Human Growth and Development Reviewer

Chapter 1: Gametogenesis

Gametogenesis
- Process of forming male (sperm) and females (oocyte/egg)
- Starts from Primoridial Germ Cell (PGCs)

Primordial Germ Cells
- Development begins with fertilization
- Male gamete (sperm) and female gamete (oocyte) give rise to a zygote

Chromosome theory of inheritance
- Traits of a new individual are determined by specific genes on chromosomes inherited from the father and the mother
- Humans have approximately 35,000 genes on 46 chromosomes

Mitosis
- The process where one cell divides
- Giver rise to 2 daughter cells (genetically identical to parent cells) = 24 chromosomes
- Each chromosomes replicates its deoxyribonucleic acid (DNA) “photocopy”
- Replication phase

Phases of Mitosis
- **Prophase - “Pack”** chromosome coils and condense DNA **“Prepare”** Spindle fibers form to move chromosomes
- 2 sister chromatids, joined together at the centromere
- **Metaphase-** Chromosome line up at the equatorial plane
- Each attached by microtubules extending from centromere to centriole, forming mitotic spindle
- Centromere of each chromosome divides, marks the beginning of **Anaphase**

- **Anaphase-** Migration of chromatids to opposite poles of the spindle

- **Telophase-** Chromosomes have reached the opposite side of the cell. Uncoils, Cytoplasm divides, produces 2 daughter cells.

Meiosis 1
- Male and female germ cells replicates their DNA at the beginning
- Each of the 46 chromosomes is duplicated into sister chromatids
- Homologous chromosomes align themselves in pairs
- “Synapsis”
- **Cross over-** Prophase 1 of meiosis, homologous chromosomes exchange pieces of DNA. New combinations of genetic information, the chiasma is the X-shaped poin where exchange occurs

Meiosis 2
- the 2 cells from meiosis divide again
- The sister chromatids separate
- Each cell divides into 2

  Results: 4 cells total, 23 chromosomes each, each chromosome has 1 chromatid

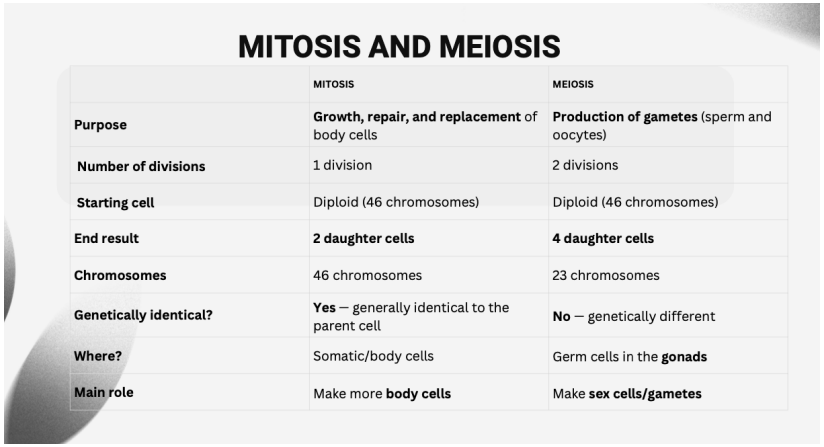
Polar Bodies

Oogenesis (female)

- 1 primary oocyte
- Only 1 becomes mature oocyte
- The other 3 polar bodies disappear

Spermatogenesis

- 1 primary spermatocyte
- All 4 become sperm cells
- 2 sperm carry X, 2 sperm carry Y



MITOSIS AND MEIOSIS

	MITOSIS	MEIOSIS
Purpose	**Growth, repair, and replacement** of body cells	**Production of gametes** (sperm and oocytes)
Number of divisions	1 division	2 divisions
Starting cell	Diploid (46 chromosomes)	Diploid (46 chromosomes)
End result	**2 daughter cells**	**4 daughter cells**
Chromosomes	46 chromosomes	23 chromosomes
Genetically identical?	**Yes** – generally identical to the parent cell	**No** – genetically different
Where?	Somatic/body cells	Germ cells in the **gonads**
Main role	Make more **body cells**	Make **sex cells/gametes**

Chromosomal and Genetic Abnormalities

- chromosomal abnormalities are a major cause of congenital malformations and spontaneous abortions.

A. Numerical

- occur due to nondisjunction (failure of homologous chromosomes and chromatids to separate) during meiosis.

1. Trisomy 21 (Down Syndrome)

- extra copy of **<u>chromosomes 21</u>**
- Usually caused by meiotic nondisjunction
- **MANIFESTATIONS**
  - growth and development
  - intellectual disability
  - upward-slanting eyes and epicanthal folds
  - flats facial appearance
  - small ears
  - Hypotonia
  - congenital heart defects
  - increased risk of infections, leukemia, and thyroid problems
  - increased risk of Alzheimer later in life

2. Trisomy 18(Edward's Syndrome)

- Those born alive usually die by age 2 months
- Incidence: **1 in 5000** newborns

- **Features:**
  - Mental retardation
  - Congenital heart defects
  - Low-set ears
  - Flexion of fingers and hands

- micrognathia, renal anomalies, syndactyly, and malformations of the skeletal system

3. Trisomy 13 (Patau Syndrome)

- Incidence: **1 in 20,000 live births**
- Over 90% of infants die in the first month after birth

- Features
  - mental retardation
  - holoprosencncephaly
  - congenital heart defects
  - deafness
  - cleft lip and palate

4. Klinefelter Syndrome

- **Incidence: 1 in 500 males**
- Patients have **48 chromosomes:** 44 autosomal and 4 sex chromosomes (XXXY)
- **(+) Barr Body / Sex Chromatin Body**
  - Formed by condensation of an inactive PDAX sex chromosomes

- clinical features found only in males and usually detected during puberty

- sterility
- testicular atrophy
- hyalinization of seminiferous tubules
- gynecomastia

- **Turner Syndrome**

- The only Monosomy compatible with life
- Patients appear <u>female</u> in appearance
- Characterized by the absence of ovaries (gonadal dysgenesis) and a short stature

- **Features:**

- Webbed neck
- Lymphedema of the extremities
- skeletal deformities
- a broad chest with widely spaced nipples

B. STRUCTURAL ABNORMALITIES

- usually result from chromosomal breakage
- Breaks are caused by environmental factors (viruses, radiation, drugs)
- Partial deletion
  - Broken piece of a chromosome is lost and the infants with partial deletion of a chromosome is abnormal

CRI-DU-CHAT SYNDROME

- Partial Deletion of the short arm of chromosome 5
- Features:
  - cat liken
  - Microcephaly
  - Mental retardation
  - Congenital heart disease

ANGELMAN SYNDROME

- Deletion on the maternal chromosome

- **Features:**
  - Mental retardation
  - Cannot speak

- Poor motor development
- Prone to unprovoked and prolonged periods of laughter

PRADER-WILLI SYNDROME

- Deletion on the paternal chromosome

- Features:
  - Hypotonia
  - Obesity
  - Mental
  - retardation
  - Hypogonadism
  - Cryptorchidism

MILLER-DIEKER SYNDROME

- Deletion on either parental chromosome
- Features:
  - Lissencephaly
  - Developmental delay
  - Seizures
  - Cardiac and facial abnormalities

SHPRINTZEN SYNDROME

- Deletion on either parental chromosome
- **Features:**
  - Palatal defects
  - Conotruncal heart defects
  - Speech delay
  - Learning disorders
  - Schizophrenia-like disorder

FRAGILE X SYNDROME

- CGG repeats on the site on the long arm of the **X chromosome**
- **Males** are affected more than females
- Second to Down Syndrome as a cause of mental retardation because of chromosomal abnormalities
- Features:
  - Mental retardation
  - Large ears
  - Prominent jaw Pale
  - blue irise

Morphological changes during maturation of gametes (oogenesis and spermatogenesis)

Oogenesis 1

- Maturation of Oocytes begins before birth
- Primordial germ cell (PGCs) migrate to the female gonad and differentiate into Oogonia
- Follicular cells originate from the ovarian surface and form clusters around oogonia
- Primary oocytes form when oogonia stop dividing by mitosis and arrest in prophase of meiosis 1
- Primoridial follicle consists of one surviving oocye surrounded by a single layer of flat epithelial follicular cells

Oogenesis 2

- **Maturation of oocytes continues at puberty**
- Primary oocytes enter the biplotene stage
- Due to Oocyte Maturation Inhibitor (OMI)- a substance secreted by follicular cells

Oocyte number and aging
- At birth: 700,000-2 million total number of primary oocytes
- Beginning of puberty: 400,000 are present
- Increase maternal age= high risk and vulnerable to damages

Follicular development
- As primary oocyte begins to grow — Surrounding follicular cells change from flat to cuboidal and produce a stratified epithelium of granulosa cells — becomes a primary follicle

Follicle structure
- Granulosa cells rest on a basement membrane separating them from surrounding stromal cells that form theca folliculi
- Granulosa cells and the oocyte secrete a layer of glycoproteins on the surface of the oocyte, forming zona pellucida
- Zona Pellucida- Glycoproteins

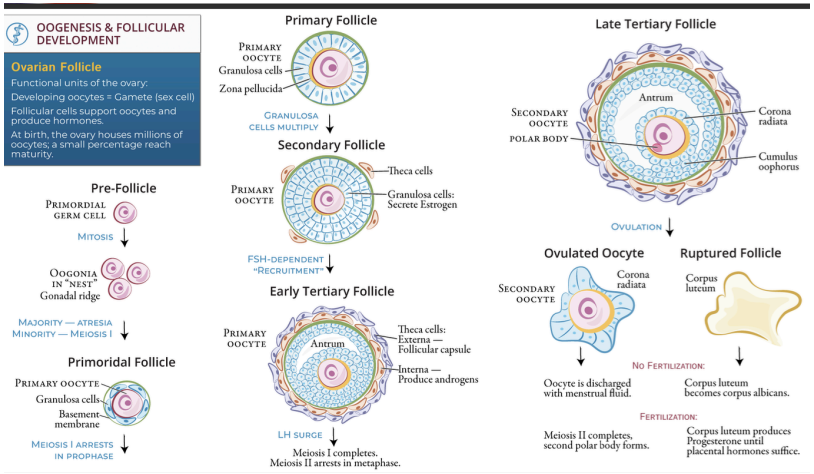
Theca layers
- As the follicles continue to grow, cells of the theca folliculi organize into:
- Theca interna - inner layer of secretory cells, composed of cells having characteristics of steroid secretion, rich in blood vessels.
- Theca externa - outer fibrous capsule, gradually merges with the ovarian stroma

Secondary Follicle
- As development continues, fluid filled spaces appear between granulosa cells and the follicle becomes a secondary follicle
- At maturity, the secondary follicle may be 25 mm or more in diameter

Ovulation and meiosis
- When matures, a surge in Luteinizing Hormone (LH) induces a preovulatory growth phase
- Meiosis 1 is completed
- Results in formation of 2 Daughter cells of unequal size, each with 23 double structures chromosomes

Daughter cells
- 1 secondary cells: receives most of the cytoplasm, cell membrane lies in the perivitelline space
- 1st polar body: receives none of the cytoplasm, cell membrane lies between zona pellucida

Meiosis 2 Arrest
- The cell then enters meiosis 2 but arrest in metaphase approximately 3 hours before ovulation
- Meiosis 2 is completed only if the oocyte is fertilized, otherwise the cell degenerates approximately 24 hrs after ovulation.



Spermatogenesis

- Maturation begins at puberty
- Spermatogonia are transformed into spermatozoa
- At birth, germ cells in the male can be recognized in the sex cords of the testis as large, pale cells surrounded by supporting cells
- Supporting cells become sustentacular or sertoli cells
- Before puberty, the sex cords acquire lumen and become the semeniferous tubules at the same time, primordial germ cells gives rise to **spermatogonial stem cells**
- **Type A spermatogonia**: Production marks the initiation of spermatogenesis, Undergo a limited number of mitotic divisions to form a clone of cells.
- **Type B Spermatogonia**: Formed by the last cell division of type A, Further divide to form primary spermatocyte.
- **Primary Spermatocytes:** Enter a prolonged Prophase (22 days) followed by rapid completion of meiosis 1 and the formation of secondary spermatocytes.
- **Secondary spermatocytes:** immediately begin to form haploid **spermatids.**

Sertoli Cells

- Where spermatogonia and spermatids remain embedded throughout their development
- **Support and protect the germ cells**, participate in their nutrition, and assist in the release of mature spermatozoa.

Luteneizing Hormones (LH)

- Produced by Anterior Pituitary gland to regulate.
- LH binds to receptors — s**timulates testosterone production** — Binds sertoli cells to promote spermatogenesis

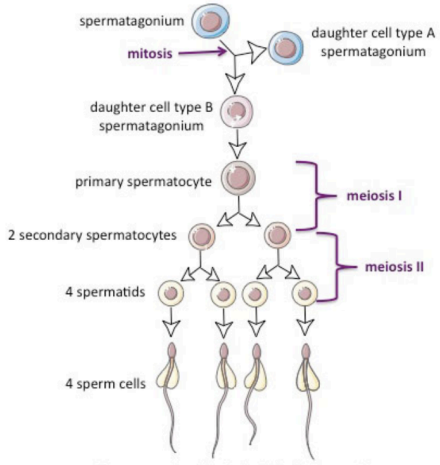
Follicle Stimulating Hormone

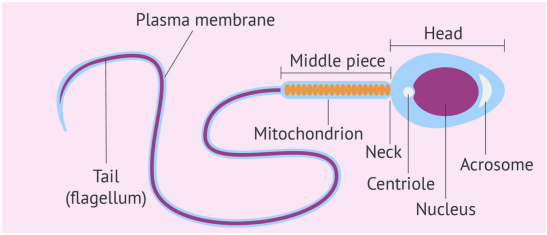
- Its binding to the sertoli cells **stimulates testicular fluid production** and synthesis of intracellular androgen receptor proteins

Results:

- Formation of the acrosome
- Covers half of the nuclear surface and contains enzymes to assist in penetration of the egg and its surrounding layers
- Condensation of the nucleus
- Formation of the neck, middle piece and tail

- Shedding of the most of the cytoplasm
- 64 days for spermatogonium to develop into a mature
- spermatozoon





Chapter 3: 2nd week of development: Bileminar Germ Disk

Day 8:

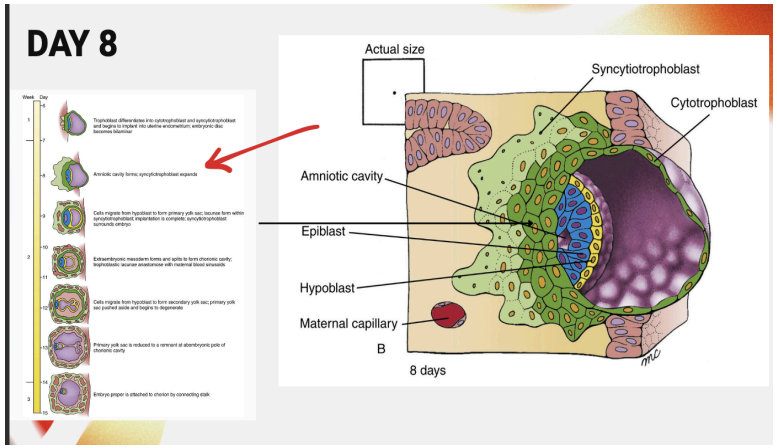
- He blastocyst is partially embedded in the endometrial stroma
- The trophoblast has differentiated into 2 layers:

Outer layer- Multinucleated zone without distinct cell boundaries, the **syncythiotrophoblast**

Inner layer- Mononucleated cells, the **cytotrophoblast**

Differentiated into:

- **Hypoblast layer-** layer of small cuboidal cells adjacent to the blastocyst cavity
- **Epiblast layer-** a layer of high columnar cells adjective to the amniotic cavity



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Day 9

- The blastocyst is more deeply embedded in the endometrium
- The trophoblast shows considerable progress in development
- **Lucnar Stage:** phase of trophoblast development when vacuoles fuse and form a large lacunae
- **Exocoelomic cavity or primitive yolk sac-** lined by a thin membrane originating from the hypoblast

Days 11 and 12

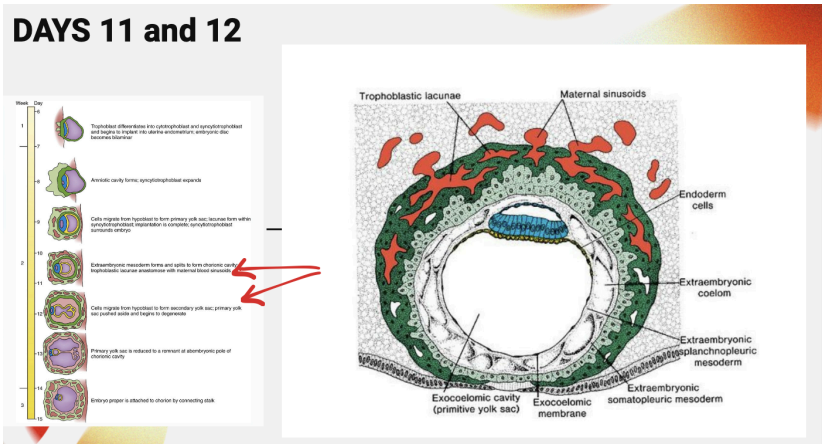
- The blastocyst is completely embedded in the endometrial stroma
- The blastocyst now produces a slight protrusion into the lumen of the uterus
- The trophoblast is characterized by lacunar spaces in the syncytium that form an intercommunication network
- Cells of the syncytiotrophoblast penetrate deeper into the stroma and erode the endothelial lining of the maternal capillaries
- These capillaries are known as **sinusoids**
- Establishment of the uteroplacental circulation: happens when the trophoblast continues to erode more and more sinusoids, maternal blood begins to flow through the trophoblastic system

Extraembryonic Mesoderm

- Loose connective tissue formed by cells derived from yolk sac cells
- Fills all of the space between the trophoblast externally and the amnion and exocoelomic membrane
- It can be divided into two parts
- **Extraembryonic somatic mesoderm**- lines the cytotrophoblast and amnion
- **Extraembryonic splanchnic mesoderm-** this lines the yolk sac

Extraembryonic Coelom or Chorionic Cavity

- A new space formed by the large cavities developing into the extraembryonic mesoderm
- Surrounds the primitive yolk and amniotic cavity



- Bleeding may occasionally occur at the implantation site as a result of increased blood flow into lacunar spaces
- The trophoblast is characterized by **villous structures**
- Hypoblast produces additional cells that migrate along inside of the **exocoelomic membrane** these cells proliferate and gradually form a new cavity within the exocoelomic cavity

Secondary yolk sac or definitive yolk sac

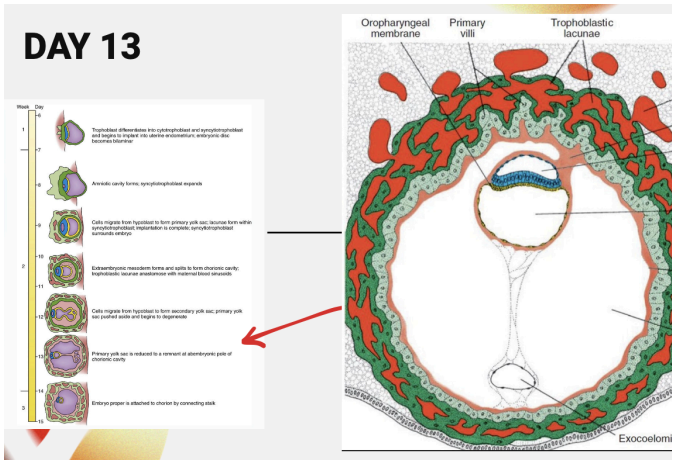
- New cavity formed inside the exocoelomic cavity or primitive yolk sac

Extraembryonic coelom

- Expands and form a large cavity/ chorionic cavity

Connecting stalk

- The only place where extraembryonic mesoderm traverses the chorionic cavity
- Becomes the umbilical cord with the development of blood vessels

- 

Chapter 4: 3rd week of development: trileminar germ disc

1. **Gastrulation: Formation of Embryonic mesoderm and endoderm**
    - The process that establishes all **three layers** in the embryo
        - Ectoderm
        - Mesoderm
        - Endoderm

    - Begins with formation of the primitive streak on surface of the epiblast
    - Primitive streak:
    - In a 15 to 16 day embryo, it is visible as a narrow groove with slightly bulging region on either side
    - Primitive node: cephalic end of the streak
    - **Invagination:** inward movement when the cells of the epiblast migrate toward the primitive streak — embryonic endoderm
    - Some cells come to lie between the epiblast and newly created endoderm to form **mesoderm**
    - Cells remaining in the epiblast then form the ectoderm
    - Epiblast- during gatrulation, it is the source of the germ layers, cells in these layer will give rise to all of the tissues and organs in the embryo
2. **Formation of the notochord**
    - **Pre-notochordal cells**
    - Found in the primitive pit
    - Move forward cephalad until they reach the prechordal plate
        - Forms between the tip of the notochord and the buccopharyngeal membrane
        - Importance for induction of the forebrain
    - **Notochord plate**

      Formed by the two cell layers of the midline of the embryo
    - **Neurenteric canal**

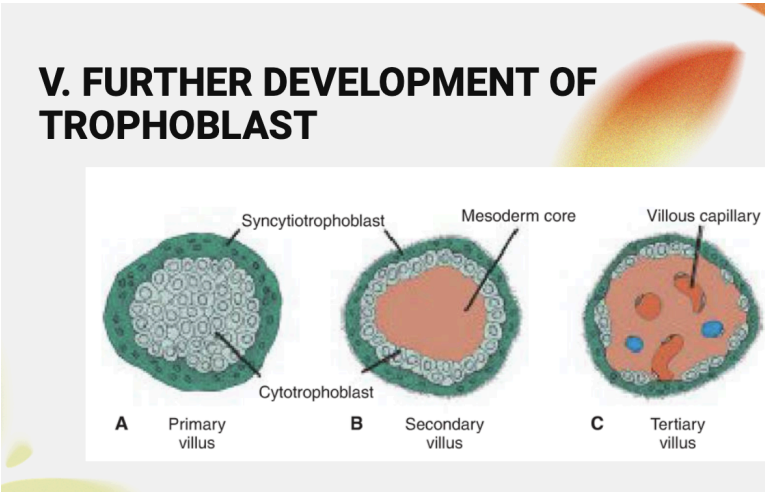
      Connects the amniotic and yolk sac cavities where the primitive pit forms an indentation in the epiblast
    - **Cloacal membrane**
    - Formed at the caudal end the embryonic disc
    - Consists of tightly adherent ectoderm and endoderm cells
    - **Allantoenteric Diverticulum or allantois**
    - Formed by the posterior wall of the yolk sac
    - Appears on the 16th day of development

- May be involved in abnormalities of bladder development
- Takes place before and during the period of gastrulation.
- **Anterior Visceral Endoderm (AVE)**
    - Expresses genes essential for head formation including transcription factor: OTX2, LIM1, HESX1
    - And secreted factor: **Cerberus**
    - These genes establish the cranial end of the embryo before gastrulation
- **Nodal**
    - A member of the transforming growth factor beta family
    - Initiate and maintains the primitive streak
    - Once the streak is formed, a number of genes regulate formation of dorsal and ventral mesoderm and head and tail structure

3. **Establishment of the body axes**
    - **Bone morphogenetic protein-4 (bmp-4)**
        - Secreted throughout the embryonic disc
        - Along with fibroblast growth factors (FGF), mesoderm will be ventralized to contribute to kidneys, blood, and body wall mesoderm
    - **Hepatocyte nuclear factor 3- Beta (HNF-3 beta)**
        - Maintains the node and later induces regional specificity in the forebrain and midbrain area
        - Without this, embryos fail to gastrulate properly and lack forebrain and midbrain structures
    - **Transcription factor goosecoid**
        - Contributes to regulation of head development
    - **Brachyury (T) gene**
        - Controls the regulation of dorsal mesoderm formation in mid and caudal regions of embryo
    - **Fibroblast Growth Factor**
        - Secreted by cells in the node and primitive streak and induces expression of nodal but only on the left side of the embryo
    - **Embryonic Disc**
        - Initially flat and almost round
        - Gradually becomes elongated,, with a broad cephalic and a narrow caudal end
    - **End of 4th week**
        - Primitive streak shows regressive changes, rapidly shrinks and soon disappears

5. **Further Development of trophoblast**
    - **Primary villi-** Consist of a cyrotrophoblastic covered by a syncytical layer
    - **Secondary villi-** Formed by the penetration of the mesodermal cells of the core primary villi and growth toward the decidua
    - **Tertiary villus-** “Definitive placental villus”, Capillaries in this structure will make contact with capillaries

developing in mesoderm of the chronic plate and in the connecting stalk



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Stem / Anchoring Villi

- Villi that extend from the **chorionic plate → decidual plate**.
- Their main job is to **anchor/support** the developing structure.
- **Remember: Stem = Anchor**

Free / Terminal Villi

- These **branch from the stem villi**.
- They are where **nutrient and substance exchange** happens.
- **Remember: Terminal = Exchange**

Chorionic Cavity

- The **chorionic cavity gets larger** as development continues.
- By around the **19th–20th day**, the embryo is connected to the trophoblastic shell by a **connecting stalk**.

Umbilical Cord

- The **connecting stalk develops into the umbilical cord**.
- It connects the **placenta and embryo/fetus**.