From Egg to Embryo

- Pregnancy – events that occur from fertilization until the infant is born
- Conceptus – the developing offspring
- Gestation period – time of development (about 280 days) technically from the last menstrual period until birth
- Embryonic period: fertilization to week 8 (embryo)
- Fetal period: week 9 to birth (fetus)
- At birth, conceptus is called an infant
Accomplishing Fertilization

- Sperm must reach the ovulated secondary oocyte
- The oocyte is viable for 12 to 24 hours after ovulation
- Sperm retain their fertilizing power for 24 to 48 hours after ejaculation
- For fertilization to occur, coitus must occur no more than two days before ovulation
  - And no later than 24 hours after ovulation
  - At which point the oocyte is about 1/3 the way down the length of the uterine tube
- Fertilization – when a sperm fuses with an egg (secondary oocyte) to form a zygote (the first cell of the new individual)
Sperm Transport and Capacitation

- Sperm must travel just 5 inches
- Fates of ejaculated sperm:
  - Leak out of the vagina immediately after deposition
  - Destroyed by the acidic vaginal environment
  - Fail to make it through the cervix (thick cervical mucus must first be made fluid by estrogen)
  - Dispersed in the uterine cavity by uterine contractions
  - Destroyed by uterine phagocytic leukocytes
- 200-3000 sperm make it up the uterine tube by reverse peristalsis
- Sperm must undergo capacitation before they can penetrate the oocyte
Capacitation

- Capacitation: enhanced sperm motility and process whereby the sperm’s membranes become fragile so the hydrolytic enzymes in their acrosomes can be released
  - Secretions in the uterine tract breakdown the sperm’s membranes
  - Sperm possess olfactory receptors and egg releases signaling molecules (chemotaxis)
Acrosomal Reaction and Sperm Penetration

- An ovulated oocyte is encapsulated by:
  - The corona radiata and zona pellucida both of which the sperm must penetrate

- Sperm releases hyaluronidase which weakens cell-cell contacts between granulosa cells

- Sperm head then bind to the ZP3 glycoprotein of the zona pellucida

- Zona pellucida acts as a sperm receiver and triggers the acrosomal reaction
Acrosomal Reaction and Sperm Penetration

- Acrosomal reaction
  - Involves the breakdown of the acrosome and the release of acrosomal enzymes near the oocyte which digest holes through the zona pellucida
  - Requires the release of enzymes from hundreds of sperm acrosomes to digest the zona pellucida
- A single sperm will ultimately breaches the membrane and fuse with the oocyte’s membrane receptors
Acrosomal Reaction and Sperm Penetration

- Once a sperm makes contact with the oocyte’s membrane:
  - Its nucleus is pulled into the oocyte’s cytoplasm
  - Beta protein finds and binds to receptors on the oocyte membrane causing…
  - The Alpha protein to insert into the membrane
  - Contents of the egg and sperm then mix
  - The area where the sperm enters determines the future right and left halves of the fetal body
Blocks to Polyspermy (Entry of Several Sperm)

- Once sperm enters the egg, the egg’s endoplasmic reticulum releases Ca++ into the cytoplasm activating the egg for cell division
- Ca++ flux also causes the cortical reaction where granules located in the egg’s plasma membrane release enzymes (ZIPs) into the extracellular space beneath the zona pellucida
Blocks to Polyspermy (Entry of Several Sperm)

- Zonal inhibiting proteins (ZIPs) destroy sperm receptors preventing further sperm entry
- ZIPs also bind water causing the zona pellucida to swell and detach any sperm attached to the receptors
- Finally, if polyspermy occurs, the embryo dies
Completion of Meiosis II and Fertilization

- After sperm enters egg it loses its tail and midpiece
- The male pronucleus forms
- The secondary oocyte, stimulated by the Ca++ surge:
  - Completes meiosis II
  - Casts out a second polar body
- The ovum nucleus swells forming the female pronucleus
- The two pronuclei approach each other
- The mitotic spindle forms between them
- The pronuclei membranes rupture releasing the chromosomes
- The male and female chromosomes combine forming the diploid zygote (fertilized egg)
- The chromosomes replicate followed by the 1\textsuperscript{st} mitotic division of the conceptus
Events Immediately Following Sperm Penetration

Figure 28.3
Zygote to Blastocyst Implantation: Cleavage & Blastocyst Formation

- **Cleavage**: Period of rapid mitotic divisions
- Produces small cells with high surface:volume ratio enhancing uptake of nutrients & O2
- After 36 hrs.: blastomere forms (2 identical cells)
- After 72 hrs.: 16 or more cells (morula)
- By day 3-4: 100 cells are seen floating free in the uterus
Zygote to Blastocyst Implantation: Cleavage & Blastocyst Formation

- Blastocyst accumulates fluid within an internal cavity
- The zona pellucida breaks down
- Blastocyst “hatches” with the lack of a zona pellucida
- Blastocyst consists of:
  - A fluid-filled hollow sphere consisting of a single layer of flattened cells (trophoblast cells) which are involved with placental formation
  - and 20-30 rounded cells (inner cell mass) located at one side which will become the embryonic disc
Cleavage: From Zygote to Blastocyst

(a) Zygote (fertilized egg)
(b) 4-cell stage 2 days
(c) Morula 3 days
(d) Early blastocyst 4 days
(e) Implanting blastocyst 6 days

- Sperm
- Inner cell mass
- Blastocyst cavity
- Trophoblast
- Fertilization (sperm meets egg)
- Uterine tube
- Oocyte (egg)
- Ovary
- Uterus
- Endometrium
- Cavity of uterus

Figure 28.4
Implantation

- Blastocyst floats in the uterus for 2-3 days receiving nourishment from glycogen-rich uterine secretion

- Integrin and selectin proteins of the trophoblast binds to the extracellular components (collagen, fibronectin, lamina) of the endometrial cells as well as to the selectin-binding carbohydrates on the inner uterine wall located high in the uterus
Implantation

- Trophoblast cells secrete digestive enzymes and growth factors against the endometrium surface which thickens with characteristics of an acute inflammatory response

- The trophoblast proliferates forming 2 distinct layers:
  - Cellular trophoblast (Cytotrophoblast): cells in the inner layer which retain their plasma membranes
  - Syncytial trophoblast (Synctiotrophoblast): cells in the outer layer that lose their plasma membranes
    - form a multi-nuclear cytoplasmic mass
Implantation of the Blastocyst

(a)

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

(b)

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

- Syncytial trophoblast: invades the endometrium and digest the uterine cells it contacts
- The blastocyst burrows into the cavity and is covered up by endometrial cells
- 2/3 of all zygotes fail to implant or spontaneously abort
- Successful implantation takes 5 days and is completed by day 12 after ovulation
- Menses must be prevented during this time
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 – a membrane developed from trophoblasts after implantation, continues this hormonal stimulus
- Thus, the conceptus takes over the hormonal control of the uterus
Hormonal Changes During Pregnancy

Figure 28.6

- Human chorionic gonadotropin
- Estrogens
- Progesterone

Relative blood levels

Gestation (weeks)

Ovulation and fertilization

Birth
Placentation

- The formation of the placenta

- Between the second and third month, the placenta:
  - Assumes the role of progesterone and estrogen production
  - Is providing nutrients and removing wastes

- Formation of the placenta from:
  - Embryonic trophoblastic tissues
  - Maternal endometrial tissues
Placentation

- The chorion develops fingerlike villi, which:
  - Become vascularized
  - Extend to the embryo as umbilical arteries and veins
  - Lie immersed in maternal blood
- Decidua basalis – part of the endometrium that lies between the chorionic villi and the stratum basalis
Placentation

- Decidua capsularis – part of the endometrium surrounding the uterine cavity face of the implanted embryo

- The placenta is fully formed and functional by the end of the third month
Placentation

- Barriers to free passage of substances between embryonic and maternal blood supplies are embryonic barriers: e.g.
  - The chorionic villi
  - The endothelium of embryonic capillaries

Thus, embryonic and maternal blood supplies do not mix
Decidua basalis

(g)

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Placentation

- Throughout pregnancy, estrogen and progesterone levels continue to rise encouraging growth and further differentiation of the mother's mammary glands.

- The placenta also secretes other hormones – human placental lactogen, human chorionic thyrotropin, and relaxin.
Placentation

Figure 28.7a–c

(a) 7½-day implanting blastocyst
(b) 12-day implanted blastocyst
(c) 16-day embryo
Placentation

(d) 4 1/2-week embryo

Lumen of uterus

Decidua basalis
Maternal blood
Chorionic villus
Umbilical blood vessels in umbilical cord
Amnion
Amniotic cavity
Yolk sac
Extraembryonic coelom
Chorion
Decidua capsularis

Figure 28.7d
Placentation

(f) 13-week fetus
Gastrula to Fetus: Germ Layers

- Gastrula phase: when the 3 primary germ layers form and the extraembryonic membranes develop
  - The three primary germ layers are: ectoderm, endoderm, and mesoderm
- Before becoming three-layered, the inner cell mass subdivides into the upper epiblast and lower hypoblast
  - These layers form two of the four embryonic membranes
Formation and Roles of the Extraembryonic Membranes

- The extraembryonic membranes form during the first 2-3 weeks and include: amnion, yolk sac, allantois, and the chorion

- Amnion – develops when the cells of the epiblast transform into a transparent membranous sac (the amnion) which becomes filled with amniotic fluid
  - Provides a buoyant environment that protects the embryo
  - Helps maintain a constant homeostatic temperature
  - Prevents embryo’s parts from touching one another and fusing together
  - Amniotic fluid comes from maternal blood, and later, fetal urine
Embryonic Membranes

- Yolk sac – forms from cells of the primitive gut and hangs from the ventral surface of the embryo

- Functions:
  - Forms part of the digestive tube
  - Produces earliest blood cells and vessels
  - Is the source of primordial germ cells
Embryonic Membranes

- Allantois – a small outpocketing at the caudal end of the yolk sac
  - Structural base for the umbilical cord
  - Becomes part of the urinary bladder
- Chorion – helps form the placenta
  - Is the outermost membrane enclosing the embryonic body and all other membranes
Gastrulation: Germ Layer Formation

- During the 3\textsuperscript{rd} week, the two-layered embryonic disc becomes a three-layered embryo
- The primary germ layers are ectoderm, mesoderm, and endoderm
- Involves cellular rearrangements and migrations
- Begins with the appearance of the primitive streak
  - Primitive streak – raised dorsal groove that establishes the longitudinal axis of the embryo
Gastrulation

- Notochord – formed from mesodermal cells
  - Serves as the first axial support
KU Game Day!!

- Thur. 3:30 pm
Primary Germ Layers

- The 3 layers serve as primitive tissues from which all body organs will derive
  
  - Ectoderm – forms structures of the nervous system and skin epidermis
  
  - Endoderm – forms epithelial linings of the digestive, respiratory, glands and urogenital systems
  
  - Mesoderm – forms all other tissues

  - Endoderm and ectoderm are securely joined and are considered epithelia
Primary Germ Layers

Figure 28.8a–e

(a) Embryo (See Figure 28.7b)
(b) ... turned 90°
(c) 3-D view
(d) Section view in (e)

(e) Bilayered embryonic disc, lateral-superior view
Primary Germ Layers

Figure 28.8e–h
Organogenesis: Differentiation of the Germ Layers

- Gastrulation sets the stage for organogenesis, the formation of body organs
- By the 8\textsuperscript{th} week all organ systems are recognizable
Specialization of Ectoderm

- Neurulation – the first event of organogenesis gives rise to the brain and spinal cord
- Ectoderm over the notochord thickens, forming the neural plate
- The neural plate folds inward as a neural groove with prominent neural folds
Specialization of Ectoderm

- By the 22\textsuperscript{nd} day, neural folds fuse into a neural tube, which pinches off into the body.
- The anterior end becomes the brain; the rest becomes the spinal cord.
- By the end of the 1\textsuperscript{st} month, 3 primary brain vesicles (fore-, mid-, and hindbrain) are obvious.
- The remaining ectoderm becomes the skin epidermis.
Specialization of Ectoderm: Neuralization

(a) 17 days

(b) 19 days

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Figure 28.9a, b
Specialization of Ectoderm: Neuralization

(c) 20 days

(d) 22 days

Figure 28.9c, d
Specialization of Endoderm

- As the endoderm folds, it encloses part of the yolk sac
- The tube of endoderm is the primitive gut which is the epithelial lining of the G.I. tract
- The pharynx, esophagus, stomach and intestines become apparent followed by the oral and anal openings
Folding of the Embryonic Body

Figure 28.10a–d
Endodermal Differentiation

5-week embryo

- Pharynx
- Parathyroid glands and thymus
- Thyroid gland
- Esophagus
- Trachea
- Right and left lungs
- Stomach
- Liver
- Pancreas
- Gallbladder
- Small intestine
- Large intestine
- Connection to yolk sac
- Umbilical cord
- Allantois
Specialization of the Mesoderm

- First evidence is the appearance of the notochord, which is replaced later by the vertebral column.

- Three mesoderm aggregates appear lateral to the notochord.
  - Somites, intermediate mesoderm, and double sheets of lateral mesoderm.
Specialization of the Mesoderm

- The 40 pairs of somites have three functional parts:
  - **Sclerotome** – produce the vertebrae and ribs
  - **Dermatome** – help form the dermis of the skin on the dorsal part of the body
  - **Myotome** – form the skeletal muscles of the neck, trunk, and limbs
Specialization of the Mesoderm

- Intermediate mesoderm forms the gonads and the kidneys
- Lateral mesoderm consists of somatic and splanchnic mesoderm
Specialization of the Mesoderm

- Somatic mesoderm forms the:
  - Dermis of the skin in the ventral region
  - Parietal serosa that lines the ventral body cavity
  - Bones, ligaments, and dermis of the limbs

- Splanchnic mesoderm forms:
  - The heart and blood vessels
  - Most connective tissues of the body
  - The walls of the digestive & respiratory tracts
  - Thus, the lateral mesoderm forms the ventral body cavity
Specialization of the Mesoderm

(a) Ectoderm
   Somite
   Intermediate mesoderm
   Notochord
   Endoderm

(b) Somatic mesoderm
   Coelom
   Future gut (digestive tube)
   Lateral fold
   Splanchnic mesoderm

(c) Dermatome
   Myotome
   Sclerotome
   Kidney and gonads (intermediate mesoderm)
   Splanchnic mesoderm
   • Visceral serosa
   • Smooth muscle of gut
   • Peritoneal cavity (coelom)

Neural tube
   Epidermis (ectoderm)
   Gut lining (endoderm)
   Neural tube (ectoderm)
   Limb bud
   Parietal serosa
   Dermis

Yolk sac

Figure 28.12
End of Embryonic Period

- By the end of the embryonic period (8 weeks):
  - The embryo is about 1” long
  - The bones have begun to ossify
  - Skeletal muscles have formed and are contracting
  - The blood supply is provided by the placenta
  - The lungs and kidneys are in place
  - The heart & liver are maneuvering into their places
Development of Fetal Circulation

- By the end of the 3rd week:
  - The 1st blood cells arise in the yolk sac
  - The heart is pumping by 3 ½ weeks
  - Circulatory shunts are placed so blood can bypass the liver and lungs (next slide)
  - The embryo has a system of paired vessels
  - The vessels forming the heart have fused
Development of Fetal Circulation

- Unique vascular modifications seen in prenatal development include umbilical arteries and veins, and three vascular shunts (occluded at birth)
  - Ductus venosus – venous shunt that bypasses the liver
  - Foramen ovale – opening in the interatrial septa to bypass pulmonary circulation
  - Ductus arteriosus – transfers blood from the right ventricle to the aorta
Circulation in Fetus and Newborn

Figure 28.13
Effects of Pregnancy on the Mother: Anatomical Changes

- The reproductive organs become more vascularized

- Placental production of the hormone relaxin causes pelvic ligaments and the pubic symphysis to relax, widen and become more flexible

- Typical weight gain is about 28 pounds
Pregnancy and the mother

- Vitamin supplements containing folic acid help prevent risk of having a baby with neurological problems

- Mom needs only about 300 extra calories/day to sustain proper fetal growth

- This must be acquired with quality food...not just more food
Effects of Pregnancy: Metabolic Changes

- The placenta secretes human placental lactogen (hPL) which works with estrogen and progesterone to stimulate the maturation of the breasts for lactation

- hPL promotes the use of fatty acid metabolism for the mother sparing glucose for use by the fetus
Effects of Pregnancy: Physiological Changes

- GI tract – morning sickness occurs due to elevated levels of estrogen and progesterone

- Heartburn – esophagus is displaced and the stomach is crowded by the growing uterus causing acid reflux into the esophagus

- Urinary system – urine production increases to handle the additional fetal wastes
  - Uterus compresses the bladder leading to more frequent urination
Effects of Pregnancy: Physiological Changes

- Respiratory system – nasal congestion may occur
  - Dyspnea (difficult breathing) may develop late in pregnancy
- Cardiovascular system – blood volume increases 25-40%  
  - Blood pressure and pulse increase
  - Venous pressure from lower limbs is impaired, resulting in varicose veins
Parturition: Initiation of Labor

- Parturition (birth) occurs w/i 15 days (280 days from the last menstrual period)

- During the last few weeks of pregnancy, estrogen reaches a peak:
  - Stimulates the myometrial cells of the uterus to form abundant oxytocin receptors
  - Antagonizes progesterone’s quieting influence on the uterine muscles

- Thus, the myometrium begins to contract (Braxton Hicks contractions) e.g. false labor
Parturition: Initiation of Labor

- As birth nears, fetal cells produce more oxytocin causing the placenta to release prostaglandins causing powerful uterine contractions

- Contractions become more vigorous

- Mother’s hypothalamus signals for the release of oxytocin by the posterior pituitary

- Together, elevated levels of oxytocin & prostaglandins trigger rhythmic expulsive contractions of true labor
Parturition: Initiation of Labor

- Positive feedback with the hypothalamus:
  - Greater contractile force causes release of more oxytocin which causes greater contractile force
- Fetal fibronectin begins to change from sticky substance to a lubricant
Parturition: Initiation of Labor

Estrogen

from ovaries
Induces oxytocin receptors on uterus

Oxytocin

from fetus and mother's posterior pituitary

Stimulates uterus to contract
Stimulates placenta to make prostaglandins
Stimulate more vigorous contractions of uterus

Positive feedback
Stages of Labor: Dilation Stage

- From the onset of labor until the cervix is fully dilated by the baby’s head (10 cm)
- Contractions begin at the top of the uterus and move toward the vagina
- Initial contractions are 15–30 minutes apart and 10–30 seconds in duration
- Contractions become more vigorous and rapid
- The baby’s head moves into the cervix
- The amnion ruptures, releasing amniotic fluid (breaking of the water)
- Engagement occurs as the infant’s head enters the true pelvis
- Head rotates so that it lies in the anteroposterior line
- Longest stage lasting 6-12 hours
Stages of Labor: Dilation Stage
Stages of Labor: Expulsion Stage

- Lasts from full dilation to delivery of the infant
- Strong contractions occur every 2–3 minutes and last about 1 minute
- Lasts about 1-2 hrs. for the 1st birth, 20 min. for subsequent births
- Crowning occurs when the largest dimension of the head distends the vulva
- Episiotomy may be done at this time to prevent tearing
- Once the head is delivered, the rest of the body passes fairly easily
- The umbilical cord is clamped and cut
- Breech birth: often requires forceps
- Cesarean section: delivery thru the abdominal and uterine walls
Episiotomy
Stages of Labor: Expulsion Stage

Figure 28.17c
Stages of Labor: Placental Stage

- The delivery of the placenta is accomplished within 30 minutes of birth
- Uterine contractions occur after delivery of infant causing detachment of the placenta
- Afterbirth – the placenta and its attached fetal membranes are removed with a gentle tug on the umbilical cord
- All placenta fragments must be removed to prevent postpartum bleeding
Stages of Labor: Expulsion Stage

Uterus

Placenta (detaching)

Umbilical cord

Figure 28.17d
Extrauterine Life

- The neonatal period lasts 4 weeks after birth
- At 1-5 minutes after birth, the infant’s physical status is assessed based on five signs: heart rate, respiration, color, muscle tone, and reflexes
- Each observation is given a score of 0 to 2
- Apgar score – the total score of the above assessments
  - 8-10 indicates a healthy baby
  - Lower scores reveal problems
First Breath

- Once carbon dioxide is no longer removed by the placenta, central acidosis occurs.

- This excites the respiratory centers to trigger the first inspiration.

- This requires tremendous effort – airways are tiny and the lungs are collapsed.

- Once the lungs inflate, surfactant in alveolar fluid helps reduce surface tension.
Occlusion of Fetal Blood Vessels

- Umbilical arteries and vein constrict and become fibrosed

- As the pulmonary circulation becomes functional:
  - Left heart pressure increases & right heart pressure decreases causing the pulmonary shunts to close
  - The foramin ovale closes and its edges fuse to the septal wall (complete within 1 year)
  - All special circulatory adaptations of the fetus are functionally occluded within 30 minutes after birth
Lactation

- The production of milk by the mammary glands
- Rising levels of placental estrogen, progesterone and lactogen toward the end of pregnancy stimulate the mother’s hypothalamus to release prolactin-releasing hormone (PRH)
- The anterior pituitary responds by releasing prolactin
Lactation

- Colostrum
  - Solution rich in vitamin A, protein, minerals, and IgA antibodies
  - Is released the first 2–3 days
  - Is followed by true milk production
- After birth, PRL release wanes and milk production persists based on mechanical stimulation
- Oxytocin causes the let-down reflex
- Oxytocin binds to myoepithelial cells surrounding the mammary glands
Breast Milk

- Advantages of breast milk for the infant
  - Fats and iron are better absorbed
  - Its amino acids are metabolized more efficiently than those of cow’s milk
  - Beneficial chemicals are present – IgA, other immunoglobulins, complement, lysozyme, interferon, and lactoperoxidase
  - Interleukins and prostaglandins are present, which prevent overzealous inflammatory responses
  - Its natural laxatives help cleanse the bowels of meconium
Have a Great Summer!