells and blood vessels
Extraembryonic Membranes

3. Allantois: a small outpocketing at the caudal end of the yolk sac
   – Structural base for the umbilical cord
   – Becomes part of the urinary bladder

4. Chorion: helps form the placenta
   – Encloses the embryonic body and all other membranes
Implanting 7½-day blastocyst. The syncytiotrophoblast is eroding the endometrium. Cells of the embryonic disc are now separated from the amnion by a fluid-filled space.

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Gastrulation

- Occurs in week 3, in which the embryonic disc becomes a three-layered embryo with ectoderm, mesoderm, and endoderm
- Begins with appearance of primitive streak, a raised dorsal groove that establishes the longitudinal axis of the embryo
Gastrulation

• Cells begin to migrate into the groove
  – The first cells form the endoderm
  – Cells that follow push laterally, forming the mesoderm
  – Cells that remain on the embryo’s dorsal surface form the ectoderm

• Notochord: rod of mesodermal cells that serves as axial support
Figure 28.9

Amnion
Bilayered embryonic disc
Yolk sac
Cut edge of amnion
Left
Right
Head end
Primitive streak
Tail end
Ectoderm
Mesoderm
Endoderm

(a) Bilayered embryonic disc, superior view

(b) Frontal section
(c) 3-D view
(d) Section view in (e)

(f) 14-15 days

(g) 16 days

Primitive streak
Epiblast
Hypoblast
Primary Germ Layers

• The primitive tissues from which all body organs derive
• Ectoderm $\rightarrow$ nervous system and skin epidermis
• Endoderm $\rightarrow$ epithelial linings of the digestive, respiratory, and urogenital systems
• Mesoderm $\rightarrow$ forms all other tissues
• Endoderm and ectoderm are considered epithelia
Organogenesis

• Gastrulation sets the stage for organogenesis: formation of body organs and systems

• At eighth week
  – All organ systems are recognizable
  – End of the embryonic period
Specialization of Ectoderm

• Neurulation
  – First major event of organogenesis
  – Gives rise to brain and spinal cord
  – Ectoderm over the notochord forms the neural plate
  – Neural plate folds inward as a neural groove with neural folds
Specialization of Ectoderm

- By the 22nd day, neural folds fuse into a neural tube
  - Anterior end → brain; the rest → spinal cord
- Neural crest cells → cranial, spinal, and sympathetic ganglia, and adrenal medulla
Figure 28.10a

(a) 17 days. The flat three-layered embryo has completed gastrulation. Notochord and neural plate are present.
(b) 20 days. The neural folds form by folding of the neural plate, which then deepens, producing the neural groove. Three mesodermal aggregates form on each side of the notochord (somite, intermediate mesoderm, and lateral plate mesoderm).
(c) 22 days. The neural folds have closed, forming the neural tube which has detached from the surface ectoderm and lies between the surface ectoderm and the notochord. Embryonic body is beginning to undercut.
End of week 4. Embryo undercutting is complete. Somites have subdivided into sclerotome, myotome, and dermatome, which form the vertebrae, skeletal muscles, and dermis respectively. Body coelom present.
Specialization of Endoderm

- Embryonic folding begins with lateral folds
- Next, head and tail folds appear
- Endoderm tube forms epithelial lining of the GI tract
- Organs of the GI tract become apparent, and oral and anal openings perforate
- Mucosal lining of respiratory tract forms from pharyngeal endoderm
Figure 28.11a

Tail

Amnion

Head

Yolk sac

Ectoderm

Mesoderm

Endoderm

(a)

Trilaminar embryonic disc
Lateral fold

Future gut (digestive tube)
Figure 28.11c

- Somites (seen through ectoderm)
- Tail fold
- Head fold
- Yolk sac
Figure 28.11d

Primitive gut

Foregut

Hindgut

Neural tube

Notochord

Primitive gut

Foregut

Yolk sac

(d)
<table>
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<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 inch); 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>
<td>13–16 weeks</td>
<td>Cerebellum becoming prominent; general sensory organs differentiated; eyes and ears assume characteristic position and shape; blinking of eyes and sucking motions of lips occur</td>
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<td>(month 4)</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>16 weeks</td>
<td>Approximate crown-to-rump length at end of interval: 140 mm</td>
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<td>17–20 weeks</td>
<td>Vernix caseosa (fatty secretions of sebaceous glands) covers body; lanugo (silky hair) covers skin</td>
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<td>(month 5)</td>
<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>Quickening occurs (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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<td>21–30 weeks (months 6 and 7)</td>
<td>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)</td>
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<td>Myelination of spinal cord begins; eyes are open</td>
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<td>Distal limb bones are beginning to ossify</td>
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<td>Skin is wrinkled and red; fingernails and toenails are present; tooth enamel is forming on deciduous teeth</td>
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<td>Body is lean and well proportioned</td>
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<td>Bone marrow becomes sole site of blood cell formation</td>
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<td>Testes reach scrotum in seventh month (in males)</td>
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<td></td>
<td>Approximate crown-to-rump length at end of interval: 280 mm</td>
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<td>30–40 weeks (term) (months 8 and 9)</td>
<td>Skin whitish pink; fat laid down in subcutaneous tissue (hypodermis)</td>
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<td>Approximate crown-to-rump length at end of interval: 360 mm (14 inches); weight: 3.2 kg (7 lb)</td>
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At birth
Effects of Pregnancy: Anatomical Changes

- The uterus expands, occupying most of the abdominal cavity
- Lordosis occurs with the change in the center of gravity
- Weight gain of ~13 kg (28 lb)
- Relaxin causes pelvic ligaments and the pubic symphysis to relax to ease birth passage
Effects of Pregnancy: Physiological Changes

• GI tract
  – Morning sickness due to elevated levels of estrogen and progesterone
  – Heartburn and constipation are common

• Urinary system
  – ↑ Urine production due to ↑ metabolism and fetal wastes
  – Stress incontinence may occur as bladder is compressed
Effects of Pregnancy: Physiological Changes

• Respiratory system
  – Estrogens may cause nasal edema and congestion
  – Tidal volume increases
  – Dyspnea (difficult breathing) may occur later in pregnancy
Effects of Pregnancy: Physiological Changes

• Cardiovascular system
  – Blood volume increases 25–40%
  – Blood pressure and pulse rise
  – Venous return from lower limbs may be impaired, resulting in varicose veins
Parturition

• Parturition giving birth to the baby
• Labor events that expel the infant from the uterus
Initiation of Labor

- During the last few weeks of pregnancy
  - Fetal secretion of cortisol stimulates the placenta to secrete more estrogen
  - Causes production of oxytocin receptors by myometrium
  - Antagonizes calming effects of progesterone, leading to Braxton Hicks contractions in uterus
Lactation

• Production of milk by the mammary glands
• Toward the end of pregnancy
  – Placental estrogens, progesterone, and lactogen lead to release of prolactin.
Lactation

• Colostrum
  – Yellowish secretion rich in vitamin A, protein, minerals, and IgA antibodies
  – Released the first 2–3 days
  – Followed by true milk production

• Suckling initiates a positive feedback mechanism

• Oxytocin causes the letdown reflex
Figure 28.19

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

Inhibits hypothalamic neurons that release dopamine. Hypothalamus releases prolactin releasing factors (PRF) 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 lactiferous glands.

↑ Milk production

Positive feedback

Start

Hypothalamus releases prolactin to blood.
Advantages of Breast Milk

• Fats and iron are easily absorbed; amino acids more easily metabolized, compared with cow’s milk

• Beneficial chemicals: IgA, complement, lysozyme, interferon, and lactoperoxidase

• Interleukins and prostaglandins prevent overzealous inflammatory responses
Advantages of Breast Milk

• Natural laxative effect helps eliminate bile-rich meconium, helping to prevent physiological jaundice
• Encourages bacterial colonization of the large intestine