Quick Notes on Fertilization, Pre-embryonic Period, Embryonic Period, and Fetal Period

- Gestation = amount of time to develop to birth.

Pregnancy = condition of being pregnant.

Gestational age is the common term used during pregnancy to describe how far along the pregnancy is. It is measured in weeks, from the first day of the woman's last menstrual cycle to the current date. Normal gestation = 40 weeks or 280 days.

Developmental (Embryonic or Fetal) Age is the number of days since conception. Usually 2 weeks less than Gestational age, as (normally) ovulation occurs 14 days after menstruation. 38 weeks or 266 days. 38 weeks = 8.7 months (let's round up, shall we? 9 months)

- Pre-embryonic Stage - First 2 Weeks

- Female reproductive tract has many protections against pathogen invasion. Sperm must get past this.
  * pH of vaginal environment, white blood cells, cervical mucus plug, etc.
  * Recall: oocyte surrounded by corona radiata (follicular cells) and zona pellucida
  * Hundreds of millions of sperm in ejaculate. Semen contains alkaline solution, fructose, fibrinogen.
  * Only a few hundred will reach oocyte. Male infertility is often low sperm count. Varicocele (varicose veins of the testes)

- Capacitation: To fertilize egg, the sperm must undergo *capacitation*

  Last step in the maturation of spermatozoa and is required to render them competent to fertilize an oocyte.

  Remove the “acrosomal sperm head membrane”:
  1. Greater binding between sperm and oocyte
  2. Reveal acrosome.

- Fertilization

  Acrosomal reaction of capacitated sperm
  * The enzyme-filled “cap” of the sperm, called the acrosome, releases its stored digestive enzymes.
  * Penetrates granulosa cells then zona pellucida surrounding egg

  Prevention of polyspermy
  * Fast block: depolarize the oocyte’s membrane
  * Slow block: cortical reaction


Fertilized egg now called a *zygote*. 
- **Cleavage** - mitotic divisions that occur for 3 days after fertilization

  Zygote splits into 2 daughter cells. Repeated mitosis, but cluster of cells same size as original oocyte.

- Morula stage (solid ball of cells). Morula free in uterine cavity for 4-5 days. Enters uterus.

  * Zona pellucida disintegrates to release blastocyst, which will eventually implant.

- Dizygotic (fraternal) twins
  2 eggs are ovulated and fertilized (2 zygotes)  
  As different as any other siblings

- Monozygotic (maternal) twins
  1 egg is fertilized (1 zygote) but embryoblast splits into two  
  Genetically identical siblings (must be same sex)

- Implantation of Blastocyst

  Blastocyst attaches to uterine wall 6 days after ovulation  
  Endometrium completely encloses embryo

  Ectopic Pregnancy - Blastocyst implants outside uterus  
  "tubal pregnancy": 1 type  
  abdominal pregnancies result in live birth by Cesarian section

- Embryo: all 3 primary germ layers present

  Embryogenesis: the germ layers and embryonic membranes

  Gastrulation: Development of 3 primary germ layers  
  1. Flattening of embryoblast into embryonic disc  
  2. Form the 3 germ layers: Ectoderm, endoderm, and mesoderm in primitive streak  
  3. At same time, form the embryonic membranes.

  Organogenesis: Germ layers differentiate into organs and organ systems  
  Presence of “adult organs” marks the beginning of fetal stage

Here’s the embryonic membranes we’ll discuss:

- Yolk sac - hangs from ventral side of embryo, greatly reduced later as we rely on umbilical cord (umbilicus) and placenta.

  Contributes to GI tract, blood cells and germ cells

- Chorion - outermost membrane  
  Chorionic villi form fetal portion of the placenta.  
  More in next section.

- Allantois - foundation of umbilical cord and urinary bladder

- Amnion - transparent sac filled with fluid  
  Protects embryo from trauma, temperature changes, adhesions and provides freedom of movement  
  Forms from maternal plasma filtrate and fetal urine. When a woman’s “water breaks", the sac is ruptured and this fluid is released.
Amniocentesis: take a sample of this fluid to look for chromosomal abnormalities, fetal infections.

As development continues:

- **Derivatives of endoderm**
  - Epithelium of gut and respiratory, and glands

- **Derivatives of mesoderm**
  - Skeleton, muscle, cartilage, blood

- **Derivatives of ectoderm**
  - Epidermis, nervous system
  - Neural groove and fold – first to appear in embryo
  - Spina bifida: posterior portion fails to close. Anencephaly: anterior portion fails to close.
  - Somites (pre-muscles) next adult structures to appear on side of fold.

Embryo begins receiving its nutrients from placenta

The Placenta - Surface facing fetus is smooth and connected to fetus by umbilical cord. Substances pass through by diffusion, facilitated diffusion, active transport and receptor-mediated endocytosis.

- Fetal and maternal blood do not mix. Placenta = fuse fetal contribution (Chorion), which develops from the same blastocyst that forms the fetus, and the maternal contribution to the placenta (Decidua basalis), which develops from the endometrium
  - Maternal contribution: Uterine surface consists of villi and decidua basalis region of endometrium
  - Fetal contribution: Chorionic villi - Extensions of syncytiotrophoblast into endometrium by digestion and growth of “roots” of tissue.

Embryonic tissue extends into chorionic villi to form embryonic blood vessels.

Pools of maternal blood that merge in “venous lakes” and surround villi.

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**SIDELINE: Some pathology terms related to the placenta:**

*These terms are often confused and synonymized. For the exam, just know the definitions of the conditions, and anything in bold. Many of these are mainly due to maternal infections before/during pregnancy scarring the uterine wall. Nowadays, previous cesareans and other scarring (surgical or not) is the main cause.*

- **Antepartum bleeding:** Most common cause = rupture of marginal sinus. Usually not dangerous for mother, but can lead to premature birth.

- **Placenta abruptio** is a pregnancy problem in which the placenta separates too early from the wall of the uterus.

- **Placenta previa:** Implantation too close to the os cervix (“Opening” of the cervix), causing the placenta to grow over the opening of the cervix.

- **Preeclampsia and eclampsia:** characterized by high maternal blood pressure and a large amount of protein in the urine.

  Pre-eclampsia increases the risk of death for both the mother and the baby. If left untreated, it may result in seizures at which point it is known as eclampsia.

Highest risk factors: high pre-pregnancy BP, diabetes mellitus and obesity.
SIDELINE: Congenital Anomalies & Teratogens

For the exam, know the definitions of the terms teratogen and congenital. Know the 4 variables affecting outcomes, and know the 6 categories of teratogens. Know the example of thalidomide. Know what might make a chemical/drug a teratogen. Know the examples given of microorganisms/infections that are teratogens.

Teratogens are viruses, chemicals, ionizing radiation or other agents that cause anatomical deformities in fetus.

A congenital disorder, also known as a congenital disease, deformity, birth defect, or anomaly, is a condition existing at or before birth regardless of cause. 3% of newborns.

Variables affecting outcome:

Timing - Some teratogens cause damage only during specific days or weeks in early pregnancy

Critical period - in prenatal development, the time when a particular organ or other body part is most susceptible to teratogenic damage

Dosage and amount of exposure is everything!

Interaction

Genetic variability

Causes of teratogenesis can broadly be classified as:

1. Toxic substances, such as, for humans, drugs in pregnancy and environmental toxins in pregnancy.

Size and solubility

* Thalidomide (unformed arms or legs)

* Fetal alcohol syndrome, smoking

2. Vertically transmitted infection.

Microorganisms that can cross the placenta include:

- Herpes simplex, rubella, cytomegalovirus, HIV

3. Lack of nutrients. For example, lack of folic acid in the nutrition in pregnancy for humans can result in spina bifida.

4. Physical restraint.

5. Ionizing radiation (including x-rays)

6. Maternal antibodies/hormones crossing the placenta
- The Fetus and Neonate

Organogenesis

Formation of organs from primary germ layers

At 8 weeks, all organs are present in 3 cm long fetus

Fetal Development I am going to use “developmental age”, not “gestational age”.

Fetus = from 8 weeks until birth. Organs mature to support external life

*Important landmarks:*

At 8 weeks (end of embryonic period)

* All body systems present in rudimentary form. Cardiovascular is fully functioning.
* All major brain regions present
* Skeleton just beginning to ossify. Joints and toes distinguishable.

9 – 12 weeks (third month)

* Head is ½ size of the fetus
* Skin epidermis and dermis obvious
* Sex readily detected from genitals

13 – 16 Weeks (fourth month)

* Body beginning to outgrow head
* Face looks normal
* Most bones are now distinct, and joint cavities are present

17 – 20 weeks (fifth month)

* Vernix caseosa (fatty secretions of sebaceous glands)
* Fetal position
* “Quickening” (mother feels spontaneous muscular contractions)
* Limbs proportional

21 - 30 weeks (sixth and seventh months)

* Great increase in weight
* Testes descend into scrotum if male

31 – 38 weeks (eighth and ninth months)

* Kidneys, lungs, liver matures.
* Mostly gaining weight
- Meconium: The earliest stool of a fetus. Composed of materials ingested during the time the infant spends in the uterus: mostly amniotic fluid.

- Fetal circulation
  * Umbilical-placental circuit via umbilical cord
  * Circulatory shunts
    Ductus venosus connects to inferior vena cava
    Foramen ovale connecting right and left atria
    Ductus arteriosus connects pulmonary trunk to aorta

The Neonate or Newborn

- Transitional period
  First 6-8 hours heart and respiratory rate increase and body temperature falls

- Circulatory Adaptations:
  * Umbilical arteries and veins become ligamentous

- Thermoregulation and Metabolism
  * Brown fat deposited during weeks 17 to 20 fetal life
    Role: produce heat for organisms (like newborns) that can’t shiver
    Mitochondria breakdown pyruvic acid and release only heat

- Water balance
  * Kidneys not fully developed at birth

- Premature Infants
  * Infants born weighing less than 5.5 lb.
  * Infants born before 7 months suffer from Respiratory distress syndrome
    Insufficient surfactant causing alveolar collapse with exhalation
  * Thermoregulatory problems due to undeveloped hypothalamus -- keep in incubator
  * Edema, deficiency of clotting and jaundice from bile

Aging is all changes occurring with the passage of time -- growth, development and degeneration
Senescence is the degeneration that occurs after the age of peak functional efficiency

*If time permits, we will look at the material in the “Notes on Aging and Senescence”*