GENERAL EMBRYOLOGY

Human Embryology and Congenital Malformations

Objective: *To assist students in the analysis of normal relationships of different structure in the body and to explain malformations and their consequences.*

Content: Development of the gastro-intestinal tract, including rotation of the gut and its fixation; development of the pancreas, liver, gall bladder, kidneys, urethras, urinary bladder, urethra and their malformations; prostate, uterus, uterine tubes, external genitalia – males and females. Development and descent of the testis and ovary; bronchial and congenital abnormalities including bronchial fistulae. Development of the face and respiratory tract;

Development of the endocrine glands: pituitary, supra-renal, thyroid glands and their abnormalities.

Development of the nervous system: neural tube and its sub-divisions; neural crest and its derivatives; hydrocephalus, anencephaly, spina bifida occulta, meningo coel and meningo-myelocoel; the eye and ear.

TEXTBOOKS:

•*The **Developing Human, Clinically Oriented Embryology,*** 8th ed. by Moore and Persaud, 2008, Saunders.

•***Medical Embryology*** 12th Edition or Any other Textbook by T.W. Sadler, 2012, Lippincot; Williams & Wilkins. (http://thepoint.lww.com/sadler12e)

Course Instructor: ***Dr. Salah A. Martin***

Introduction

- **Embryology** is the study of development from conception till birth.
- It is sometimes referred to as **developmental anatomy.**
- Development begins with the fusion of male and female gametes.
- These cells are produced in the gonads by **gametogenesis.**
- During ejaculation, the male deposits millions of spermatozoa in the female reproductive tract.
- The spermatozoa must migrate through the female reproductive tract to find and fertilize the ovum that has been released from the ovary.

Age of Fetus

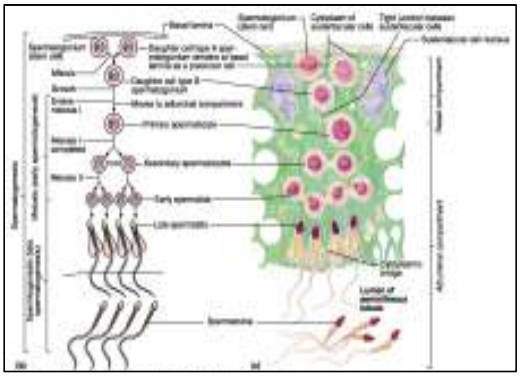
- A "full-term" **human pregnancy** ranges from 216 to 306 days with a modal length of **266** days.
- **Fertilization age** of the fetus uses the event of fertilization as time zero.
- **Menstrual age** uses the start of the mother's **last normal menstrual period** (LNMP) as time zero, meaning that **menstrual age is approximately two weeks older than fertilization age**.

PRE-FERTILIZATION EVENTS

- Gametogenesis
  - Female Gametogenesis (Oogenesis)
  - Male Gametogenesis (Spermatogenesis)
- Gamete Transport
- Ovulation
- Transport of Sperm in Female
- Aneuploidy

Spematogenesis

- The sequence of events that produces sperm in the **seminiferous tubules** of the testes
- Each cell has two sets of chromosomes (one maternal, one paternal) and is said to be diploid (2*n* chromosomal number)
- Humans have 23 pairs of homologous chromosomes
- Gametes only have 23 chromosomes and are said to be haploid (*n* chromosomal number)
- Gamete formation is by meiosis, in which the number of chromosomes is halved (from 2*n* to *n*)



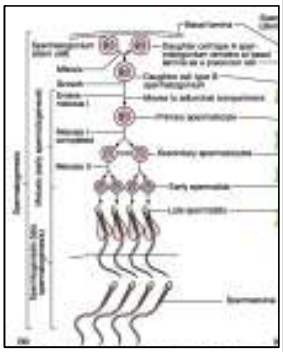
- Cells making up the walls of **seminiferous tubules** are in various stages of cell division
- These **spermatogenic cells** give rise to sperm in a series of events
  - **Mitosis of spermatogonia**, forming **spermatocytes**
  - **Spermatids** formed from **spermatocytes** by meiosis
  - **Spermiogenesis** – **spermatids** forming **sperm**

Mitosis of Spermatogonia

- **Spermatogonia** – outermost cells in contact with the epithelial basal lamina
- **Spermatogenesis** begins at puberty as each mitotic division of **spermatogonia** results in **type A** or **type B** daughter cells
- **Type A** cells remain at the basement membrane and maintain the germ line
- **Type B** cells move toward the lumen and become primary **spermatocytes**

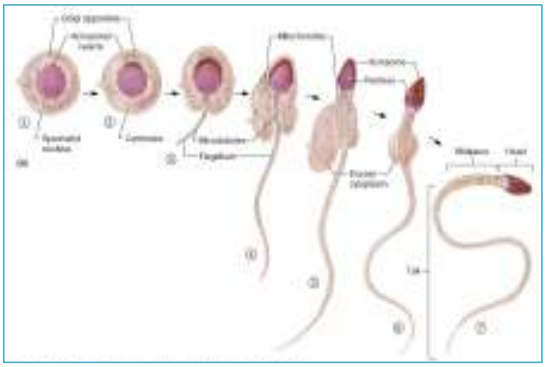
Spermatocytes to Spermatids

- **Primary** s**permatocyte**s undergo **meiosis I**, forming two haploid cells called **secondary spermatocytes**
- Secondary spermatocytes undergo **meiosis II** and their daughter cells are called **spermatids**
- Spermatids are small round cells seen close to the lumen of the tubule



Spermiogenesis: Spermatids to Sperm

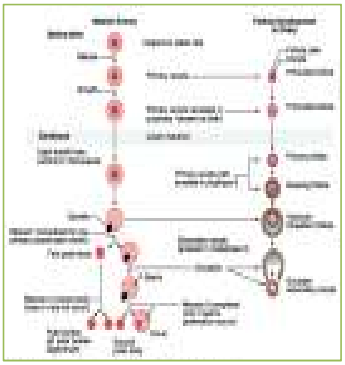
- Late in spermatogenesis, spermatids are **haploid** but are **nonmotile**
- **Spermiogenesis** – spermatids lose excess cytoplasm and form a tail, becoming sperm
- Sperm have three major regions
  - **Head** – contains DNA and has a helmetlike **acrosome** containing **hydrolytic enzymes** that allow the sperm to penetrate and enter the egg
  - **Midpiece** – contains mitochondria spiraled around the tail filaments
  - **Tail** – a typical flagellum produced by a centriole



Oogenesis

- Production of female sex cells by meiosis
- In the **fetal period,** oogonia (2*n* ovarian stem cells) multiply by mitosis and store nutrients
- **Primordial follicles** appear as oogonia are transformed into **primary oocytes**
- **Primary oocytes** begin meiosis **but stall in prophase I.**
- **At puberty,** one activated **primary oocyte** produces two haploid cells
  - **The first polar body**
  - **The secondary oocyte**

- The secondary **oocyte arrests** in metaphase II and is **ovulated**
- If penetrated by sperm:
  - The second oocyte **completes meiosis II,** yielding:
    - **One large ovum** (the functional gamete)
    - A tiny second **polar body**

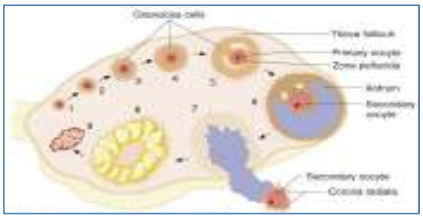


Ovarian Cycle

- Monthly series of events associated with the maturation of an egg
- **Follicular phase** – period of follicle growth (days 1–14)
- **Luteal phase** – period of **corpus luteum** activity (days 14–28)
- Ovulation occurs **midcycle**

Follicular Phase

- The **secondary follicle** becomes a **vesicular follicle**
  - The **antrum** expands and isolates the **oocyte** and the **corona radiata**
  - The full-size follicle (vesicular follicle) bulges from the external surface of the ovary
  - The **primary oocyte** completes meiosis I, and the stage is set for **ovulation**



Ovulation

- Under the influence of **estrogen released during the first half of the menstrual cycle**, three changes take place in the uterine tubes to facilitate its capture of the egg:
  1. The uterine tubes move closer to the ovaries (**physical approximation**)
  2. The fimbriae on the ends of the tubes beat more rapidly (**increased fluid current**)
  3. The number of ciliated cells in the epithelium of the fimbriae increase (**increase in ciliation**)

Luteal Phase

- After **ovulation,** the ruptured follicle collapses, **granulosa cells** enlarge, and along with internal **thecal cells**, form **the corpus luteum**
- The corpus luteum secretes **progesterone** and **estrogen**
- If **pregnancy does not occur**, the corpus luteum degenerates in 10 days, leaving a scar (**corpus albicans**)
- If **pregnancy does occur**, the corpus luteum produces hormones until the placenta takes over that role (at about 3 months)

Establishing the Ovarian Cycle

- During childhood, ovaries grow and secrete small amounts of **estrogens** that **inhibit the hypothalamic release of GnRH**
- **As puberty** nears, **GnRH** is released; **FSH** and **LH** are released by the pituitary, which act on the ovaries
- These events continue until an adult cyclic pattern is achieved and **menarche** occurs

Hormonal Interactions During the Ovarian Cycle

- **Day 1** – **GnRH** stimulates the release of **FSH** and **LH**
- **FSH** and **LH** stimulate follicle growth and maturation, and low-level estrogen release
- Rising estrogen levels:
  - **Inhibit the release of FSH and LH**
  - **Prod the pituitary to synthesize and accumulate these gonadotropins**
- Estrogen levels increase and high estrogen levels have a positive feedback effect on the pituitary, causing a sudden **surge of LH**

- The **LH spike simulates** the primary oocyte to complete meiosis I, and the secondary oocyte continues on to metaphase II
- Day 14 – LH **triggers ovulation**
- LH transforms the ruptured follicle into a **corpus luteum**, which produces **inhibin**, **progesterone**, and **estrogen**
- These hormones **shut off FSH** and **LH release** and declining LH ends luteal activity
- Days 26-28 – decline of the ovarian hormones
  - Ends the **blockade of FSH and LH**
  - **The cycle starts anew**

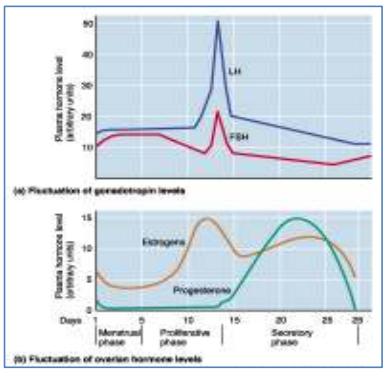
Uterine (Menstrual) Cycle

- Series of cyclic changes that the **uterine endometrium goes** through each month in response to **ovarian hormones** in the blood
- **Days 1-5: Menstrual phase** – uterus sheds all but the deepest part of the endometrium
- **Days 6-14: Proliferative phase** – endometrium rebuilds itself
- **Days 15-28: Secretory phase** – Endometrium prepares for implantation of the embryo

Menses

- If **fertilization does not** occur, **progesterone levels fall**, depriving the endometrium of hormonal support
- **Spiral arteries** kink and go into spasms and endometrial cells begin to die
- The functional layer begins to **digest itself**
- **Spiral arteries** constrict one final time then suddenly relax and open wide
- The rush of blood fragments weakened capillary beds and the **functional layer sloughs**

Gonadotropins, Hormones, and the Ovarian and Uterine Cycles



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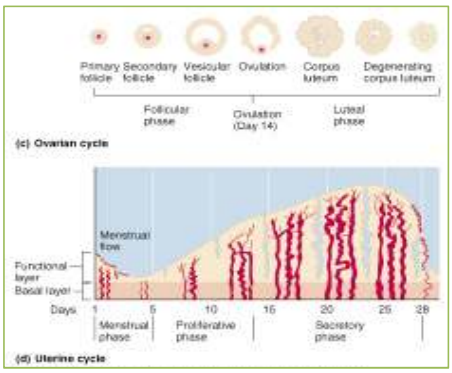


Female Sexual Response

- The **clitoris**, vaginal mucosa, and breasts engorge with blood
- **Vestibular glands** lubricate the vestibule and facilitate entry of the **penis**
- **Orgasm** – accompanied by muscle tension, increase in pulse rate and blood pressure, and **rhythmical contractions** of the uterus
- **Females** do not have a refractory period after orgasm and can experience multiple orgasms in a single sexual experience
- **Orgasm** is not essential for conception

Transport of Sperm in Female

- Sperm are deposited in the upper vagina and must overcome several obstacles to reach an egg in the **ampulla** of one of the **uterine tubes**.
- Sperm lose their ability to fertilize an egg after **3 - 3½ days**.
- The egg itself is viable for only about **24 hours**.

Aneuploidy

- Aneuploidy is an abnormal number of chromosomes that can result from either **unbalanced chromosomal translocations** or **nondisjunction during meiosis II**.
- Most chromosomal abnormalities are incompatible with life.
- However, some combinations do result in live offspring, and trisomies involving chromosomes 13, 14, 15, 21 and 22 (groups D and G chromosomes) are relatively common birth defects.

Abnormality Karyotype

- Down Syndrome: Trisomy 21
- Turner Syndrome: X
- Triple-X Syndrome: XXX
- Klinefelter Syndrome: XXY
- Jacob Syndrome: XYY

Turner Syndr

Monosomy X (45,X). Characteristically broad, "webbed" neck. Stature reduced, edema in ankles and wrists.

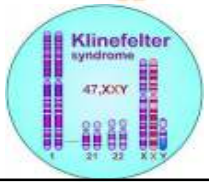
Relatively normal lives – but no functional ovaries. 1 in 6,000 birth affected.

Klinefelter Syndron

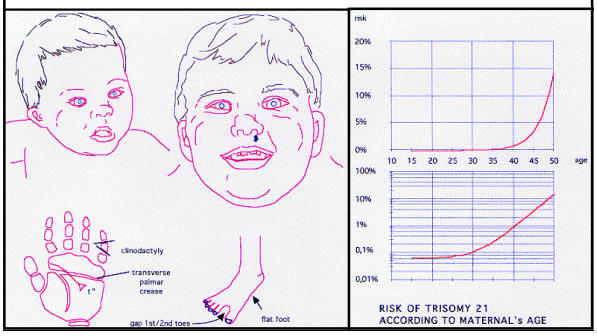
XXY karyotype. Non-disjunction in meiosis (maternal or paternal) ⇒ ovum: XX; sperm: XY

Usually normal – may be tall and have small testes. Infertility due to absent sperm.

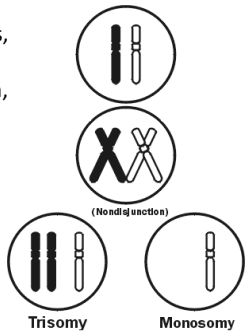
1 in 1,500 males affected.



TRISOMY 21: Most frequent viable autosomal aneuploidy



- **Down syndrome** results from **trisomy 21** that occurs in approximately **1/500** live births, and is characterized by growth retardation, mental retardation, and specific somatic abnormalities.
- **Aneuploidy of the sex chromosomes** can also occur, and certain karyotypes are associated with characteristic syndromes.

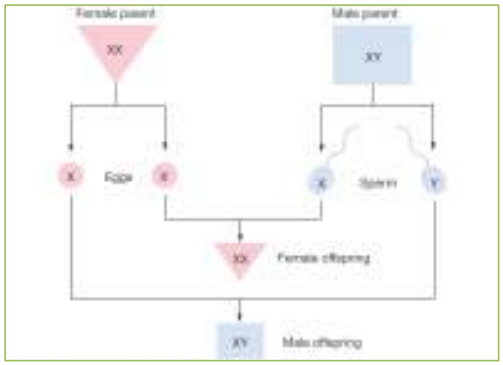


Syndromes Associated with Aneuploidy of the Sex Chromosomes

Karyotype	Syndrome	Frequency	Description
45,X (XO)	Turner syndrome	1/5000 female live births	Phenotypic female, gonadal dysgenesis and sexual immaturity after puberty, infertility
XXY	Klinefelter's syndrome	1/1000 male live births	Phenotypic male, gonadal dysgenesis and sexual immaturity after puberty, infertility
XYY (XXYY)	XYY syndrome	1/1000 male live births	Phenotypic male, behavioral abnormalities

Determination of Gender

- Although genetic sex (XX or XY) is determined at fertilization, the embryo's gender is not distinguishable for the first six weeks of development.
- This is known as the **indifferent period of development**.
- Characteristics of either **male** or **female genitalia** can often be **recognized by week twelve** of development.



Sex Determination

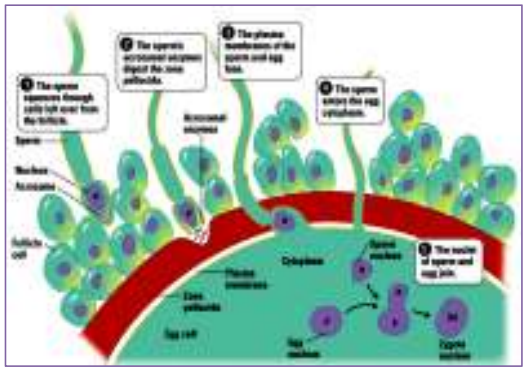
- **Early gonad** (< 6 weeks) is bipotential (indifferent gonad)
  - **SRY** (Sex-determining Region of Y chromosome) gene on Y-chromosome codes for a protein that directs the gonad to become a **testis**
  - If **no SRY**, gonad becomes **ovary.**
  - Note that sex hormones are not yet produced!
- Testes produce **Anti-Mullerian Hormone, Testosterone** and **DHT** which results in the development of male accessory organs
- Ovaries develop due to absence of **SRY** and **AMH**
  - **Estrogen** directs development of f**emale accessory organs**

FIRST WEEK (DAY 1-7)

BEGINNING OF HUMAN DEVELOPMENT

Fertilization

- At **ovulation**, a secondary **oocyte**, **zona pellucida**, and **corona radiata** of follicle cells are discharged from the ovary and drawn into the **infundibulum** of the uterine tube.
- Here, a **spermatozoan** can penetrate the **zona pellucida** and **secondary oocyte**.
- In this process, **acrosome enzymes aid** in the penetration of **corona radiata** and **zona pellucida,** and **a cytoplasmic response** of the **secondary oocyte** leads to a **zonal reaction** that prevents the penetration of other spermatozoa.



Capacitation

- Changes take place in the **glycoprotein coat** of sperm as they travel up the female reproductive tract.
- These changes are absolutely essential for fertilization.
- Thus, to perform successful *in vitro* fertilization you must add some tissue extracted from the female reproductive tract in addition to the sperm and egg extracted from the parents.
- Only a tiny fraction of sperm actually reaches the **ampulla** of the **uterine tube** to be near the egg.

Penetration of Corona Radiata and Zona Pellucida

- The sperm uses both **chemical** and **physical means** to penetrate the **egg's corona radiata**:
  1. **The action of membrane-bound enzyme hyaluronidase on its coat, and**
  2. **Swimming motion of its flagellum.**
- Once inside the corona radiata, the sperm binds to the **species-specific ZP_3 receptor** on the **egg's glycoprotein coat**.

Acrosomal Reaction,

- This triggers the **acrosomal reaction,** or the release of enzymes stored in the sperm's acrosome (e.g. **acrosin**).
- These enzymes help the sperm penetrate the **zona pellucida**.
- Once the sperm has penetrated the outer layers it fuses with the plasma membrane of the egg and releases its contents inside.
- The head and the tail of the sperm degrade, so that **all mitochondria** in the embryo **(and all mitochondrial DNA) come from the mother**.

Cortical Reaction

- Entry of a sperm into the egg triggers changes that prevent **polyspermy** (fertilization of an egg by more than one sperm).
- These changes are known as the **cortical reaction** and include the following as represented in the following table..

Phase	Description
Fast block	**Electrical depolarization of the egg's surface** (–70Mv +10Mv) works for a short time to repel other sperm electrostatically.
Slow block	A wave of Ca^{++} ions released from the point of sperm entry spreads through the egg. This causes **cortical granules in the egg to release their contents**. Polysaccharides in the cortical granules reach the outside of the egg and form a physical barrier to sperm penetration. Enzymes in the granules break down the ZP3 receptors in the zona pellucida and also further harden the coat.

Fusion of Pronuclei

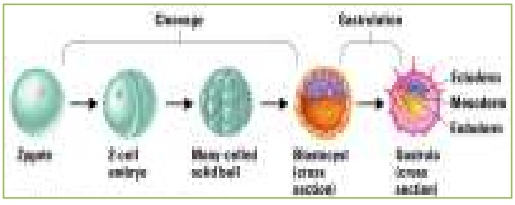
- DNA in the **male pronucleus** is packed very tightly with **protamines** to make it compact enough to fit inside a sperm.
- These protamines are replaced by **histones** inside the egg, unpacking the **DNA.**
- Afterwards the male and female **pronuclei fuse** and the egg completes **its second mei**otic division, resulting in a second **polar body**.
- The **fertilized egg** is now known as the **zygote** ("together").

Consequences of Fertilization

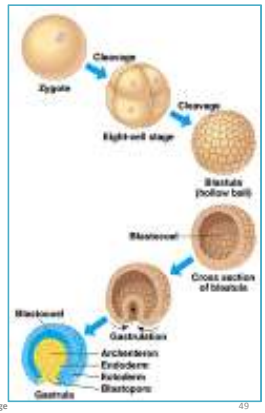
- The **union** of the **spermatozoan** and the **secondary oocyte** in the process of **fertilization** brings about the following major physical consequences:
  1. Reactivation of the secondary oocyte
  2. Completion of the second meiotic division with formation of the second polar body
  3. Establishment of the **zygote** (fertilized ovum) with diploid number(46) of chromosomes.
  4. Establishment of the **meiotic spindle** for the first cleavage division, and
  5. The **determination of the gender** of the new individual.

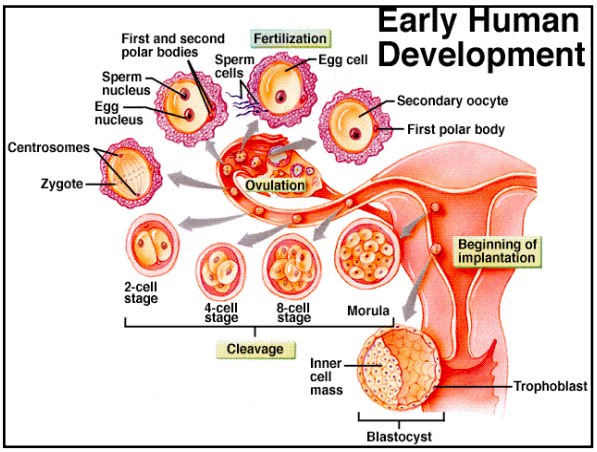
Cleavage

- The zygote undergoes a number of **ordinary mitotic divisions** that increase the number of cells in the zygote but not its overall size.
- Each cycle of division takes about 24 hours.
- The individual cells are known as **blastomeres**.



- At the 32-cell stage the embryo is known as a **morula** (L. “mulberry”), a solid ball consisting of an **inner cell mass** and an **outer cell mass**.
- The **inner cell mass** will eventually become the **embryo and fetus**, while the **outer cell mass** will eventually become part of the **placenta**.



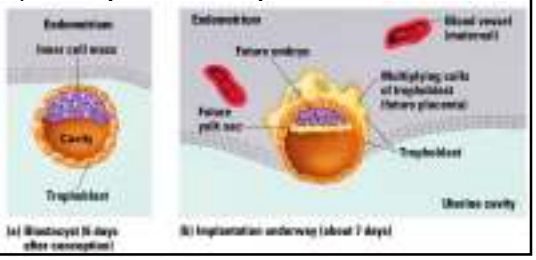


Blastocyst Formation

- **Compaction**
  - The **cells on the outside of the morula form tight intercellular junctions** and express ion channels to create an impermeable barrier.
- **Cavitation**
  - **A fluid-filled cavity forms inside the morula**.
  - This cavity is known as the **blastocyst cavity** or **blastocoele**, and the morula is now called a **blastula** or **blastocyst**.
  - The inner cell mass is now known as the **embryoblast** and the outer cell mass becomes the **trophoblast**.

Implantation

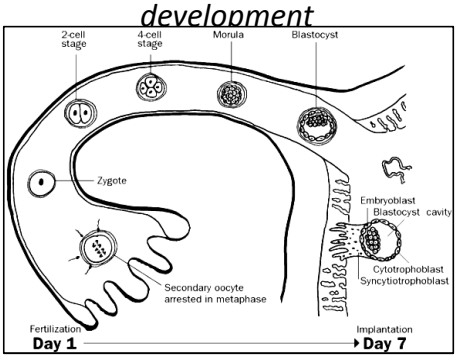
- **The blastula sheds its zona pellucida**.
- This is required for implantation to occur.
- One function of the **zona pellucida** is to prevent **premature implantation.**



Attachment and Invasion

- The embryo attaches to and invades into the maternal endometrium.
- The trophoblast differentiates into the **cytotrophoblast** and the **syncytiotrophoblast**.
- The **embryo typically implants in the posterior superior wall of the uterus**.
- The response of the maternal endrometrial cells to the invading embryo is called the **decidual reaction**.

Summary of the first week of development



Ectopic Pregnancy

- The **bastocyst implants** in a location other than the uterus.
- This can present as an **acute surgical emergency** for the mother after the fetus begins to outgrow its confines:
- *Common Sites of Ectopic Pregnancy are indicated in the following Table*

Site of implantation	Likely reason
Upper and middle part of the uterine tube	Embryo probably lost its zona pellucida prematurely. Most common ectopic location.
Ovary	The egg was never released from the ovary.
Abdominal cavity	Probably caused by defect in egg capture process. Rarely, an asymptomatic ectopic fetus can die and calcify to become a **lithopedeon** ("stone baby").

Placenta Previa

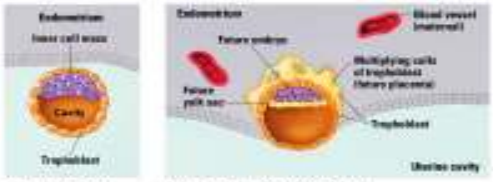
- The embryo implants in the **lower part of the uterus towards the cervix**.
- This makes it easy for the placenta to tear, and the mother can die from hemorrhage, or the placenta may grow to obstruct the cervical canal.
- This is diagnosed with ultrasound, and the baby is delivered via Cesarean section.

SECOND WEEK (DAY 8-14)

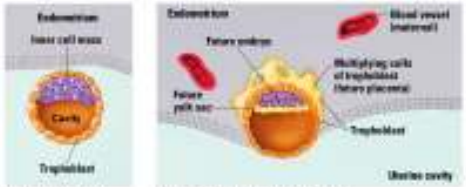
FORMATION OF THE BILAMINAR EMBRYONIC DISC

Trophoblast

- As the **blastocyst embeds** itself in the endrometrium it differentiates into two layers:
  1. the **cytotrophoblast** (inner)
  2. and **syncytiotrophoblast** (outer).
- The **syncytiotrophoblast** invades into the **maternal endometrium,** and in this sense it is more invasive than any tumor tissue.

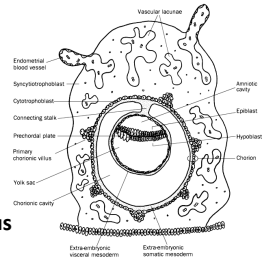


- As it comes into contact with blood vessels it creates **lacunae**, or spaces which fill with maternal blood.
- These lacunae fuse to form **lacunar networks**.
- The maternal blood that flows in and out of these networks exchanges nutrients and waste products with the fetus, forming the basis of a **primitive uteroplacental circulation**.



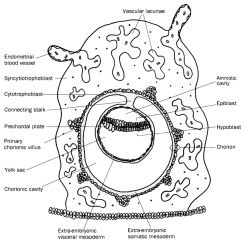
Syncytiotrophoblast

- The syncytiotrophoblast is **acellular** and does not expand mitotically.
- The syncytiotrophoblast produces **human chorionic gonadotrophin** (hCG), a glycoprotein hormone that stimulates the production of **progesterone** by the **corpus luteum**.



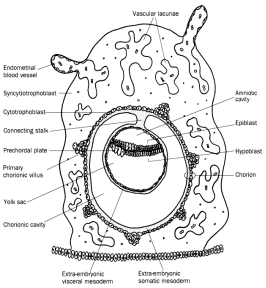
Cytotrophoblast

- The **cytotrophoblast** is cellular and expands mitotically into the syncytiotrophoblast to form **primary chorionic villi**.
- Cells from these villi can be removed for early genetic testing at some risk to the fetus (**chorionic villus sampling**).



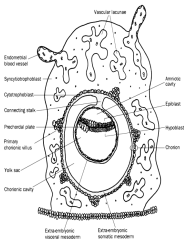
Embryoblast

- After implantation, the **inner cell mass** subdivides into a bilaminar disc consisting of the **hypoblast** and **epiblast**.



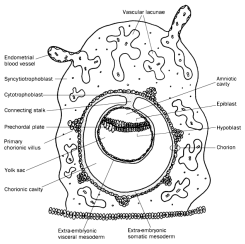
Hypoblast

- Hypoblast cells migrate along the inner surface of the cytotrophoblast and will form the **primary yolk sac**.
- The primary yolk sac becomes reduced in size and is known as the **secondary yolk sac**.
- In humans the yolk sac **contains no yolk** but is important for the transfer of nutrients between the fetus and mother.



Epiblast

- Epiblast cells cavitate to form the **amnion**, an extra-embryonic epithelial membrane covering the embryo and amniotic cavity.
- Cells from the epiblast will also eventually form the **body** of the embryo.



Extra-embryonic Mesoderm

- Extra-embryonic mesoderm cells migrate between the **cytotrophoblast** and **yolk sac** and **amnion.**
- **Extraembryonic somatic mesoderm** lines the cytotrophoblast and covers the amnion is.
- **Extraembryonic somatic mesoderm** also forms the **connecting stalk** that is the primordium of the **umbilical cord**.
- **Extraembryonic visceral mesoderm** covers the yolk sac.
- At the end of the second week it is possible to distinguish the dorsal (amniotic cavity) from the ventral (yolk sac) side of the embryo.

Clinical Correlations

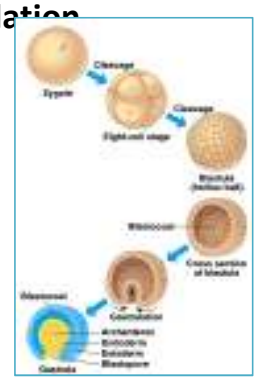
- **Early pregnancy testing**
- hCG produced by the syncytiotrophoblast can be detected in maternal blood or urine as early as **day 10** of pregnancy and is the basis for pregnancy tests.
- **Hydatidiform mole**
- A blighted blastocyst leads to death of the embryo, which is followed by hyperplastic proliferation of the trophoblast within the uterine wall.
- **Choriocarcinoma**
- A malignant tumor arising from trophoblastic cells that may occur following a normal pregnancy, abortion, or a hydatidiform mole.

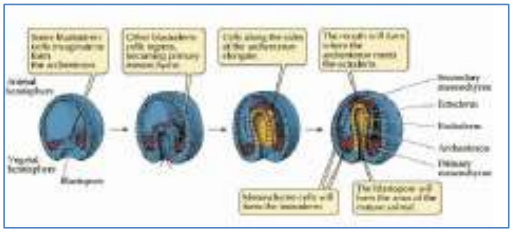
WEEK 3-8
EMBRYONIC PERIOD

- **Third Week** is involved in the **formation of the Human Embryo**
- The **Fourth to the Eighth Week** is concerned with **the Development** of **Tissues. Organ, and Form**

Gastrulation

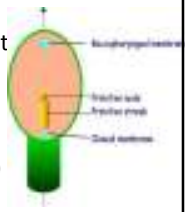
- Gastrulation is the conversion of the epiblast from a bilaminar disc into a **trilaminar embryonic disc** consisting of **ectoderm**, **mesoderm**, and**endoderm**.
- Gastrulation begins with the formation of the **primitive streak**.





Primitive Streak

- The **primitive streak** is a **linear band of thickened epiblast** that first appears at the **caudal** end of the embryo and **grows cranially**.
- At the cranial end its cells proliferat to form the **primitive knot** (**primitive node)**.
- With the appearance of the **primitive streak** it is possible to **distinguish cranial** (primitive knot) and caudal (**primitive streak**) ends of the **embryo**.



Notochordal Process

- Mesenchymal cells migrate from the primitive knot to form a midline cellular cord known as the **notochordal process**.
- The notochordal process grows cranially until it reaches the prechordal plate, the future site of the **mouth**.
- In this area the ectoderm is attached directly to the endoderm without intervening mesoderm.
- This area is known as the **oropharyngeal membrane**, and it will break down to become the **mouth**.
- At the other end of the primitive streak the ectoderm is also fused directly to the endoderm.
- This is known as the **cloacal membrane** (**proctodeum)**, or primordial **anus**.

Notochord

- The **notochord** is a cellular chord that develops by transformation of the **notochordal process**.
- The **notochord** will eventually become the ***nucleus pulposis*** of each **intervertebral disk**.
- The **embryonic three germ layers** give rise to the **many tissues** and **organs of the embryo:**

Ectoderm: Adult Derivatives of the Surface ectoderm

- Lens of eye
- Adenohypophysis (anterior pituitary gland)
- Utricle, semicircular ducts, and vestibular ganglion of CN VIII
- Epithelial lining of external auditory meatus
- Olfactory placode.

- Epithelial lining of: anterior two thirds of tongue, the hard palate, sides of the mouth, ameloblasts, and parotid glands and ducts
- Mammary glands
- Epithelial lining of lower anal canal
- Epithelial lining of distal penile urethra
- Epidermis, hair, nails, sweat and cutaneous sebaceous glands

Ectoderm: Adult Derivatives of Neuroectoderm

- All neurons within the CNS
- All glial (supporting) cells within the CNS
- Retina
- Pineal gland
- Neurohypophysis (posterior pituitary gland)

Ectoderm: Adult Derivatives of Neural Crest

- Postganglionic sympathetic neurons within the sympathetic chain ganglia and prevertebral ganglia
- Postganglionic parasympathetic neurons within the ciliary, pterygopalatine, submandibular, otic, enteric ganglia, and ganglia of the abdominal and pelvic cavities
- Sensory neurons within the dorsal root ganglia, Schwann cells
- Pia mater and arachnoid membrane
- Chromaffin cells of the adrenal medulla
- Melanocytes

- Bony structures of the face and neck: Maxilla, zygomatic bone, palatine bone, vomer, mandible, hard palate, incus, malleus, stapes, sphenomandibular ligament, styloid process, stylohyoid ligament, hyoid bone, frontal bone, parietal bond, sphenoid bone, and ethmoid bone
- Odontoblasts
- Aorticopulmonary septum
- Parafollicular cells of thyroid
- Dilator and sphincter pupillae muscles
- Ciliary muscle
- Carotid body

Mesoderm: Adult Derivatives of Paraxial mesoderm

- Skeletal muscles of trunk
- Skeletal muscles of limbs
- Skeletal muscles of head and neck
- Extraocular muscles
- Intrinsic muscles of tongue
- Vertebrae and ribs
- Cranial bone
- Dermis
- Dura mater

Mesoderm: Adult Derivatives of Intermediate mesoderm

- Kidneys
- Testes and ovaries
- Genital ducts and accessory sex glands

Mesoderm: Adult Derivatives of Lateral mesoderm

- Sternum, clavicle, scapula, pelvis, and bones of the limbs
- Serous membranes of body cavities
- Lamina propria, muscularis mucosae, submucosa, muscularis externae, and adventitia of the gastrointestinal tract

- Blood cells, microglia, Kupffer cells
- Cardiovascular system
- Lymphatic system
- Spleen
- Suprarenal cortex
- Laryngeal cartilages

Adult Derivatives of Endoderm

- Epithelial lining of the auditory tube and middle ear cavity
- Epithelial lining of the posterior third of the tongue, floor of the mouth, palatoglossal and palatopharyngeal folds, soft palate, crypts of the palatine tonsil, and sublingual and submandibular glands and ducts
- Principal and oxyphil cells of the parathyroid glands
- Epithelial reticular cells and thymic corpuscles
- Thyroid follicular cells

- Epithelial lining and glands of the trachea, bronchi, and lungs
- Epithelial lining of the gastrointestinal tract
- Hepatocytes and epithelial lining of the biliary tree
- Acinar cells, islet cells, and the epithelial lining of the pancreatic ducts
- Epithelial lining of the urinary bladder
- Epithelial lining of the vagina
- Epithelial lining of the female urethra and most of the male urethra

Development of Somites

- As the notochord and neural tube form, the mesoderm alongside them forms longitudinal columns called **paraxial mesoderm**.
- These columns divide into paired cubical bodies called **somites**.
- The somites develop in pairs; the first pair develops near the cranial end of the notochord around the end of the third week.

- Additional pairs of somites develop in a caudal direction from days 20 to 30 (**period of somite development**) and the number of somites is sometimes used as a criterion for determining an embryo's age.
- The somites give rise to most of the axial skeleton (vertebral column, ribs, sternum, and skull base) and associated musculature, as well as to the adjacent dermis.

PLACENTA AND EXTRAEMBRYONIC MEMBRANES

- The placenta is a fetomaternal organ.
- The fetal portion of the placenta is known as the **villous chorion**.
- The maternal portion is known as the **decidua basalis**.
- The two portions are held together by **anchoring villi** that are anchored to the decidua basalis by the cytotrophoblastic shell.

Decidua

- The endometrium (lining of the uterus) of the mother is known as the **decidua** ("cast off"), consisting of three regions named by location.

Region	Description
Decidua basalis	Region between the blastocyst and the myometrium
Decidua capsularis	Endometrium that covers the implanted blastocyst
Decidua parietalis	All the remaining endometrium

- As the embryo enlarges, the decidua capsularis becomes stretched and smooth. Eventually the decidua capsularis merges with the decidua parietalis, obliterating the uterine cavity.

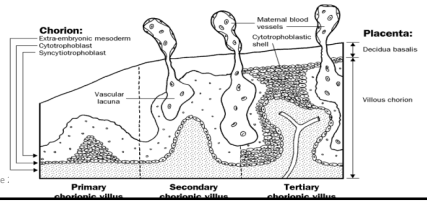
Placental Membrane: Functions

- The **placental membrane** separates maternal blood from fetal blood.
- The fetal part of the placenta is known as the **chorion**.
- The maternal component of the placenta is known as the **decidua basalis**.
- **Oxygen and nutrients** in the maternal blood in the intervillous spaces diffuse through the walls of the villi and enter the fetal capillaries.

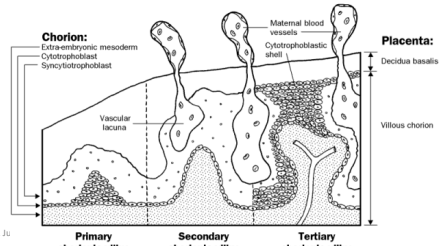
- **Carbon dioxide and waste products** diffuse from blood in the fetal capillaries through the walls of the villi to the maternal blood in the intervillous spaces.
- Although the placental membrane is often referred to as the **placental barrier**, many substances, both helpful and harmful, can cross it to affect the developing embryo.

Placental Membrane: Structure

- **Primary chorionic villi are solid** outgrowths of cytotrophoblast that protrude into the syncytiotrophoblast.
- **Secondary chorionic villi have a core of loose connective tissue**, which grows into the primary villi about the third week of development.



- **Tertiary chorionic villi contain embryonic blood vessels** that develop from mesenchymal cells in the loose connective tissue core.
- These blood vessels connect up with vessels that develop in the chorion and connecting stalk and begin to circulate embryonic blood about the **third week** of development.



Amniotic Fluid

- Amniotic fluid has three main functions:
1. it protects the fetus physically,
2. it provides room for fetal movements, and
3. helps to regulate fetal body temperature.
- Amniotic fluid is produced by **dialysis of maternal and fetal blood** through blood vessels in the placenta.
- Later, production of **fetal urine** contributes to the volume of amniotic fluid and **fetal swallowing** reduces it.
- The water content of amniotic fluid turns over every three hours.

Umbilical Cord

- The umbilical cord is a composite structure formed by contributions from:
  - Fetal connecting (body) stalk
  - Yolk sac
  - Amnion
- The umbilical cord contains the **right** and **left umbilical arteries**, the **left umbilical vein**, and mucous connective tissue.
- Presence of only one umbilical artery may suggest the presence of cardiovascular anomalies.

Multiple Pregnancy: **Dizygotic Twins**

- **Dizygotic twins** are derived from two zygotes that were fertilized independently (i.e., two oocytes and two spermatozoa).
- Consequently, they are associated with two amnions, two chorions, and two placentas, which may (65%) or may not (35%) be fused.
- Dizygotic twins are only as closely genetically related as any two siblings.

Multiple Pregnancy: **Monozygotic twins**

- **Monozygotic twins** (30%) are derived from one zygote that splits into two parts.
- This type of twins commonly has two amnions, one chorion, and one placenta.
- If the embryo splits early in the second week after the amniotic cavity has formed, the twins will have one amnion, one chorion, and one placenta.
- Monozygotic twins are genetically identical, but may have physical differences due to differing developmental environments (e.g., unequal division of placental circulation).

Placenta Previa

- The fetus implants in such a way that the placenta or fetal blood vessels grow to block the internal os of the uterus.

Erythroblastosis Fetalis

- Some erythrocytes produced in the fetus routinely escape into the mother's systemic circulation.
- When fetal erythrocytes are Rh-positive but the mother is Rh-negative, the mother's body can form antibodies to the Rh antigen, which cross the placental barrier and destroy the fetus.
- The immunological memory of the mother's immune system means this problem is much greater with second and subsequent pregnancies.