# Topic 5. The cell - chemical composition. Hyaloplasm (Cytosol)

In the cell we can find:

- organic compounds (complex molecules carbon-containing) and inorganic compounds (water and minerals are among the most important)

## Organic compounds:

### 1. Carbohydrates

- the three basics elements of this molecule are carbon, hydrogen and oxygen (C, H & O)
- they can be found as monosaccharides (glucose), disaccharides (sucrose) or polysaccharides (starch, glycogen and cellulose)
- the monosaccharides and disaccharides carbohydrates are found in cell in the chloroplast, mitochondrion or cytoplasm
- the polysaccharides are found in plastid, cytoplasm or cell wall
- the carbohydrates have the functions of energy source and storage, strengthen plant cell walls and providing tough exterior covering
- Polysaccharides can be demonstrated in a cell using the PAS (periodic acid Schiff) reaction
  (↳ PAS is a staining technique (coloring technique) used in histology)

### 2. Lipids

- the 4 basics elements of this molecules are carbon, hydrogen, oxygen and phosphorus (in phospholipids) (C, H, O & P)
- composed by hydrocarbon rings and long hydrocarbon side chain
- they are relatively insoluble in water and are hydrophobic substances. They're soluble in non-polar (organic) solvents like chloroform, methanol and ethanol
- they have high energy content and are metabolised (verstoffwechseln → um-bzw abbau einer Substanz durch körpereigene Enzymsysteme) to release calories
- Lipids are electrical insulators, insulating axons
- the fats and oils are found in the cytoplasm, the phospholipids and steroids are found in the cell membrane and the waxes in the cell surface. The fats are hydrolysed by lipase enzymes, to produce fatty acids and glycerol. Fats are bad conductors of heat
- Examples of lipids are — fats (esters of fatty acids and glycerol) and oils, phospholipids, steroids (cholesterol, testosterone), waxes (esters of long chain fatty acids and long chains alcohol)
- the lipids have the functions of energy storage, cell membrane components, chemical messengers and protection
- phospholipids → components of cell membranes
- Glycolipids → unlike phospholipids, they have no phosphate group. But they do have hydrophobic region containing two hydrocarbon tails

## 3. Proteins

- the 4 basic elements of this molecules are carbon, hydrogen, oxygen, nitrogen and sometimes sulphur and phosphorus (C, H, O, N & sometimes S and P)

- they are very large molecules of linked monomers called amino acids

- there are 20 types of aminoacids, they can be classified as essential and non-essential

- the amino acids are the smallest unit of the proteins, and their major funtion is the building of blocks of proteins, but also are the precursors (Prä kursor → Wegbereiter) for the biosynthesis of some biological molecules, part of coenzymes, metabolic intermediates and neurotransmitters (excitatory, inhibitory)

- the proteins are organized in four levels:
  - Primary structure: the amino acid sequence
  - Secondary structure: regularly repeating local structures stabilized by hydrogen-bonds
  - Tertiary structure: formation of protein subunits by folding
  - Quaternary structure: the assembly of subunits, the structure formed by several protein molecules (polypeptide chains)

- the proteins make up 60% of dry cell mass (15% on a wet-weight basis) and determine the shape and structure of the cell also serve as main instruments of molecular recognition and catalysis

- structurally, proteins can be divided into:
  - simple proteins: albumins, histones, collagen
  - compound proteins: glycoproteins, lipoproteins, nucleoproteins

- functionally proteins can be divided into - Structural proteins, enzymes, transport proteins, defence proteins and contractile proteins

Some example of proteins:

- messenger proteins and antibodies, which are found in ribosomes, endoplasmic reticulum, Golgi apparatus and vesicles

- recepter proteins and transport proteins, which are found in the cell membrane

- structural proteins, which are found in the cell surface

- enzymes, which are found throughout the cell → the functions of the proteins are immunity, communication, transport materials, support cell and body, structure and speed up chemical reactions

## 4. Nucleic Acids

- they're made up of 5 basics elements - carbon, hydrogen, oxygen, nitrogen and phosphorus (C, H, O, N, P)

- there are two types of nucleic acids
  Deoxyribonucleic Acid
  - DNA, which is found in the nucleus, chloroplast and mitochondrion. The funtion of the DNA is to store hereditary information
  Ribonucleic Acid
  - RNA, which is found in the nucleus, cytoplasm and ribosome. There are three types of RNA - rRNA, tRNA and mRNA

    > ribosomal RNA (rRNA)
    > transfer RNA (tRNA)
    > messenger RNA (mRNA)

  the function of the RNA is to decode hereditary informations

# Inorganic compounds

## 1. Water

- Water is the most abundant component (reichlich vorhandene Komponente) of cells & organisms, making up 70% of a cell
- Water molecules are cohesive (bindend) - hydrogen bonds form between the hydrogen atoms and the oxygenations of water molecules
- it is an excellant solvent (Lösungsmittel)
- it has an high specific heat
- Aquaporins are integral membrane proteins (Membranproteine, die zum Teil in eine Membran eingebettet sind oder diese ganz durchdringen) that forms pores in the membrane of cells. They selectively conduct water molecules in and out of cells
- Water forms 90% of the $\boxed{\text{protoplasm}}$ → the colourless material comprising the living part of a cell, including the cytoplasm, nucleus and other organelles
- it is a transport medium
- it is a medium in which all chemical reactions in cells take place
- it can be used to regulate temperature in organisms
- it can be a reactant in reactant in reactions

## 2. Mineral salts

- Chlorides, carbonates of sodium, phosphates, nitrates, etc. are dissolved as ions in the cytoplasm and in the vacuols of plant cells
- Assist in chemical reactions by helping enzymes to funtion
- essential for functioning of cell membrane and nerve and muscle cells. For example, Calcium ions with membrane channels, impulse transmission and muscle contraction

## Hyaloplasm (Cytosol)

- forms 70% of total volume of the protoplasm
- the cytosol is composed of 90% water and macromolecules
- it is the final liquid produced by $\boxed{\text{differential centrifugation}}$ → process by which organelles are seperated by their sedimentation rate
- it is a translucent fluid with a pH 6.8, also is the substratum for cytoplasmic funtions

## Processes occuring in the cytoplasm:

- Glycolysis occurs in the cytoplasm: Glucose is a phosphorylated by adding phosphate from molecule ATP. This creates Hexose Phosphate and $\boxed{\text{ADP}}$ → Adenosine diphosphate. This process is repeated, $\boxed{\text{ATP}}$ → Adenosine triphosphate is once again added and hexose bisphosphate is produced. Hexose bisphosphate is then split into 2 triose phosphate (3C).
- Translation occurs in the cytoplasm with tRNA, ribosomes and mRNA.

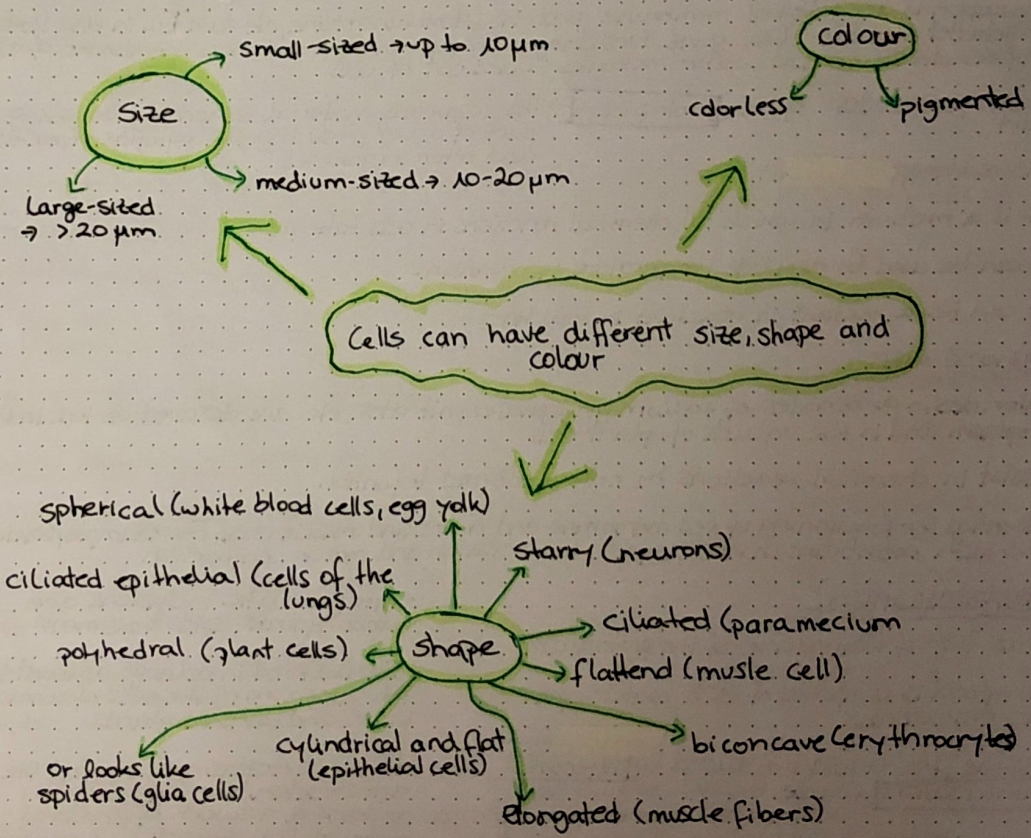
- cytoplasmatic inclusions are carbohydrates, lipids & pigments
- Fat is stored in a large amount in the cytoplasm of the cells of connective tissue and adrenal glands
- In the cytoplasm, we can find the cytoskeleton. The cytoskeleton contains a network of structural proteins that consists of 3 components — microtubules, microfilaments and intermediate filaments. These structural proteins not only provide the form and shaping of the cell, but also play an important role in cytoplasmic and cellular movement

# Topic 6. The cell – external morphology

Most mammalian cells (→ Säugetierzellen) in culture can be divided into 3 basic categories based on their morphology.

These are:

- Fibroblastic cells – bipolar or multipolar cells and grow attached to a substrate
- Epithelial like cells – polygonal shape and grow attached to a substrate in discrete patches
- Lymphoblastic cells – spherical shape (→ kugelförmig) and grow on suspension, without attaching to a surface



# Topic 7. The cell – internal morphology and organisation

## Levels of organisation:

- Atom – molecule or compound – organelle – cell – tissue – organ – organ system – organism
- Each item represents a different level of organization
- organelles only operate within a cell and their activity only affects the cell
- tissue operates on a higher level of organization as it is composed of many cells that work together to perform that tissue's function in the body
- two or more tissue types occur in organs, which represent yet a higher level of organization

## Major cell ability:

1. cell reproduces by cell division
2. the functioning of a cell depends upon its ability to extract and use chemical energy stored in organic molecules
3. cell responds to stimuli such as changes in temperature, pH or levels of nutrients
4. cell contents are contained by a cell surface membrane

## Cell hierarchy:

Comparison of Procaryotic and Eucaryotic Organisms

| | Procaryotes | Eucaryotes |
|---|---|---|
| organism | bacteria & cyanobacteria | protists, fungi, plants and animals |
| cell size | generally 1 to 10 μm in linear dimension | generally 5 to 100 μm in linear dimension |
| Metabolism | anaerobic and aerobic | aerobic |
| Organelles | few or none | nucleus, mitochondria, chloroplasts, endoplasmatic reticulum etc. |
| DNA | circular DNA in cytoplasm | very long linear DNA molecules containing many noncoding regions; bounded by nuclear envelope |
| RNA and protein | RNA & protein synthesized in same compartment | RNA synthesized and processed in nucleus; proteins synthesized in cytoplasm |
| Cytoplasm | no cytoskeleton; cytoplasmic streaming, endocytosis and exocytosis all absent | cytoskeleton composed of protein filaments; cytoplasmic streaming, endocytosis & exocytosis |
| Cell division | chromosomes pulled apart by attachments to plasma membrane | chromosomes pulled apart by cytoskeleton spindle apparatus |
| Cellular organization | mainly unicellular | mainly multicellular, with differentiation of many cell types |

| | Eukaryotic cells | Prokaryotic cells |
|---|---|---|
| Compartmentalized | YES | NO |
| Cytoskeleton | YES | NO |

# Cellular architecture

## 1. Plasma membrane

- this membrane enclosing a cell is made up of two phospholipids layers making up a phospholipid bilayer. it has two different parts to it – a hydrophilic phosphate head and a hydrophobic lipid tail – amphipathic

- the phospholipids are arranged so that the tails face each other on the inside and the heads face (down) towards the outside of the membrane

- there are pores or channels in the cell's plasma membrane which are made up of certain proteins that control the movement of water and nutrients in and out of the cell

- proteins make up a large part of the membrane. there are integral proteins, transmembrane proteins or peripheral proteins. Integral proteins are incorporated (eingetragen) directly within the lipid bilayer, whereas peripheral proteins are bound to one of the membrane surfaces. Transmembrane surfaces often form channels

- Membrane proteins which are components of large enzyme complexes are usually less mobile, especially those involved in the transduction of signals. Such protein complexes are located in specialised membrane patches called lipid rafts with higher concentrations of cholesterol and saturated fatty acids.

- Cholesterol makes the bilayer more fluid but decreases permeability of water soluble molecules

### Functions of plasma membrane:

- physical barrier → protects cellular contents and supports cell structure

- selective permeability → regulates the passage of materials into and out of the cell and facilitating the transport of specific molecules
  ↳ erleichtern

- communication → contains receptors that recognise and respond to molecular signals

- electrochemical gradient → establishes and maintains schaffen & aufrechterhalten an electrical charge across the plasma membrane

- keeps the ion content of the cytoplasm constant, which differs from that of the extracellular fluid

## 2. Nucleus

- the nucleus is the control centre of the cell. It is the largest organelle in the cell and it contains the DNA of the cell. Inside the nucleus there is another organelle called the nucleolus, which is responsible for making ribosomes

- the circles on the surface of the nucleus are the nuclear pores. these are where ribosomes, mRNA etc. move in and out of the cell

# Cytoplasm-Organelles

## 1. Endoplasmic Reticulum (ER)

- it is a network of membranes/cisternae throughout the cytoplasm of the cell. the endoplasmic reticulum acts as a transport system

### Rough Endoplasmic Reticulum (RER)

- the RER consists parallel stacks of flattened cisternae, with the membrane attached to the nuclear envelope and attached ribosomes

- the ribosomes are shown by basophilic stains

- RER produces most of the proteins to be used in membranes, organelles and export. It is a site for protein synthesis and protein exocytosis by vesicles

Smooth Endoplasmic Reticulum (SER)

- the SER is continuous with the RER, yet less abundant. It is not basophilic. SER cisternae are more tubular, rather than flattened cisternae of RER

- the function of the smooth endoplasmic reticulum is to synthesize lipids and steroids in the cell, drug detoxification and transport proteins from the RER

- Proteins from the RER move into the SER and are then sent by the SER to the Golgi body in vesicles

2. Ribosomes

- organelles that help in the synthesis of proteins. Some ribosomes are found in the cytoplasm, but most are attached to the rough endoplasmic reticulum. A ribosome has two subunits of different sizes bound to a strand of mRNA

3. Golgi complex

- Golgi complex completes post translational modifications of proteins produces in the RER and then packages and sends these proteins to their proper destinations

- In the most cells, the Golgi complex is located near the nucleus the golgi has two sides - cis face and trans face. The cis face is where transport vesicles merge with the Golgi, and the trans face is where the vesicles carry completed protein products to organelles away from the Golgi.

4. Mitochondrion

- It is a membrane-bound organelle with many enzymes specialised for aerobic respiration and production of ATP

- it packages the energy from the food into ATP molecules. every type of cell has different amounts of mitochondria, depending on the cell's energy needs. E.g. intestinal epithelial cells have more due to active transport using ATP

- Mitochondria also functions in cellular apoptosis, which results in rapid cell death. New mitochondria originate by growth and division of pre-existing mitochondria. mitochondria are only received maternally

- mitochondrial matrix contains a small circular chromosome of DNA, ribosomes, mRNA and tRNA.

- can be seen by a light microscope

5. Chloroplast

- this is the organelle in which photosynthesis takes place. the light energy of the sun is converted into chemical energy. chloroplasts are found only in plant cells

6. Vesicles

- these organelles helps store and transport products produced by the cell

7. Vacuole

- the vacuole contains large amounts of water and stores other important materials such as sugars, ions and pigments

## 8. Cytoskeleton

- consists of microtubules, microfilaments and intermedia filaments. these protein polymers determine the shape of cells and aid the movement of organelles, cytoplasmic vesicles and the cell itself

OTHERS:

## 9. Peroxisomes

- they are sperical organelles, enclosed by a single membrane produce enzymes like catalase, which breaks down hydrogen peroxide which is potentially damaging to the cell

- collect and safely break down chemicals that are toxic to the cell

## 10. Centrioles

- these are only found in animal cells and come into action when the cells divide, helping with the organization of chromosomes

## 11. Lysosomes

- created by the Golgi apparatus and contain degradative enzymes which breaks down large molecules and dead organelles into smaller useful molecules for the cell

# Topic 8. The cell membrane - structure and functions. Glycocalyx (Cell coat)

The cell membrane is a structure based on a two-ply [zweilagig] sheet of lipid molecules about 8-10 nm thick, embeded with proteins, semi permeable and asymmetric cell membrane. Cell membranes are both present in eukaryotic and prokaryotic cells. It works as a barrier between the inner and outer surface of a cell.

## Functions of the cell membrane:

1. Communication: The plasma membrane plays an important role in the response of a cell to external stimuli, a process known as signal transduction. Membranes posses receptors that are capable of recognising and responding to different molecules. The interaction of a plasma membrane receptor with an external ligand may cause the membrane to generate a signal that stimulates or inhibits internal activities.
2. Intercellular interaction: The plasma membrane allows cells to recognise and signal each other, to adhere when needed and to exchange materials & information
3. Physical barrier: Phospholipids bilayer seperates substances inside and outside the cell, also establishes a flexible boundary, protects cellular contents & supports cell structure
4. Providing a selectively permeable barrier: membranes prevent unrestricted exchange of molecules from one side to the other.

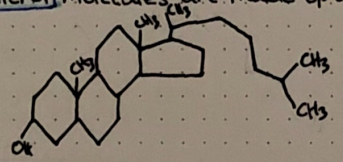
## Chemical components:

The cell membrane is composed of 3 different types of molecules:
1. Lipids (phospholipids, cholesterol, glycolipids)
2. Carbonhydrates (glycoproteins, glycolipids and glycocalyx)
3. Proteins (hydrophobic in the structure and hydrophilic as receptors and enzymes)

## 1. Lipids (20-40%)

1.1. Phospholipids are the basic structure of a cell membrane. A single phospholipid molecule has two different parts, hydrophilic head and hydrophobic tail. The phospholipids of a cell membrane are arranged in a double layer called the lipid bilayer

1.2. Cholesterol molecules are made up of four rings of hydrogen and carbon atoms. They are hydrophobic and are found among the hydrophobic tails in the lipid bilayer. Cholesterol molecules are important for maintaining the consistency of the cell membrane. They also keep the phospholipids tails from coming into contact and solidifying (verfestigen). This ensures that the cell membrane stays fluid & flexible.




1.3. Glycolipids (2-10%) have a short carbonhydrate chain covalently attached and they are found on the outer surface of the cell. The glycolipids mainly have communicative role, often acting as markers for cellular recognition. Additionally they provide stability for the cell and help cells to join other cells to form tissues.

## 2. Carbonhydrates (10%)

2.1. Glycolipids (1.3.)

2.2. Glycoproteins are integral membrane proteins. They have short carbohydrate chains covalently attached which are exposed on the outer surface of the cell. Integral proteins are those which penetrate the hydrophobic region of the cell membrane. Most of the integral proteins are transmembrane proteins which span the entire plasma membrane.
Glycoproteins play a crucial part in cell-cell recognition and have important roles in protection and the immune response, reproduction, structural integrity & cell adhesion.

2.3. Glycocalyx is basically the outer part of the cell surface, it carries a negative charge and it is made up by the glycolipids and glycoproteins. It has many functions. Based on structure and type of carbonhydrates in the glycocalyx, the body can recognize the cells and determine whether they should be there. Protect cell membranes from physical or chemical damage, enabling the immune system to recognize foreign organisms and cancer cells. It is also important for cell recognition in immunological responses and transplants. It binds cells to prevent tissue breakdown.

## 3. Proteins (50% or less)

3.1. **Transport proteins** are membrane proteins. The cell membrane is the site where materials are exchanged between the cell and the environment. These proteins control movement of substances into and out of the organelles and between the cell and its external environment. There are three types of transport proteins:

1. pumps → transport ions: $Na^+$, $K^+$ and ATPase.
2. carries → transmembrane proteins (transport via diffusion and exchange).
3. channels → allows the passage of small ions and molecules, don't require ATP and they go with the concentration gradient

3.2. **Structural proteins** link membranes, cytoplasm and the nucleus allowing for communication. These proteins are associated with movement and affect the shape of the cell. There a 5 families of proteins, classified in

- $Ca^{2+}$-dependant (cadherins, selectins and integrins)
- $Ca^{2+}$-independant (immunoglobin)

3.3. **Receptor proteins** help in communication with the cell's external environment. Each receptor can bind to a specific extracellular molecule what activates an intracellular process, in which the receptor relays a signal to targets within the cell. There are neurotransmitter receptors, hormone receptors, immune receptors & endocytosis receptors.

3.4. Enzymes in the membrane can transform a molecule into another form. There are 30 different types of enzymes.

3.5. Scaffold proteins have regulatory and morphogenetic functions. They have a crucial role in regulating key signal pathways and helping to localise pathway components in specific areas of the cell.

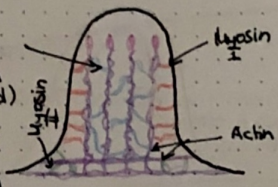
# Topic 9. The cell membrane - specialised structures of the cell membrane, intercellular junctions

Specialited structures of the cell membrane are used in cell movement, phagocytosis & absorption. Most of these extensions are based on actin filaments

## Types

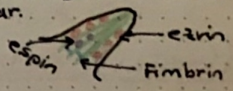
### 1. Microvilli:

- 1 µm high & 0,1 µm wide
- contains bundle of actin filaments (20-30 tighty bonded)
- core is attached to plasma membrane through Myosin II & $Ca^{2+}$
- fingerlike extensions derived from cell surface




### 2. Stereocilia:

- non-motile microvilli, up to 120 µm
- limited to ductus epididymis & have receptive functions in the ear → sensory hair cells of the inner ear.




### 3. Cilia & flagella:

- motile move substances around cell
- made out of microtubules
- covered by extension of plasma membrane

| Kinocilia: | Senscilia: | Flagellum: |
|---|---|---|
| - 2-10 µm = length | - non-motile microvili | - l = 100-200 µm |
| - 0,3-0,5 µm = Ø (diameter) | - single primary cilia | - 1 flagellum per cell |
| - basal body (9x3+0) | - 9x2+0 | - only in spermatozoa |
| - 9x2+2 | | |

### 4. Basal infoldings:

- increase basal surface area
- allow more transport proteins & channels to be present
- concentrated mitochondria for energy

### 5. Lamellipodia

- cytoskeletal protein actin projection on the leading edge of the cell

### 6. Filopodia

- slender cytoplasmic projections that extended beyond the leading edge of lamellipodia in migrating cell

### 7. Invadopodia

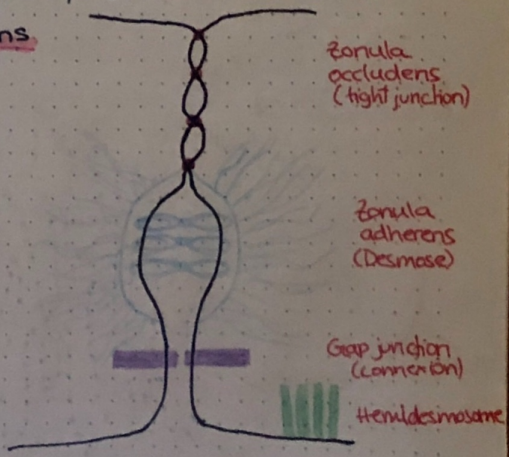
- protrusions in the cell membrane of some cells that are rich in actin and extend into the extracellular matrix

## Kartagener's syndrome

Immotile ciliary syndrome of kartagener causes a defect in the action of cilia lining the resperatory tract and the fallopian tube due to the absence of dynein arms in axoneme

## Intercellular junctions

1. Occluding junctions (barriers):
   - > tight junction (zonula occludens)
   - > occluding strip (fascia occludens)
   - > occluding spot (macula occludens)
2. Anchoring (adhering) junction:
   - > focal adhesion (punctum adherens)
   - > belt desmosome (zonula adherens)
   - > spot desmosome (macula adherens)
3. Communicating junctions:
   - > gap junction (nexus)
   - > synapse



# Topic 10. Membranous cell organelles - endoplasmatic reticulum (ER)

**General:**
- Biosynthesis of proteins and lipids
- acts as transport system for proteins and lipids
- network of intercommunicating membrane sacs → so called cisternae
- in cytoplasm of cells

Rough Endoplasmatic Reticulum

**RER (with Ribosomes):** → developed in exocrine gland cells, blast cells, plasma cells & neurons.
- involved in protein synthesis
- is a transport system
- moves Protein molecules from the RER into the SER
- starts glycolisation of glyco proteins
- starts phospholipids synthesis

Smooth Endoplasmatic Reticulum

**SER (without Ribosomes)** → developed in in cells of adrenal cortex, liver cells, skeletal & cardiac muscle cells, nerve & glandular cells
- involved in diverse metabolic processes
  - synthesis of lipids
  - carbohydrate metabolism
  - detoxification of drugs and other poisons
  - synthesis of steroid hormones
  - regulation of $Ca^{2+}$ concentration

⇒ not accurate because

RER is found near the cytoplasm of the eukaryotic cells.

while SER is found near the cell membrane.

**Accurate Sketch:**

# Topic 11. Membranous cell organelles - mitochondria

**General:**
- sperical or filamentous organelles
- double membrane bound organelle with cristae
- 0,5 - 1 µm diameter & varied lengths
- membrane-bound organelle that moves through the cytoplasm via microtubles in cytoskeleton
- transforms the chemical energy of the metabolites presented in the cytoplasm compounds
- approximately 50% is dissipated as heat → used to maintain the body temperature
- no mitochondria in RBC

**Functions:**
- Cellular Apoptosis → controlled "suicide" of the cell by gene expression
- Steroid synthesis
- storage of $Ca^{2+}$ - ions

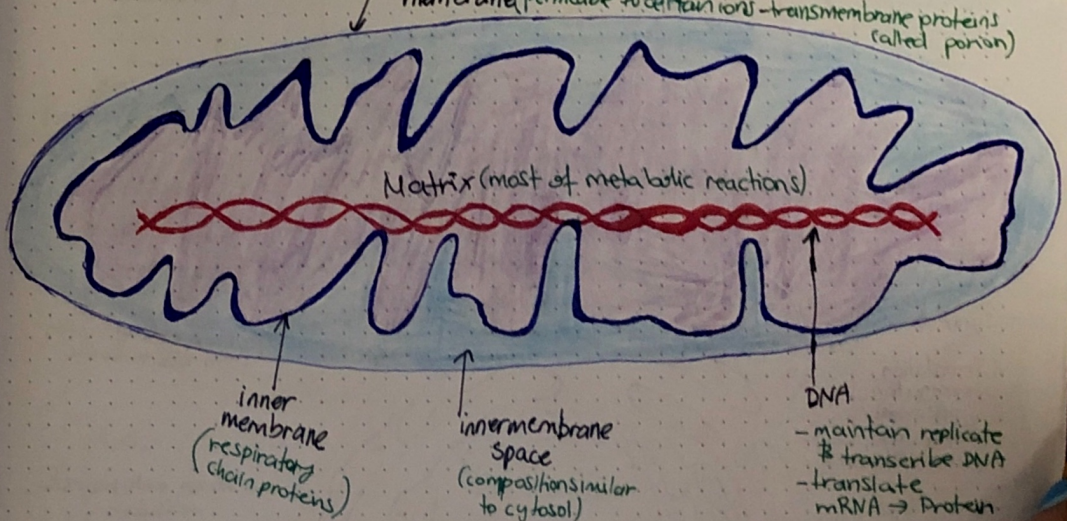
**Mitochondria are composed of 4 structures:**

**outer mitochondrial membrane**
- major intrinsic protein
  - ↳ resistant to tryptic digestion
  - ↳ appears to form channels for the passage of solute
- has receptor for proteins & polypeptids
- has many enzymes
- lacks at elementary particles that are prominent in the inner mitochondrial membrane

**inner mitochondrial membrane**
- folded → forms cristae
- lipid bilayer
  - ↳ contains phospholipids
  - ↳ is highly impermeable to ions
- selectively permeable to small molecules
  - ↳ needed by enzymes in the matrix
  - e.g. CoA
- oxidative phosphorylation is carried out by enzymes of the electron transport chain embedded in the inner membrane
  - ↳ produces ATP
    - ↳ occurs by chemiosmosis

**intermembranous space**
- $H^+$ electro-chemical gradient is set up
- the protein cytochrome c is released here into the cell cytoplasm
- concentration of small molecules such as ions & sugars in the inner space of the membrane are the same as the concentration in the cytoplasm
- but the composition of the proteins is different

**matrix**
- rich in proteins
- contains some DNA & RNA
- found here:
  - enzymes for the krebs cycle & fatty-acid-beta-oxidation
- DNA is double stranded
- 3 types of RNA
  - tRNA
  - rRNA
  - mRNA



# Topic 12. Membranous cell organelles - Golgi apparatus. Secretory vesicles, coated vesicles.

## General:

- packaging organelle like the ER
  ↳ post office of the cell
- post-translational modification of proteins and then packages & sends them to their proper destination
  ↓
  three main destinations:
  1. inside the cell to the lysosomes
  2. plasma membrane
  3. outside the cell

  destination is chosen based on the proteins function
- the Golgi has 3 compartments
  I. Curved stack of flattened cisternae
  II. Cis face with vesicles
  III. Trans face with large condensing vacuoles
- Golgi has two faces
  1. Cis face &
  2. trans face

## Function:

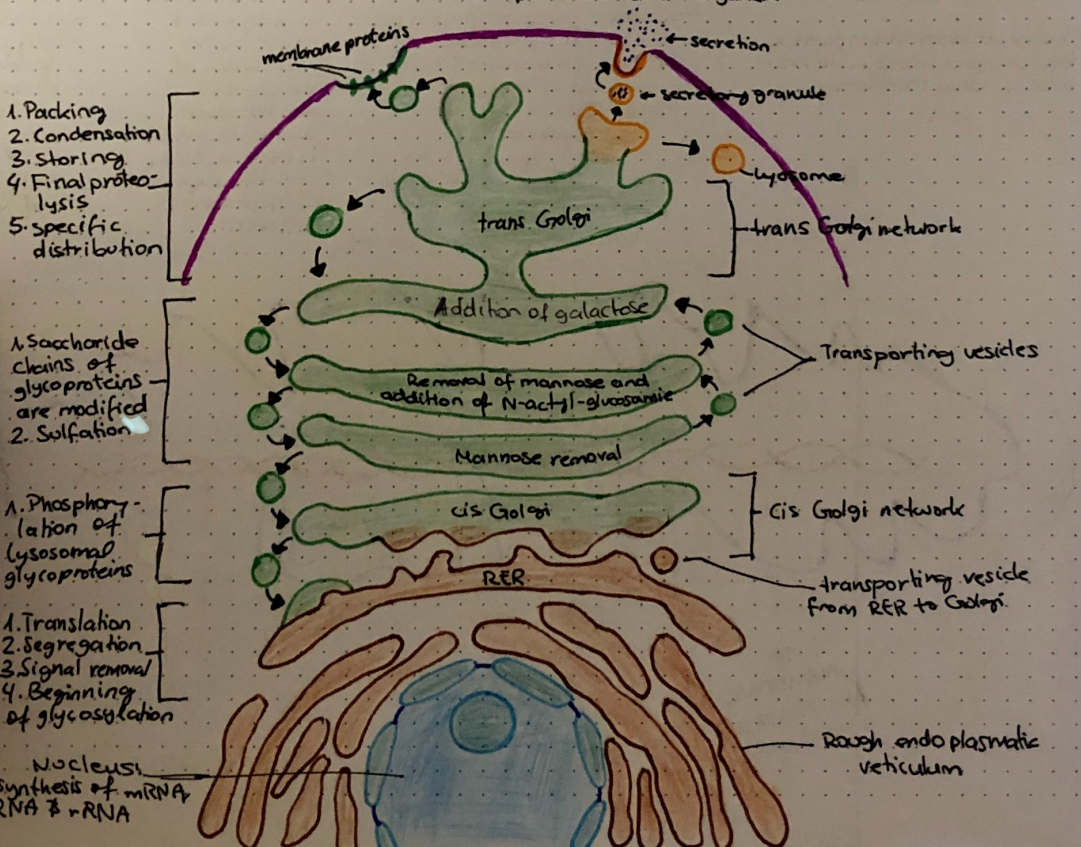
1. takes products from the RER
2. transported to the vesicles
3. vesicles are delivered into the cis golgi network
4. here the products are checked

4.1 any products that have been delivered wrongly, including chemicles that should've stayed in the RER
5. are send back packed into vesicles

4.2 proteins & lipids that have been delivered correctly
6. are passed into the cisternae of the golgi stack
↓
processed & sorted in an orderly sequence

## Vesicles:

I. Transport vesicles: (in this case from RER to Golgi) move molecules inside the cell
II. Secretory vesicles: contain material that has to be exerted from the cell
III. coated vesicles: coated with proteins & lysosome; makes them specific to a particular doner organelle.



# Topic 13. Membranous Cell organelles – Lysosomes. Peroxisomes

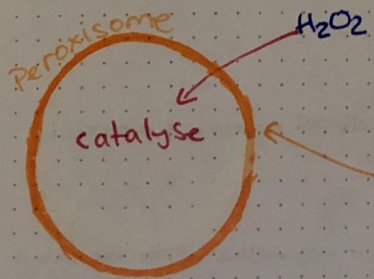
## General (Lysosomes)

- sperical, single membrane bound vesicles containg 40 different hydrolytic enzymes
- slightly larger & visible with a light microscope → after staining
- lysosomes digest (break down) various molecules and substances
- two different processes:
  - Autophagy ("self-eating")
    - digest parts of cell or other cells
      - > organelles that are no longer functional
      - > macrophagus of immune system
  - Crinophagy
    - digest excess secretory products
      - ↳ eg. if a cell produces too much hormones, the excess hormones will be broken down by the lysosomes
- afte the lysosome finishes, breaking down the molecules, it will release into the cytoplasm the building blocks that have just formed:
  - ↳ didn't form building blocks → but broke down the molecules down into their most basic, basic parts → those basic parts are put into the cytoplasm and be reused
    - ↳ eg. lysosomes digest extra hormones → those extra hormones are made up of proteins → they'll break those proteins down into the individual amino acids → and those amino acids will be released into the cytoplasm → & they'll be used for something else

## General (Peroxisomes)

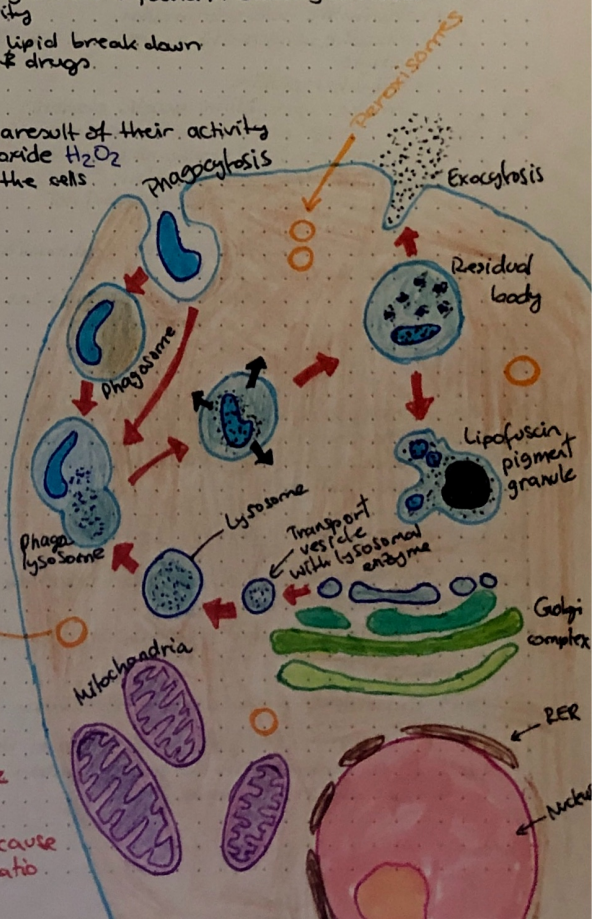
- small, spherical single membrane bound organelles → found in eukaryotic cells
- responsible for a variety of metabolic activity
  - ↳ in some cells they're essential for lipid break down
  - ↳ help liver cells detoxify chemicals & drugs
- they carry out a very important task
  - ↓ So what do they do?
  - • there are various enzymes in a cell → as a result of their activity they produce a by-product → hydrogen peroxide $H_2O_2$
  - • hydrogen peroxide is pretty dangerous for the cells
  - • so what peroxisomes will do is
    1. they're going to isolate it → hydrogen peroxide endsup in the peroxisome
    2. each peroxisome has an enzyme known as „catalase" → this enzyme is able to break down hydrogen peroxide
    3. Catalase breaks down hydrogen peroxide into water and oxygen

So peroxisome protect the cell from the damaging effects of hydrogen peroxide by isolating it & then breaking it down into water & oxygen




$$H_2O_2 \xrightarrow{\text{catalyse}} H_2O + \frac{1}{2} O_2$$

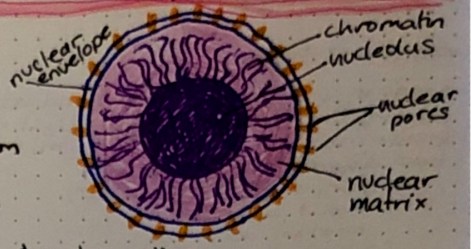
↓ only because of the ratio



# Topic 14. Cell nucleus - structure of interphase nucleus: chromatin, nucleolus & nuclear matrix

## Structural components:

- Nuclear envelope
- Chromatin
- Nucleolus
- Nuclear matrix (nucleoplasm)
- Nuclear pores - pathway between nucleus & cytoplasm




## Chromatin:

- complex of DNA, histones (basic protein) & non-histone proteins (acidic protein)
- interphase nucleus: classified into heterochromatin & euchromatin

### I. Heterochromatin (stains dark with HE)

- highly condensed
- transcriptionally inactive
- only present in eukaryotes
- 3 locations:
  - marginal chromatin - is found in the periphery of the nucleus
  - karyosomes - are found dispersed around the nucleus
  - nucleolar-associated chromatin - found in association with the nucleolus
- 2 types of heterochromatin:
  - constitutive heterochromatin:
    - > inactive, condensed & occurs in all cells & stages
    - > highly repetitive
    - > makes upreplitive genetic elements
      - ↳ eg. centromere & telomeres
    - > plays role in chromosome structure
  - facultative heterochromatin:
    - > also inactive & condensed, but not repetitive
    - > has inconsistant chromosomal localization
    - > region: barr body
      - ↳ used to identify sex of the fetus

### II. Euchromatin

- more dispersed (verstraut)
- is transcriptionally active
- chromatin is stretched out
  - ↳ so the genetic information in the DNA can be read & transcribed
- most active portion of the genome in the nucleus
- lightly packed form of chromatin with less DNA
- presented in both eukaryotes & prokaryotes
  - ↳ cells with & without a nucleus

## Structure of chromatin

- organised at several levels
- nucleosom: basic structure of chromatin
  - ↳ complex of 146 base pairs of DNA wound around 8 histone molecules (protein core)

## Nucleolus:

- non-membranous, intranuclear structure only present in the interphase of the nucleus
- Largest structure in the nucleus (eukaryote cells)
- rRNA & ribosome synthesi and assembly
- composed of RNA & protein

## Nuclear matrix (Nucleoplasm)

- material enclosed by the nuclear envelope, without nucleolus & chromatin
- fibrious network
  - ↳ contains nuclear proteins, DNA & RNA
- 3 functions
  - ↳ main function: to serve as a substance for organelles inside the nucleus
  - ↳ helps maintain the shape & structure of the nucleus
  - ↳ plays an important in the transportation of materials that are vital to the cell metabolism & function

# Topic 15. Ultrastructural organisation: structure of the nuclear envelope & nuclear pores

## Nuclear pores:

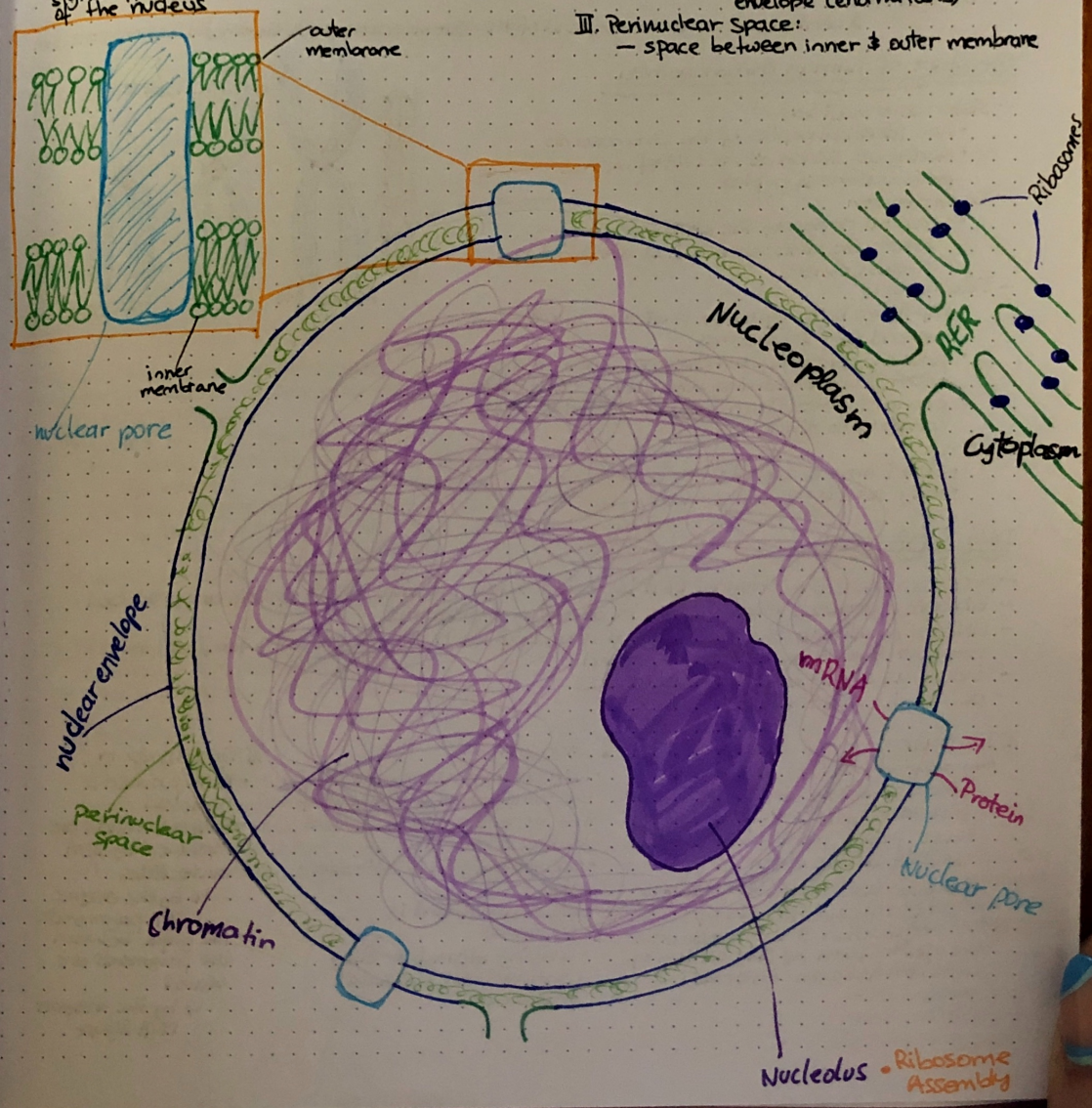
- spans both membranes, the outer membrane and the inner membrane.
- these pores are what the nuclear envelope semipermeable
  - ↳ it serves as a transport spot, where different molecules & proteins can enter or leave the nucleoplasm
- nuclear pores are very selective in letting different proteins inside the nucleoplasm, therefore the nuclear pore recognizes special signals on different proteins and only with the presence of these signals, proteins can be transported into & out of the nucleus

## Nuclear envelope:

I. Outer nuclear membrane:
- faces cytoplasm
- is close to RER
- it's made out of ribosomes & vimetin filaments

II. Inner nuclear membrane:
- faces the nucleoplasm
- is covered by nuclear lamina
  - ↳ composed of nuclear laminas A, B & C
  - ↳ play a role
    - in rapid breakdown of the nuclear envelope (start mitosis)
    - reassembly of the nuclear envelope (end mitosis)

III. Perinuclear space:
- space between inner & outer membrane



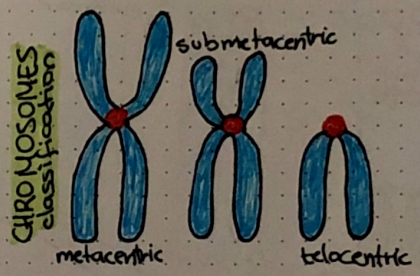
# Topic 16. Cell nucleus – chromosomes, structure & replication of DNA

## Chromosomes in General:

- organised package of DNA
- found in the nucleus
- different organism → different number of chromosomes
- humans have 23 pairs of chromosomes
  - ↳ 22 pairs of numbered chromosomes (autosome)
  - ↳ 1 pair of sex chromosomes X & Y
- chromosomes are classified by the position of the centromere:
  - metacentric:
    > centromere is in the middle of the chromosome, the arms are equal in length
  - submetacentric:
    > centromere is closer to the middle of the chromosome than to one of the end, the arms differ in length
  - telocentric:
    > centromere is at the very end of the chromosome, each chromatid has only one arm

## Structure of human chromosomes:

- sister chromatids:
  - two identical copies of the chromosome
  - during cell division all the DNA of each chromosome is copied
- Centromere:
  - centeral region of the chromosome
    - ↳ here the sister chromatids are joined to each other
- Telomeres:
  - repetitive DNA sequence that are situated at the tip of chromosomes
  - prevent damage from chromosomes & stop them from becoming attached to each other
  - protect genes from getting deleted as cells continue to divide
- Arm:
  - short arm is called p-arm
  - long arm is called q-arm




## DNA Replication:

- process where the original DNA is copied → two identical copies of DNA are produced
- biological process that occurs in all living organisms
- DNA is made up of two identical strands, & each strand acts as a template to produce the complementary strand
- known as semi-conservative process
- occurs in 3 stages:

### I Initiation

- ds DNA unwinds by breaking the H bonds between the complementary base pairs, producing ss DNA (single strand)
  - ↳ because initiator proteins bind to the origin of replication & two replication forks form by the action of DNA helicase enzyme

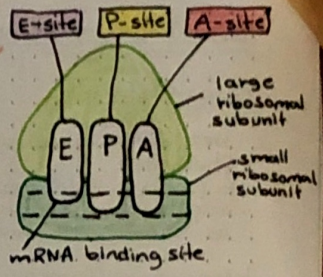
### II. Elongation

- DNA polymerase synthesise the complementary strand of two seperate chains & moves bidirectional
- occurs only in 5'-3'-direction
- leading strand is continous
- lagging strand is discontinous by okazaki fragments

### III. Termination

- RNA primer is removed
- RNA nucleotids are replaced by DNA nucleotides
  - ↳ by the enzyme DNA polymerase
- The gaps between the fragments are sealed
  - ↳ by the enzyme DNA ligase

# Topic 17: Nonmembranous cell organelles – ribosomes, polyribosomes




## Ribosomes (polyribosomes – intensely basophilic):

- cell organelle that consists of 65% RNA & 35% proteins
- responsible for assembling the proteins of the cell
- ribosomes may number in millions
  ↳ depending on the protein production level of the cell
- Eukaryotes: composed of a large (60S) subunit, small (40S) subunit
- subunits are synthesised by the nucleus
- subunits join together during protein synthesis when the ribosome attaches to mRNA
- mRNA ⟶ proteins
  Ribosomes connected to tRNA translate the protein-coding genes

## Types of ribosomes:

- there are 2 types of ribosomes in the cell, they can be free or bound to RER

**• Free ribosomes**

> found in cytosol
> usually make proteins that will function in the cytosol
> also synthesise proteins for import into the nucleus, mitochondria & peroxisomes

**• Bound ribosomes**

> bound to Rough Endoplasmatic Reticulum
> usually synthesise proteins that are exported from the cell or included in the cell membrane
> proteins are seperated during translation into the interior of the RER's membrane cisternae

## Protein synthesis – transcription & translation

- occurs through two processes; transcription & translation
- is the process in which cells make proteins

### 1. TRANSCRIPTION:

- occurs in the nucleus
- the double strand (ds) DNA is uncoiled using DNA Helicase
  ↳ breaks the H bonds between the nucleotide base pairs
- the RNA Polymerase attaches to the DNA template strand
  ↳ this joines together the RNA nucleotides that are complementary to the nucleotides on the DNA temple strand
- joined together RNA nucleotides form a strand of mRNA → blueprint for protein synthesis
- mRNA (messenger) passes out of the nucleus through the nuclear pore into the cytoplasm

### 2. TRANSLATION:

- occurs in the cytoplasm
- has 3 stages

**I. Initiation:**

- the two subunits of ribosomes attach to the mRNA sequence at the start codon AUG & form a complete ribosome to initiate protein synthesis

**II. Elongation:**

- tRNA attaches to amino acids → matches its anticodon
- the tRNA delivers the amino acid to the complementary codon on mRNA
- after delivery of the amino acid the tRNA detaches & the process is repeated

**III. Termination:**

- the ribosome reaches a stop codon (UAA, UAG, & UGA)
- termination protein bind to the ribosome
  ↳ cause is to release the polypeptide chain
- undergoes post translational modification to become a fully functioning protein

# Topic 18. Non-membranous cell organelles – microtubules & cytofilaments

## Cytoskeleton:

- three dimensional network consisting of microtubules, microfilaments & intermediate filaments
- is found in the cytosol
- helps to keep the structure of the cell & helps move things around in the cell, like organelles as well as the cell itself

## Intermediate filaments

- diameter of 10 µm
- between actin & microtubules
- no polarity
- most stable
- found in animal cells (vertebrates & invertebrates)
- composed of a family of proteins sharing the same structural features
- contribute (beitragen) to structural elements
- hold tissue like skin togther

## Microfilaments

- function in cellular movement
- two inter twisted strands of proteins → actin
- also known as actin filament
- powered by ATP
  ↳ assemble its filamentous form → serves as a track for myosin movement
  ↳ motor protein
- provide some rigity and shape to the cell
- located close to the cell membrane
- can depolymerise quickly → be broken down into its monomers
  ↳ thus enabling a cell to change its shape & move

## Microtubules

- presented in the cytoplasm of eukaryotic cells
- thickest structural protein
- hollow cylindrical structures & stiff but flexible
- length of microtubules is flexible
- made up of 13 subunits (protofilaments)
- composed of alpha- & beta-tubules dimers
- protofilaments are organised into a circular tube
- 2 ends
  - non-growing end (negative) that correspond to alpha-tubulin → embedded in microtubule-organising centre (MTOC)
  - fast growing end (positive) that correspond to beta-tubulin → embedded in the microtubules periphery

**Functions:**

1. maintain cell shape
2. associated with cell movement
3. part of transport system within the cells
4. take part in the mitotic spindle
5. provide the basis for centrioles, basal bodies, cilia & flagella

## Cilia & flagella:

- flagella are long, hair like structures → extend from the plasma membrane & are used to move an entire cell, for example sperm
- when cilia present → many of them extend along the entire surface of the plasma membrane
  ↳ short structures → used to move an entire cell (such as paramecia) or move substances along the outer surface of the cell
- only difference in length & number → share the same structural arrangements of microtubules of a ring of nine microtubule doublets surrounding a single microtubule doublet in the centre

## Centrioles:

- only found in animal cells
- composed of short microtubules lying parralel to each other & are arranged around a central cavity to form a cylinder
- play a role in cell devision → formation of mitotic spindle

# Topic 19. Non-membranous organelles - cytocentre (centrosome)

## Centrosome:

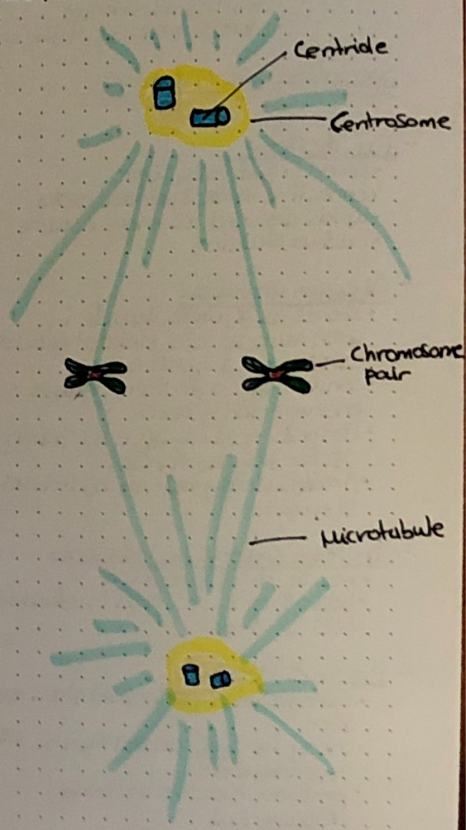
- is an organelle that serves as the main microtubule organising centre (MTOC) of animal cells
- serves also as a regulator of cell cycle progression
- composed of two orthogonally arranged centrioles, an amorphous mass of proteins & pericentriolar material
  ↳ contains (material) proteins responsible for microtubule nucleation & anchoring

## Functions of centriole:

- formation of mitotic spindle
- formation of cilia & flagella and building of their basal bodies

## Role of centrosome:

- required for survival of the organism
- associated with the nuclear membrane during prophase of the cell cycle
- mitosis: nuclear membrane breaks down → now the cytocenter can interact with the chromosomes → mitotic spindle is build
- cytocenter is only once copied per cell cycle
  ↳ each daughter cell inherits one cytocenter containing two centrioles



# Topic 20. Specialized cell organelles. Cell inclusions

## Cell inclusions:

- found in the cell cytoplasm
- produced by the cell
- or imported from the outside
- chemical substances → not permanent components of the cell
- are usually:
  - nutrients
  - sources of energy
  - stored products of the cells normal & abnormal metabolism

## Specialized cell organelles:

- **Fat droplets:**
  - found in fat cells, liver, connective tissue & adrenal cortex
  - lipids are used as energy source
  - Sudan staining
- **Glycogen granules:**
  - stored as glycogen deposits in liver, muscle cells, striated muscles, cartilage & nerve cells
  - convert glycogen into usable energy-rich glucose
  - Periodic-acid Schiff (PAS) staining
    ↳ for polysaccharides
  - Amalyse (enzyme) only hydrolyses glycogen
- **Protein/Crystalline inclusions:**
  - made up of proteins
  - testosterone is stored in glandular cells of testis
- **Pigment deposits:**
  - substances in cells that produce color
  - may be synthesized by the cells
    ↳ endogenous
  - or come outside the body
    ↳ exogenous
  - Endogenous pigments
    - > haemaglobin
    - > iron pigments (ferritin)
    - > melanin
    - > lipofuscins (found in neurons, cardiac cells & liver cells)
  - Exogenous pigments
    - > carotene
    - > dusts
    - > minerals
    - > tattoos
- **Melanin:**
  - protects the skin by tanning it
    ↳ reaction when skin is exposed to excessive UV radiation → Sun
  - abundant in epidermis
  - is a pigment in the layer of the retina (eye)
- **Haemaglobin:**
  - carries oxygen around the body in RBC
- **Lipofuscin:**
  - found in stable, non-dividing cells
    ↳ neurons & cardiac muscle
  - remaining bodies resulting from secondary lysosomes & undigested substances
  - increased quantity with age
- **Hemosiderin/Iron inclusion:**
  - from denatured ferritin proteins with a lot of atoms of bound iron
  - occurs in phagocytic cells
    ↳ especially macrophages of the liver and spleen (milz)
    ↳ results from phagocytosis of RBC

# Topic 21. Cytophysiology – vital and mitotic cycle of the cell. Amitosis, mitosis, meiosis.

## General:

- cell goes through 2 main phases to develop from a stem cell to a fully differentiated cell
- goes through mitosis → cell actively divides
- and second phase is interphase → apparent resting phase; cell prepares itself for the division
- Cell division can occur by four methods:
  1. Amitosis:
     > asexual reproduction
     > happens in unicellular organisms → bacteria
     > splitting of the nucleus is followed by the cytoplasmic restriction
  2. Endomitosis
     > chromosomes duplicate; cytoplasmic division is prevented
     > results in the duplication of chromosome number
  3. Mitosis
     > parent cell divids into two identical daughter cells
     > each receive a chromosomal set → identical to that of the parent's
  4. Meiosis
     > results in the production of 4 haploid gametes, oocytes or sperm cells

## Interphase:

- appears as a resting stage
- is actually a period of diverse activities
- very important phase → enables the next mitosis
- Last from 12h to 24h → in this time the cell synthesizes RNA, produces proteins & grows in size
- divided into four steps:
  > Gap 0 (G0)
    - cell leaves the cicle → quit dividing
    - temporary or permenant resting method
    - example: if the cell already reached the end stage of development & will no longer divide
      ↳ eg. neuron
  > Gap 1 (G1)
    - cell grows in size
    - produce RNA
    - and synthesize proteins
    - important mechanism activated → ensures that everything is ready for DNA synthesis
  > S Phase:
    - DNA replication occurs during this phase → two similar daughter cells are produced
  > Gap 2 (G2)
    - gap between DNA synthesis & mitosis
    - cell continues to grow & produces new proteins
    - last checkpoint at the end of this phase → determine if the cell can proceed to enter mitosis

## Mitosis:

- stage of cell division into two similar daughter cells
- much shorter than interphase → only 1 to 2 hours
- cell growth & protein production stops here
- one checkpoint (Metaphase) → ensures the cell is ready to complete the division

> Prophase:
- chromatin condenses → becoms visible as chromosomes
- each chromosome consists of two chromatids → joined at the centromere
- centrioles move to the opposite poles of the cell → astral fibers & spindle fibers form
- nucleoli disappears & nuclear envelop degenerates

> Metaphase:
- chromosomes align at the equator with spindle fibers → each chromosome divids longitudinally to form two chromatids
- attach at the microtubules of the mitotic spindle at the centromeres

> Metaphase/anaphas checkpoint
- checks if all the DNA is still intact & if all chromosomes are attached to the mitotic spindle

> Anaphase
- sister-chromatids of each chromosome are seperated & pulled to opposite spindle poles of the cell

> Telophase:
- chromosomes sets revert to decondensed state
- nuclear envelop & nucleoli reappear
- constriction ring develops at the equatorial plane

> Cytokinesis:
- constriction ring produces a cleavage furrow → continues until cytoplasm & its organelles are divided
  ↓
  two seperate daughter cell, each with a nucleus is formed

## Meiosis:

- two cell divions only in germ cells used to produce gametes → sperm or egg cells
- 4 haploid gametes are produced
- first interphase, then meiosis (I & II)

## Interphase:

- G1 phase - cell size increases & prepares for cell division
- S Phase - DNA replication occurs → chromosomes duplicate to form two identical sister chromatids
- G2 phase - cell produces proteins needed for meiosis & continues to increase in size

## Meiosis I

**Prophase I**
> nuclear envelope begins to dissolve
> condensation of homologous pairs
> recombination can occur → cross over

**Metaphase I**
> Homolouges chromosomes line up in double file

**Anaphase I**
> homolages chromosomes are pulled to opposite poles by the spindle
> sister chromatids remain together

**Telophase I**
> chromosomes (homolauges) unravel into its chromatin state
> nuclear membrane starts to form again
> microtubules dissolve
> cytokinesis starts

**Cytokinesis I**
> two daughter cells produced with haploid number

## Meiosis II

**Prophase II**
> nuclear envelope dissolves again & chromosomes condense too
> spindle forms

**Metaphase II**
> chromosomes align in the cell center
> spindle fibers attach to chromosomes

**Anaphase II**
> microtubules seperates chromosomes
> sister chromatids are pulled towards opposite poles of the cell by the spindle

**Telophase II**
> the two cells are becoming four → in Telophase II this process is prepared
> nuclear envelope is forming
> microtubules dissolve
> cytokinesis starts

**Cytokinesis II**
> finally the cell divids → four cells with each having two chromosomes
> gametes are formed

# Topic 22. Cytophysiology – cellular metabolism, transmembrane transport

## Metabolism

- set of chemical reactions → to maintain life
- allows the organism to grow & reproduce, maintain their structures, and respond to environmental changes
- organised into chemical pathways → regulated by enzymes
- Cellular metabolism has two types: ↳ help to maintain the ideal conditions for cells in the body ⇒ homeostasis
  - > Anabolism:
    - constructive metabolic process
    - uses energy to construct molecules → such as enzymes or nucleic acids
    - has three different basic stages
      1. production of precursors (amino acids, monosaccharides, isoprenoids & nucleotids)
      2. activation into reactive form
      3. assembly (zusammenbau) of these precursors into complex molecules
         → Example:
         - amino acid + amino acid → protein
         - glycerol + fatty acid → triglycerides
         - glucose + glucose → glycogen
  - > Catabolism
    - deconstructive metabolic process
    - cell breaks down complex molecules
    - looses / releases energy → exothermic process
    - purpose: provide the energy & components needed by anabolic reactions
    - Examples:
      - Protein → amino acids + energy
      - Triglycerides → glycerol + fatty acid + energy
      - glycogen → glucose + energy

## Transmembrane transport

- biological process → move oxygen, water & nutrients into cells / removes waste products
- active transport:
  - requires energy
  - movement of biochemicals from areas with lower concentration to areas with higher concentratio
- passive transport:
  - does not require energy
  - movement of biochemicals from areas with higher concentration to areas of low concentration

### Passive transport

a) Diffusion (simple)
- > small-non charged molecules or lipid: soluble molecules pass between the phospholipids to enter or leave the cell
- > move down their concentration gradient (high to low)
- > Oxygen, carbon dioxide & most lipids enter & leave cells by simple diffusion

b) Osmosis
- > type of simple diffusion in which water molecules diffuse → through selective permeable membrane
- > its the diffusion of water from areas of low solute concentration (hypotonic solution) to areas of high solute concentration (hypertonic solution)

c) Facilitated diffusion
- > molecules / substances move in and out of the cell through channels made of proteins in the cell membrane → membrane specialized channel
- > charged or polar molecules that don't fit between the phospholipids enter & leave through these channels

d) Filtration
- > physical or mechanical operation
- > filtrate = fluid that passes through the medium

### Active transport

a) primary active transport
- > functions with the active transport of sodium & potassium
- > pump maintains electrochemical gradient in living cells
- > the sodium-potassium pump ($Na^+$-$K^+$-ATPase) moves two $K^+$ into & three $Na^+$ out of the cell
- > result: electrical imbalance (more sodium ions outside across the membrane & more potassium ions inside)
  ↓
  contributing to the membrane potential

b) secondary active transport
- > transport methode: uses electrochemical potential difference for molecule transport
- > Endocytosis is one type: plasma membranes creates an intracellular vesicle filled with a particle to move around
  ↓
  3 types

b.1) Phagocytosis (eating):
- > ingestion of bacteria or dead cells
- > forms a vacuole with the particle

b.2) Pinocytosis (drinking):
- > takes in molecules, including water
- > vesicles fuse with lysosomes or move to opposite cell surface to fuse with the membrane & release their contents outside the cell

b.3) Receptor-mediated endocytosis
- > plasma membrane receptors bind specific substances
- > receptors & bound substances are taken up by cell in vesicles from plasma membrane

# Topic 23. Cytophysiology - cellular signalling, cellular reactivity & motility

## Cellular signalling:

- complex system of information signals
- communication is made for
  > preceiving of cell integrity
  > maintenance of optimal tissue homeostasis
  > coordination of cell actions
- in the multicellular organisms are 4 categories of chemical signalling

1. Autocrine
   - cell targets itself
   - signalling cells produce autocrine signals
   ↳ these cells can bind to the ligand that is released
   - target & signalling cell can be same / different
   - auto = self
2. Paracrine
   - act locally between nearby cells
   - move by diffusion → extracellular matrix
   - release quick responses → last only a short amount of time
   - paracrine ligand molecules are quickly degraded by enzymes or removed by neighbouring cells → to keep the respond localized
   - re-establishing the signal's concentration gradient: if the signal is removed, it will be able to diffuse quickly through the intracellular space if released again
3. Endocrine
   - originate from endocrine cells
   - signals from distant cells
   - produce a slower response → lasting effect longer
   - these ligands are called hormones → produced in one part, but affect other body regions
   - travel the large distance to their target cells via the bloodstream
   ↳ slow way to move throughout the body
   - hormones get diluted
   - present in a low concentration → when acting on target cells
4. Direct signalling across Gap junctions
   - connections between neighboring cell plasma membrane → in animal & plasmodesmata in plants
   - small signalling molecules known as intracellular mediators
   ↳ can diffuse through these water-filled channels
   - small molecules can diffuse (calcium ions); large cannot (eg. DNA or proteins)
   - specifity of the channels ensures that the cells remain independent while transmitting signals quickly & easily
   - these cells communicate the cell's state immediately to the target cell

## Cell reactivity & motility

- ability to react on the continuously changing environment; eg. temperature, light, sound, electricity
- cells answer with extra ability, conductibility & corresponding reaction; eg. movement, secretion

## Cell motility

1. Move by taxis
   - cell has the ability to attract or repel chemical substances, or light (phototaxis)
   - process calls positive or negative taxis
   - positive rectaxis = cells are moving along the direction of flow
   - negative rectaxis = cells are moving against the direction of flow
2. movement by pseudopodia
   - movement is carried out by cytoplasmic pseudopodia
   ↳ contain actin and myosin filaments & ATP
   - these filaments are on the base of the process of migration
3. movement by cilia & flagella
   - generated by the axoneme
   - both are ultrastructural identical
   - motion of flagella is propeller-like
   - motion of cilia consists of coordinated back & forth cycling
   ↳ beating of many cilia on the cell surface
4. muscular movement
   - done by actin & myosin filaments

# Topic 24. Cytophysiology - cellular growth, aging and cell death

## Cell differentiation

- all the cells of the body contain same DNA → this genetic material make every individual unique
- cell differentiation is how embryonic cells become specialized cells
- occurs through a process called gene expression
- gene expression: specific combination of genes that are turned off or on (expressed or repressed)
  - ↳ dictates how a cell functions
    - ↳ occurs because of certain signals in your body, both inside and outside the cells
    - ↳ occurs during multiple stages of development
    - ↳ cell size & shape change dramatically; so does the ability to respond to signalling molecules
- Signalling molecules bring messages to cells helping them which activities & processes to perform
  - ↳ they carry a message to a cell receptor
  - ↳ receptor interprets the message through a signal transduction pathway
  - ↳ pathway translates the message into something the cell can recognize & understand
  - ↳ cell knows now how to function
- three categories of specialized cells
  1. Fully differentiated, non-dividing cells
  2. Potentially dividing cells
  3. Not-terminally differentiated, renewal by stem cells:
     - > Unipotent cells
       - one stem cell has the capacity to differentiate into only one cell type (eg. Hepatoblasts $\xrightarrow{\text{into}}$ hepatocytes)
     - > Pluripotent cells
       - a stem cell that has the potential to differentiate into any of the three germ layers
         - ↳ endoderm (interior stomach lining, GIT, the lungs)
         - ↳ mesoderm (muscle, bone, blood, urogenital)
         - ↳ ectoderm (epidermal tissue, & nervous system)

## Cellular growth, aging & death

- growth of an organism or organ depends on cell growth not only cell division
- single-celled organisms: cell growth requires only nutrients
- in animals: cell growth & cell division both depend on signals from other cells
- extracellular growth factors bind to receptors on the cell surface → activates intracellular signalling pathways
- these pathways stimulate the accumulation of proteins & other macromolecules by increasing their rate of synthesis & decreasing their rate of degradation
- one of the most important pathways activated by growth factor receptor involves the enzyme PI 3-kinase
- cells need signals from other cells to survive → if withhold such survival factors, cells activate intracellular death program & die by apoptosis (cell suicide program)
  - ↳ ensures that cells only survive when & where they are needed
- All living cell become old and die due to:
  - > acute cellular injury
  - > programmed by gene expression changes
    - depending if the death is caused by external factors or because of programmed gene expression, there is:
      1. Necrotic cell death (necrosis): cell death is caused by external factors, such as infections, toxins or trauma
      2. Programmed cell death: apoptosis or programmed cell death is a process of a cell, mediated by an intracellular program

# Topic 25. General histology - introduction. Tissues - definition, general features & classification

## Histology:

- microscopic study of the tissues of the body and there organisation to form organs
- two main components of tissues are studied:
  - cells and
  - extracellular matrix
- importance of histology:
  - helps in understanding pathology of tissues
    ↳ in case of defective development or congential absence of an organ or tissue

## Tissues:

- human body is composed of only 4 basic types of tissue: connective tissue, muscular tissue, nervous tissue & epithelial tissue
- these tissues are formed by cells & molecules of the extracellular matrix
- tissues doesn't exist as an isolated unit but rather in association with one another & also in variable proportions, forming different organs & systems of the body
- organs can be devided into two components:
  ↳ parenchyma: cells and tissues, that are responsible for the main functions
  ↳ stroma: the supportive framework (tissue; except in the brain & the spinal cord, the stroma is made of connective tissue

## Function of the different tissues:

① Nervous tissue:
- consist of cells with intertwinning elongated (ineinandergreifend, langstreckend) processes (Neurons, Soma, dendrites, axon, ...)
- no extracellular matrix
- main function is the transmission of nervous impulses

② Muscle tissue:
- consists of elongated contractile (Langstreckend, zusammenziehbar) cells
- has a moderate amount of extracellular matrix
- main function is movement

③ Connective tissue:
- consists of several types of fixed & wandering (feststehende & wandernde) cells
- has a plenty amount of extracellular matrix
- main function is protection, support & connection of other structures (like organs)
- most common type of basic tissue

④ Epithelial tissue:
- consists of aggregated polyhedral (eng gruppierten, vielflächigen) cells
- has a small amount of extracellular matrix
- main function is the lining of surface or body cavities & the glandular secretion

- also of great function are the free cells found in body fluids such as blood & lymph

## General properties of all the tissues:

- regeneration
- degeneration / deterioration
- atrophy: reduction of the cell volume and/or number of cells in a given tissue
- aplasia: defective development or congential absence of an organ or a tissue
- hypotrophy: increase in cell number from cell proliferation
- hypertrophy: increase in cell size
- metaplasia: change in cell form / type
- neoplasia: abnormal growth of tissue, forming a mass called a tumor

Muscle tissue can be further devided into:

1) Skeletal muscle - contains bundles of very long multinucleated cells; striated; quick voluntary contractions
2) Cardiac muscle - contains elongated, often branched (verzweigt) cells bound to one another at intercalated discs; striated; vigiorous (starke) involuntary contractions
3) Smooth muscle - consist of collections of fusiform cells; not striated; slow - involuntary contractions

Epithelial tissue can be further devided into:

1) covering, lining & protecting epithelia (skin)
2) absorption (intestines)
3) secretion (epithelial cells of glands → endo & exocrine
4) contractility (myoepithelial cells)

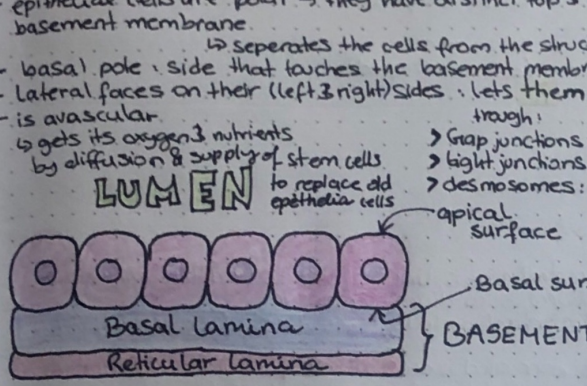
Connective tissue can be further divided into

1) Connective tissue proper (loose or dense refers to the amount of collagen present)
   ↳ loose connective tissue has much more ground substance & a relative lack of collagen
   ↳ dense connective tissue (dense irregular & dense regular)
   - dense regular connective tissue is found in structures such as tendons & ligaments and is characterized by collagen fibers arranged in an orderly parralel direction, giving it tensilestrength in one direction
   - dense irregular connective tissue provides strength in multiple directions by its dense bundle of fibers arranged in all directions
2) Specialized connective tissue
   ↳ reticular connective tissue
   - supports blood forming cells, secretory cells & lymphocytes in most lymphoid organs
   → adipose tissue → bone
   → cartilage → blood

# Topic 26. Epithelial tissue - general features, types of epithelial tissue

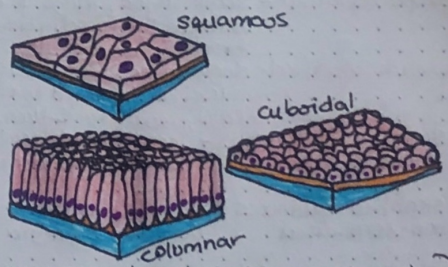
## General features:

- makes up most of the skin and the borders between different organs
- two main jobs:
  1. forming layers of cells that cover internal & external surfaces like the lining of blood vessels and skin
  2. secreting different substances either within the body or outside the body
- in some cases they are also responsible for forming the functional bulk of certain organs called parenchyma, eg. liver → 80% epithelial liver cells (hepatocytes)
- have unique jobs → depends on where we find them, but most of the time we care about them as protective layers & secreting cells
- epithelial cells are polar → they have distinct top & bottom poles oriented around a basement membrane
  ↳ seperates the cells from the structures around it
- basal pole: side that touches the basement membrane; apical pole: side that faces the lumen
- lateral faces on their (left & right) sides: lets them communicate between neighboring cells
- is avascular
  ↳ gets its oxygen & nutrients by diffusion & supply of stem cells to replace old epithelia cells
  - > Gap junctions: let really tiny particles like ions through trough
  - > tight junctions: let a few specific proteins through
  - > desmosomes: help anchor cells together




## Types of epithelial tissue

| Layer style | cell shape |
|---|---|
| simple (single layer) | squamous (squished flat) |
| pseudostratisfied (looks like multiple layers) | cuboidal (cubed shaped) |
| stratisfied (multiple layers) | columnar (column shaped) |




- simple squamous epithelium - lines blood vessels, thinness makes it ideal to pass through some substances like oxygen, but still want to keep blood contained
- simple cuboidal epithelium - for secretion of substances like in the seminiferous tubules of in the testis
- simple columnar epithelium - like in the walls of the GIT, can also secrete and absorb things
- pseudostratisfied - lining of trachea, bronchi, nasal cavity, epididymes, looks like simple columnar cells
- stratisfied squamous - mouth, oesophaagus, larynx, vagina, anal canal
- stratisfied squamous keratiniesed - epidermis
- stratisfied cuboidal - sweat glands, developing ovarian follicles
- stratisfied columnar - large ducts of salivary glands, part of urethra
- stratisfied transitional - lines urinary tract; ureters & bladder

covering epithelia

- endocrine - ductless, secrete hormones, directly into tissues & blood, eg. adrenal glands
- exocrine - tubular ducts, eg. salivary glands, prostate, mammary glands (breast)

glandular epithelia

# Topic 27. Epithelial tissue - surface / covering epithelium

## Tissues

| Layer Style | + | Cell shape |
|---|---|---|
| simple (single layer) | | squamous (squished flat) |
| pseudostratified (simple columnar - looks like multiple layers) | | cuboidal (cube shaped) |
| striatified (multiple layers) | | columnar (column shaped) |
| keratinized (filled with keratin) | | transitional (at least two cell types) |

## Covering / surface epithelia

- Simple squamous - single layer, round & central nucleus. Lining of vessels (endothelium), serous of cavities (mesothelium), pericardium, peritoneum
- simple cuboidal - single layer, large & spherical nucleus, Lines ducts of exocrine glands, ovaries & thyroid
- simple columnar - single layer, large & elongated nucleus at base. Microvilli on apical side increase SA. Found in lining of intestine & respiratory tracts. Ciliated columnar in bronchi - move mucus in one direction
- pseudostratified - single layer with cells of different sizes which might not reach the surface, nuclei at different levels & apical cilia. Lining of trachea, bronchi, nasal cavity, epididymis. Main function = protection, secretion & movement of substances
- stratified squamous keratinised - form the epidermis, cells of the epidermis get nourishment from blood vessels in the dermis. The epidermis consist of 5 layers / strata
- stratified squamous non-keratinised - found on moist surfaces & consist of only 3 layers. Lines the mouth, oesophagus, larynx & vagina, don't contain keratin
- stratified cuboidal - Lines sweat glands, ducts of large exocrine glands & cells of superficial layer are larger than basal
- stratified columnar - large ducts of largest exocrine glands, large columnar cells in superficial layer with cuboidal cells are found at the bottom. Found in salivary glands, part of urethra
- stratified transitional (urothelium) - 3 layers. Basal layer with round cells, intermediate with tennis racket cells & superficial with umbrella like cells towards lumen, usually double nuclei in superficial. Lines urinary tract - ureters & bladder. When bladder is full & membrane is stretched, it appears as stratified. Impermeable to water & ions

# Topic 28. Epithelial tissue - glandular epithelium

## Glandular epithelium

- formed by specialised epithelial cells → funtion: secretion
- one or more cells; produce & secrete product
- water-based product & contains different substances → product = secretion
- obtain needed substances from blood → transform them chemically into secretion product
- different secretion products cause contents can be proteins, lipids or complex carbohydrates
- secretory part of gland = parenchyma
- connective tissue supporting gland → stroma
- two types
  - ↳ exocrine (duct)
  - ↳ endocrine (ductless)

## Developement of glandular epithelium

- originate from all three germ layers (arises from covering epithelia & differentiates into glandular epithelia)
- Exocrine glands: originate from surface epithelium & stays connected to the surface epithelium
- Endocrine glands: connection to surface epithelium is eliminated during development
  - ↳ why they are ductless & secrete directly into the bloodstream

## Exocrine glands

- secrete their product directly or through ducts into a surface
- can be categorised according to number of cells, shape, secreted product & method of secretion:

### Number of cells

- unicellular: secretory unit consists of one cell, eg. goblet cell secreting mucous
- multicellular: secretory unit consists of multiple cells

### Shape

- simple tubular
- simple acinar
- compound tubular
- compound acinar
- compound tubuloacinar

### Method of secretion

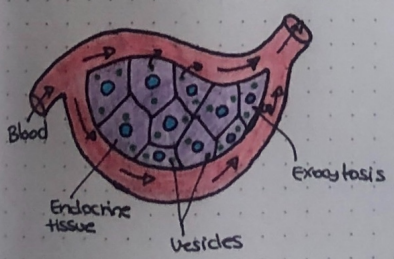
- merocrine: most of exocrine glands, and some endocrine glands; secreted in vesicles by exocytosis
- apocrine: secretory portion is released with the apical portion of the cell; remaining cell repairs itself eg. large sweat glands & mammary glands
- holocrine: secretory product is released into lumen; cell detaches itself & dies, forming the secretion; these cells are replaced by neighboring cells eg. sebaceous glands in the skin.

### Secreted product

- serous: appear as more dense, because they are rich in enzymes & secretions; pyramidal shaped cells with secretory granules at the top & around the nucleus, basophilic cytoplasm; watery fluid, eg. parotid gland, exocrine pancreas
- mucous: appear as less dense because they have less enzymes, eg. goblet; cuboidal cells & have paler cytoplasm with basally located nucleus → is flattened due to mucous vesicles pushing it into the periphery of the cell
- mixed, eg. most salivary glands

## Endocrine glands

- lack a duct system; products are hormones secreted directly into the bloodstream
- endothelium of the capillary:
  - secretes hormones, eg. thyroid gland, suprarenal gland
  - is highly vascularised
  - is fenestrated (has holes) - facilitates diffusion for large molecules of hormones into the blood



# Topic 29. Connective tissue - general features & classification

## General features

- most abundant type of the 4 basic tissues
- responsible for providing and maintaining the form of organs throughout the body
- mainly supports, connects or seperates other tissues & cells in organs, gives metabolic support
- Components: ground substance + cells + fibers
- major constituent: extracellular matrix (ECM)
- originates from the mesenchyme (embryonic tissue formed by elongated undifferentiated cells)

## Classification of connective tissue

- 2 main types; further subdivided; all are derived from the mesoderm germ layer of the early embryo
  - Embryonic connective tissue
  - Adult connective tissue

### embryonic connective tissue

**mesenchymal**
- found in embryo
- mesenchymal cells
- reticular fibers in ground substance
- stem cells

**mucous**
- umbilical cord
- collagen bundles
- fibroblasts

### adult connective tissue

#### proper

**loose**
- areolar:
  - most dominant kind
  - referencing all the space of connective tissue
  - used in papillary layer of the skin
- reticular:
  - open & airy
  - but has instead of collagen fibers, reticular fibers
- adipose:
  - shaking loose connective tissue

**dense**
- irregular
  - multiple direction strength
  - regular
  - best example: ligaments → attach bone to bone
  - exist to prevent excessive motion in one particular direction
  - single direction strength

#### specialized

**bone**
- osteocytes
  - unique to bone

**cartilage**
- chondrocytes
  - unique to cartilage

**fluid**
- blood
  - erythrocytes
    - or RBC are unique to blood
- lymph

## Topic 30. Connective tissue - with non-differentiated intercellular substance

- can be found in the embryo → embryonic connective tissue

### ① Mesenchymal Connective tissue:

- found in embryo → originate from mesenchymal (all tissues)
- mesenchymal connective tissue originates from embryonic mesenchyme
  ↳ tissue developed from mesoderm of the embryo
- consists of mesenchymal cell, fine reticular fibres and few collagen fibres in ground substance
- mesenchymal cells:
  - small spindle-shaped cells with large nucleus, prominent nucleolus & fine chromatin

### ② Mucous connective tissue:

- main component of foetal umbilical cord → wharton's jelly
- surround vessels of umbilical cord
- found in pulp of teeth & core of villus of placenta
- abundant ground substance
- richin hyaluronic acid, chondroitin sulphate & sparse collagen fibres between cells
- more viscous consistency than mesenchymal connective tissue

# Topic 31. Connective tissue - with fibrous intercellular substance (cartilage)

## Cartilage:

- flexible but strong supportive connective tissue
- Is avascular, lacking blood vessels
- does not posses the regenerative capacity of bone or other connective tissue type
- characterized by 95% ECM, with high concentrations of GAGs & proteoglycans
- Located in ears, respiratory tract, nose & forms the framework supporting softer tissues
- consists of two types of cells - chrondoblasts & chronocytes

## Cells:

① Chrondoblasts (young chrondocytes):
- originate from undifferentiated mesenchymal cells
- well developed ER in a basophilic cytoplasm
- located in the internal layer of periosteum & in depth of matrix

② Chrondocytes:
- embedded in ECM
- Synthesise & maintain all ECM components
- located in matrix cavities → lacunae
- low metabolic activity
- mitotic & synthetic activity declines with age

## Types of cartilage:

① Hyaline cartilage:
- located in trachea & bronchi, articular surfaces, larynx, costosternal junctions, collagen fibers, ground substance GAGs & proteoglycans
- covered externally by a fibrous membrane → perichondrium
- most of the collagen is type II

② Elastic cartilage:
- located in pinna of the ear, nasal cartilages, elastic & collagen fibers, ground substance GAGs & proteoglycans
- abundant network of elastic fibers in addition to a meshwork of collagen type II fibrils → gives the yellow color
- principle protein = elastin

③ fibrous cartilage:
- attachment of tendons & ligaments to hyaline cartilage
- intervertebral discs symphysis
- flexible & elastic
- ground substance GAGs & protoglycans

# Topic 32. Connective tissue - with dense intercellular substance (bones)

## Bones:

- tissue consists of widely separated cells → surround by large amounts of matrix
- 2 different types of matrix
  - organic matrix: includes collagen & elastic fibers → give strength & flexibility to the tissue
  - inorganic matrix: consists of mineral salts → give the tissue hardness

## Cells:

① Osteoblasts:
- cuboidal, columnar & polygonal in shape
- well developed RER
- production of bone intercellular matter

② Osteocytes:
- mature form of osteoblasts
- weak secretion of bone intercellular components

③ Osteoclasts:
- macrophagus of bone tissue
- giant & multinucleated
- produce lots of digestive enzymes as lysosomes
- destruction & resorption of bone fibers and ground substance

## Types of bones:

- Compact bone:
  - arranged in units → osteons or haversian system
  - osteons contain blood vessels, lymphatic vessels & nerves
- Spongy bone:
  - does not contain osteons
  - forms most of the structures of short, flat, irregular bones & the epiphysis of long bones
  - spongy bone tissue is light & supports & protects the red bone marrow

## Bone formation:

- is termed osteogensis or ossification
- Intramembranous ossification: formation of bone directly from fibrous connective tissue membranes
- Endochondral ossification: formation of bone from hyaline cartilage models
- at the epiphyseal (growth) plate: bone growth in length
- epiphysal plate has 4 zones:
  1 zone of resting cartilage
  2 zone of proliferating cartilage
  3 zone of hypertrophic cartilage
  4 zone of calcified cartilage
- Factors that affect bone growth:
  - nutrients
  - sufficient levels of specific hormones
  - adequate amount of minerals & vitamins
  - calcium & phosphorus
- vitamin c for collagen & vitamin k & b12 for protein synthesis
- Functions:
  - supporting & protecting soft tissues
  - attachment site for muscles → make movement possible
  - storage of minerals, calcium & phosphate → mineral homeostasis
  - blood cell production in red bone marrow → hemopoesis
  - energy storage in yellow bone marrow

# Topic 33. Blood & lymph - blood and lymph plasma: contents, antibodies

## Blood:

- blood tissue is a specialised form of connective tissue
- responsible for the transport & delivery of metabolites
- location:
  - blood tissues are found inside blood vessels (arteries, arterioles, capillaries, veins & venules)
  - within the heart chambers
  - white blood cells are also found in adipose tissue
  - lymphocytes can be found in the lymphatic system
- consists of different blood cells & plasma (extracellular fluid)
  - Erythrocytes (RBC) - 97%
  - Leukocytes (WBC) - 3%
  - Platelets - 1%

## Functions of blood:

- transport medium
- thermoregulation
- controls pH
- toxin removal
- regulation of electrolytes
- bodily defence
- blood clotting

## Composition of blood:

- amount: 4-6 liters, 7-8% of body weight
- composed of plasma & blood cells
- plasma proteins: albumin, globulins, fibrinogen, complement proteins
- haematocrit: volume percentage of RBC in blood
  - 36-48% in women, 42-52% in men; 44-64% in new-born baby

## Composition of blood plasma:

1. Albumin: most abundant plasma protein; made by liver; maintaining osmotic pressure
2. Alpha- & Beta-globulins: made by the liver; include transferring & other transport factors; fibronectin, lipo proteins & the proteins are entering blood from tissues
3. Gamma-globulins: antibodies secreted by lymphocytes in many directions & locations
4. Complement proteins: system of factors important in inflammation & destruction of micro organisms
5. Fibrinogen: Largest plasma protein; made by the liver; polymerises as insoluble during clotting, crops-linked fibers which block blood loss from small vessels

## Antibodies:

1. IgA: function in defense against pathogens; existing in saliva, breast milk, intestinal secrete & urogenital secrete
2. IgD: receptor for antibodies, very small amount in plasma
3. IgE: bound to the cell membrane of eosinophils & basophils; defence against parasite infection
4. IgG: 80% of all immunoglobulins; found in plasma & body secretes; only immunoglobulin which can pass to the placenta; defence & neutralisation of antigenes; immune response → secondary response; mark micro organism
5. IgM: immune response → primary response; first group of immunoglubins that appears in blood after infection; neutralisation of antigenes; can't mark microorganisms

## Lymph & its components

- is a clear-to-white fluid found between cells & tissues formed by blood plasma
- contains a variety of substances, including proteins, salts, glucose, fats, water & WBC
- main function is the transport of oxygen, nutrients & hormone to cells; also the transport of waste substances like $CO_2$ away from the cell; body cells are kept moist by the lymph
- brings plasma protein macromolecules made in the liver & hormones made in the endocrine glands to the cells, 'cause they can't diffuse into the narrow blood capillaries
- helps clear the body of cellular wastes & infective organisms
- has to be recovered back into the bloodstream to prevent blood from becoming too concentrated & to keep tissues from drowning in interstitial fluid
- blood volume decreases → means lymph returned back into the blood vascular system
- lymph nodes filter lymph → kill pathogens & produce lymphocytes
- takes lymphocytes & antibodies to the blood
- absorbs fat & fat-soluble vitamins from the intestines

# Topic 34. Morphology & function of erythrocytes, leucocytes, thrombocytes

## ① Erythrocytes (RBC):

- total number: $4.7-5 \times 10^{12}$ / litre blood
- size: 7.5 ± 0.5 µm
- diameter: 0.8 µm (centre); 2.6 µm at rim
- total surface: 140 µm² (2500 m²)
- Haemoglobin types:
  - $HbA_1$ (96-97%)
  - $HbA_2$ (2%)
  - HbF (1-2%; in new borns & 80% in adults)
  - HbS - sickle cell membrane
- plastic plasmalemma (membrane:
  - 40% lipids
  - 50% proteins
  - 10% carbohydrates
- life cycle in blood 120 days (140 in men; 109 in women)
- Haemoglobin makes 90% of dry content: 120-180 g/L
- flexible biconcave discs, allowing them to move through capillaries
- lack nucleus
- main functions:
  - $O_2$ - oxyhaemoglobin
  - CO - carboxy haemoglobin
  - $CO_2$ - carbaminohaemoglobin

## ② Leukocytes (WBC):

- total number: $4-10 \times 10^9$ / litre blood
- 2 Groups & 5 types
  - Granulocytes (polymorphonuclear)
    - > Neutrophilic granulocytes (60-70%)
    - > Eosinophilic granulocytes (2-4%)
    - > Basophilic granulocytes (0.5-1%)
  - Agranulocytes (mononuclear)
    - > lymphocytes (20-30%)
    - > Monocytes (3-8%)
- Agranulocytes
  - do not have specific granules, but they do have azurphilic granules (lysosomes)
- Lymphocytes
  - 20-40% of all WBC
  - vary in size (diameter): small (6-8 µm); medium (8-12 µm); large (12-18 µm)
  - nucleus - large spherical, hyperchromatic
  - basophilic cytoplasm with free ribosomes
  - vary in life span according to their function
  - B cells, T cells & NKC
  - involved in humoral response (B cells, plasma cells, antibodies) & cell mediated immunity (T cells)
- Monocytes
  - 3-8% of all WBC
  - size: 13-20 µm (diameter)
  - kidney shaped nucleus
  - pinocytotic vesicles & many microvilli
  - basophilic cytoplasm
  - granules: small azurphilic (lysosomes) granules
  - life span: 1-8 hours in blood; in CT months
  - perform phagocytosis
- Granulocytes
  - have two types of granules
  - have short life span of a few days & normally die by apoptosis in the CTs
    - ↳ resulting cell debris is removed by macrophagus
- Neutrophilic granulocytes
  - 60-70% of all leukocytes
  - size: 10-12 µm diameter
  - segmented nucleus: 2-5 lobes
  - 50-200 granules - specific (B granules) (80%) & azurophilic (lysosomes with acid hydrolases) (15%)
  - life span: 12-14 hours in blood; 1-4 days in CT before apoptosis
  - perform phagocytosis and are the first to appear at site of infection
- Eosinophilic granulocytes
  - 2-4% of all leukocytes
  - size: 12-17 µm
  - bilobed nucleus
  - specific granules & azurphilic (lysosomal enzymes) granules
  - life span: 6-16 hours in blood; 8-12 days in CT
- Basophilic granulocytes
  - less than 1% of all leukocytes
  - size: 10-12 µm
  - large nucleus - irregular lobes
  - specific granules (histamine) & azurphilic granules (lysosomes & hydrolic enzymes)
  - life span: 1-12 hours in blood
  - motile cells

## ③ Thrombocytes (Platelets)

- total number: $20-40 \times 10^9$ / litre blood
- size: 1.5-3.5 µm
- non-nucleated, membrane-bound cell fragments
- Ellipsoidal shape
- originate from megakaryocytes in bone marrow
- Central zone - granulomere, containing purple granules
- Transparent zone - hyalomere, containing microtubules & actin filaments
- life span: 9-12 days

# Topic 35. Erythropoesis - formation of erythrocytes

- process of making blood cells
- early embryo blood cells arise from the yolk sac mesoderm
- 2nd trimester: occurs in liver & little occurs in spleen
- 3rd trimester: occurs in bone marrow - major haemopoietic organ
- Hemopoietic stem cells
  - : single major type of pluripotent stem cell in the bone marrow → can give rise to all blood cell types
  - : rare stem cells, but proliferate & form 2 major lineages of progenitor cells:
    - > lymphoid cells - lymphocytes
    - > myeloid cells - granulocytes, monocytes, erythrocytes & megakaryocytes
- Progenitor and precursor cells
  - : progenitor cells → colony-forming units (CFUs)
  - : 4 major types
    - > CFU-E (CFU-erythrocyte) > CFU-Meg (CFU-megakaryocyte)
    - > CFU-GM (CFU-granulocytes-monocytes) > CFU-L (CFU-lymphocyte)
  - · haemopoietic tissues are blood-forming tissue → consists of reticular fibers & similarly specialised CT cells of mesenchymal origin that give rise to new blood cells
  - · two types of haemopoietic tissue:
    - > myeloid tissue - formation of most of the blood cells: RBC, granulocytes & platelets
    - > lymphoid tissue - formation of T cells & proliferation of B cells, lymph nodes & associated lymphoid tissue MALT
  - · Periods of haemopoiesis:
    - > Prenatal haematopoiesis
      - · mesoblastic (megablastic phase)
      - · hepaticnal phase
      - · medullary (myeloid phase)
    - > Post natal haematopoisis
      - · myloid phase - in red bone marrow

## Erythropoesis

- example of terminal cell differentiation, involving haemoglobin synthesis & formation of small enucleated biconcave cell
- a lot of changes take place during erythrocyte maturation:
  - : cell & nuclear volume decrease
  - : nucleoli diminish in size & disappears
  - : chromatin becomes increasingly denser until the nucleus is finally extruded from the cell
  - · gradual decrease in the number of polyribosomes (basophilia decrease) & simultaneous increase in the amount of haemoglobin (acidophilic protein)
  - : mitochondria & other organelles disappear
- 3 to 5 cell divisions until the mature erythrocyte arises → process takes 1 week
- Stages of Erythropoiesis:
  1. Proerythroblast
  2. Basophilic erythroblast
  3. Polychromatophilic erythroblast
  4. Orthochromatophilic erythroblast
  5. Reticulocyte
  6. Erythrocyte
- Stages explained

① Proerythroblast: a large cell with loose, lacy chromatin, nucleoli & basophilic cytoplasm

② Basophilic erythroblast: with more strongly basophilic cytoplasm cytoplasm & a condensed nucleus with no visible nucleolus

③ Polychromatophilic erythroblast: cell volume is reduced, polyribosomes decrease & some cytoplasmic areas begin to be filled with haemoglobin, producing regions of both basophilia & acidophilia in the cell

④ Orthochromatophilic erythroblast: the cell and nuclear volumes continue to condense & no basophilia is evident

⑤ Reticulocyte: the cell ejects the nucleus; the cell still has a small number of polyribosomes

# Topic 36: Leucopoiesis - formation of granulocytes & agranulocytes

## Granulopoiesis

- differentiation & maturation take about 11-14 days
- involves cytoplasmic changes dominated by synthesis of proteins for the azurophilic & specific granules → produced in the RER & Golgi in 2 stages
- Azurophilic granules are made first & are generally the same in all 3 granulocytes → Golgi activity than changes to produce proteins for specific granules
- stages explained:

① has a finely dispersed chromatin & nucleoli
② is characterized by its basophilic cytoplasm & azurphilic granules; different promyelocyte activate different sets of genes, resulting in lineages for three types of granules
③ specific granules gradually increase
④ metamyelocyte is formed by occupying most of the cytoplasm; mature with further condensation of the nuclei
⑤ passes through an intermediate stage, band cell, in which the nucleus is elongated

- occurs in bone marrow
- stages of granulopoiesis:
  ① Myeloblast
  ② Promyelocte
  ③ Neutrophil, eosinphil, basophil myelocyte
  ④ Neutrophil, eosinphil, basophil, metamyelocyte
  ⑤ Band cell - only for neutrophilic granulocytes
  ⑥ mature granulocyte

## Agranulopoiesis

### Monocytes

- takes 55 hours
- occurs in bone marrow
- arise from a pluripotent cell in bone marrow
- monoblast is a committed progenitor cell
- leads, due to differentiations, to the promonocyte, a large cell with basophilic cytoplasm & a large, slightly indented nucleus
- promonocytes develop into monocytes, with large amount of ER & a Golgi apparatus in which granule condensation occurs → granules are primary lysosomes
- mature monocytes enter the bloodstream, circulate for eigth hours, enters then tissue → where they mature as macrophages & function for several month

### Lymphocytes

- originate mainly in the thymus & the peripheral lymphoid organs
- all lymphocyte progenitor cells originate from bone marrow
- some migrate to the thymus
- other differentiate into B-lymphocytes in the bone marrow & than migrate to the peripheral lymph organs
- as lymphocytes mature, their chromatin becomes more compact, nucleoli becomes less visible & cell decreases in size
- Lymphoblast = first identifiable progenitor
  ↳ its a large cell capable of dividing two or three times to form pro lymphocytes
- prolymphocytes are smaller & have more condensed chromatin but none of the cell surface antigenes

## Topic 37. Thrombocytopoiesis - formation of thrombocytes (platelets)

- platelets originate from red bone narrow → dissociate from mature megakaryocytes → differentiate from megakaryoblasts (process driven by thrombopoietin
- megakaryoblast has a large kidney-shaped nucles with numerous small nucleoli
- these cells undergo endomitosis, before differentiating, with repeated rounds of DNA replication
- not seperated by cell division → resulting polyploid nucleus
- cytoplasm is homogenous & intensely basophilic
- formation of platelets: megakaryotic extend several long, branching processes called proplatelets
- penetrate into blood flow in the vessels

# Topic 38. Muscle tissue - general features. Types of muscle tissue

## General features:

- 4th basic type of tissue
- composed of cells that optimise the universal cell property of contractility
- almost all muscle cells are of mesodermal origin
- differentiate mainly by a gradual process of cell lengthening with simultaneous synthesis of myofibrillar proteins
- Sacroplasm = cytoplasm of muscle cells
- SER is sacroplasmic reticulum
- sacrolemma = muscle cell membrane & its external lamina
- muscle fiber = unit of muscle tissue
- elongated cell structure → good for contractions
- Properties of musle tissue
  - conductivity
  - contractibility
  - elasticity
  - irritability
- Functions of muscle tissue
  - movement of the body
  - body posture stability
  - volume regulation of internal organs
  - heat production
  - contraction of the skeletal musle
- three types of muscle tissue:

① Skeletal muscle ② Cardiac muscle ③ Smooth muscle

① Skeletal muscle
- contains bundles of very long, multi-nucleated cells with cross-striations
- CNS innervation
- Origin - mesoblast
- Cross-striated
- quick, voluntary contraction
- located in muscles of the head; muscles of respiration; initial & endparts of the digestive tract
- limited regeneration capacity
- involving satellite cells mainly

② Cardiac muscle
- composed of elongated, often branched cells bound to one another at intercalated discs
- origin - mesenchyme
- involuntary, vigirous contraction
- ANS innervation
- striated
- located in the walls of the heart (myocardium) & some large vessels
- very poor regenerative capacity
- 3 types of cardiac muscle cells - contractile, conductive & secretory

③ Smooth muscle
- consists of collections of fusiform cells that lack striations
- origin - mesenchyme
- non-striated
- slow, involuntary contraction
- ANS innervation
- located in the walls of hollow & tubular organs:
  - > blood vessels
  - > respiratory tract
  - > urogenital tract
- associated with hair follicles in the skin
- good regeneration capacity
- two types of muscle tissue (smooth)
  - > visceral smooth muscle:
    - small blood vessels, walls of hollow organs
    - poor nerve supply
    - abundant gap junctions
  - > multi-unit smooth muscle
    - rich nerve supply
    - allow for fine control
    - provide for very precise & graded contractions

# Topic 39. Muscle tissue - skeletal muscle tissue, Muscle contraction

## Skeletal muscle tissue

- contains bundles of very long, multinucleated cells with cross-striations
- located in muscles of head & respiration, initial & end parts of the digestive tract
- limited regeneration capacity — involving satellite cells mainly
- origin: mesoblast
- quick, voluntary contractions
- CNS innervation
- Cross striated

## Organization

- masses of fibers that make up various types of muscles are arranged in regular bundles surrounded by the epimysium
  - epi: over, mysium = muscle → external sheath of connective tissue surrounding the entire muscle
- primarily attach to bones & help move the body
- contract on voluntary basis via the somatic nervous system → move body at will, not force
- skeletal muscle muscle fibers are surrounded by endomysium

## Skeletal muscle functions

- support posture
- protects organs
- produces heat

## Skeletal muscle tissue

- each skeletal muscle is considered an organ. its made up of connective tissue layers, muscle fibers, blood vessels & nerves
- attached to bones through tendons or direct attachment
- muscle fibers are bunched together into something called fascicles, which means "bundle"
- these fascicles are surrounded by connective tissue called perimysium.
- inside the fascicles, another connective tissue layer called the endomysium surrounds individual muscle cells

## Muscle fibers

- long and cylindrical & contain several nuclei
- wrapped in a cell membrane called sarcolemma
- inside each muscle fiber, there are tiny rods called myofibrils, which are surrounded by sarcoplasm.
- myofibril: a complex organelle composed of bundles of myofilaments
- sacromere: contractile unit of myofibril that occurs in repeating segments

## Sacromeres:

- responsible for skeletal muscle contraction
- Z discs or Z lines: allow for the attachment of the thin (actin) filaments, as well as an elastic protein called titin
- each sacromere contains thin (actin) filaments & thick (myosin) filaments
- thin (actin) filaments anchor to the Z-disc.
- thick (myosin) filaments attach to an elastic, springy protein called titin, which than attaches to the Z-disc

## Muscle Contraction

1. Myosin head (thick filament) attaches to actin (thin filament
2. Working stroke - the myosin head pivots & bends pulling the thin filament towards the mid line of sacromere
3. ATP attaches to the myosin head, causing it to detach from the actin filament. The cycle then repeats

# Topic 40. Muscle tissue - smooth muscle tissue & cardiac muscle tissue

## General:

- bundles of elongated fusiform cells
- NO- striations
- single cells → central nucleus
- origin: mesenchyme
- contraction: slow & involuntary → ANS
- located in walls of hollow & tubular organs
- associated with hair follicles
- can undergo hypertrophy (enlargement)
  ↳ increase in muscle mass
- good regeneration capacity (Mitosis)
- NO sacromers but myosin
- more actin than myosin → therefore larger amount of thin filaments
- smooth muscle fibers = fusiform shape (cells)
- actin and myosin are attached in a diagonal web like structure attached to the cell membrane
  ↳ less organized than sacromers
  ↳ contraction moves in various directions
- layered in many different directions
- two types

**visceral smooth muscle**

- found in small blood vessels & walls of hollow organs
- poor nerve supply
- abundant gap junctions

**multi-unit smooth muscle**

- found in large arteries, upper respiratory tract, iris & ciliary body of eye
- rich nerve supply
- fine control
- precise & graded contractions

## Contraction:

↳ contractile apparatus: thin & thick filaments
  ↳ lattice network attached to membrane
↳ no troponin
↳ calcium binding protein activates myosine
↳ calcium ions released from ECF
↳ calcium binds to calcium binding proteins
↳ enzyme → cross-bridge formation → contraction

## Smooth muscle tissue

## Cardiac muscle tissue

## General:

- elongated, branched cells bound together by intercalated discs
- origin = mesenchyme
- contraction: involuntary & vigorous → ANS
  ↳ very strong
- found in myocardium & large vessels
- poor regeneration capacity
  ↳ mature cardiac cells don't divide

### ① cardiac muscle cells

↳ cardiummyocytes

- 3 types: contractile, conductive & secretory cells
- cylindrical, branched (with central nucleus), bound by intercalated discs (4 adjacent cells)
  ↳ intercalating disc (3 regions):
    - * Macula adherens
    - * Fascia adherens
    - * Gap junction

### ② Impulse-conducting cells

- 3 types: nodal myocytes, transitional myocytes & purkinje myocytes
  → nodal myocytes:
    - pacemaker
    - mononucleated
    - cylindrical cells with few myofibrils
    - lack sacrotubular system
  → transitional myocytes:
    - pathway between nodal & purkinje myocytes
  → purkinje myocytes:
    - large
    - mononucleated
    - few myofibrils & many mitochondria
    - abundant glycogen granules
    - well developed sacrotubular system

- another type of cardiac cells ⇒ atrial muscle cells
  → found mainly in the right atrium
  → membrane-bound granules
  → containing the hormone ANF
    ↳ atrial natriuretic factor

# Topic 41. Nerve tissue - general features. Neuroganglion cells: external & internal morphology. Neurosecretory cells

## General features:

brain, spinal cord ↑ — ↑ all the nerves branched out from CNS

- makes up CNS & PNS (Central nervous system & Peripheral nervous system)
- main component of the nervous system → brain, spinal cord & nerves
- neurons & neuroglial cells (nerve cells & glial cells)
  - → Irritability
  - → Conductivity
- movement & control of muscles & glands
- Classification:

→ CNS
- brain
- spinal cord

→ PNS
- ↳ sensory neurons (afferent) ← signals
- ↳ motor neurons (efferent) → impulses
- ! * all efferent neurons are motor neurons *!

→ ANS (Autonomic nervous system)
- involuntary
- [1] sympathetic nervous system
- [2] parasympathetic nervous system

→ SNS (Somatic nervous system)
- voluntary
- transmits impulses from CNS to skeletal muscles

- embryonic origin: neuroectoderm → ectoderm that gives rise to neural tissue

## Cells in nerve tissue

### Nerve cells/neurons

- 3 parts:
  - → dendrites: carry impulses to the cell body
  - → cell body: main part
  - → axon: carries impulses away from the cell body
- Dendrites:
  - → structure: short dendritic tree
  - → cytoplasm containing nissle bodies, neurofilaments, microtubules & mitochondria; NO Golgi
- Cell body/perikaryon:
  - → large, euchromatin nucleus
  - → prominent nucleolus
  - → organelles: nissle bodies, neurofilaments, microtubules, lipofuscin, neuromelanin & Golgi
  - → division of neurons according to number of processes
    - Multipolar (more than 2 processes)
    - Bipolar (have one dendrite & axon)
    - Unipolar (single process)
- Axon: terminal arborisation (branched ends)
  - → ends in dilation: end bulbs
    - ↳ interacts with other neurons or non-nerve cells (synapses)
  - → arises from axon hillock (→ from cell body)
  - → axolemma: plasma membrane of axon
  - → axoplasm: cytoplasm of axon
    - ↳ contains ribosomes; lacks RER & Golgi

### Neuroganglion cells

- Ganglia:
  - → avoid, contain neuronal cell bodies & surrounding glial satellite cells → supported by CT & surrounded by a dense capsule
  - → cluster of nerve cells in PNS
    - ↳ connected = plexus
  - → connect PNS & CNS
  - → transmit nerve impulses

determined by the direction of nerve impulses

**Sensory ganglion**
- receive afferent impulses → go to CNS
- associated with cranial ganglia & spinal ganglia
- each nerve cell is surrounded by satellite cells
- similar structure to Schwann cells
  - ↳ continous with them
  - ↳ envelope neuron (peripheral & central processes)
- supported by CT
- neurons are pseudounipolar
- signals nerve endings
  - ↳ from grey matter of spinal cord via synapses

**Autonomic ganglion**
- clusters of neuronal cell bodies & their dendrites
- Located in sympathetic trunk
  - ↳ some located in certain organs e.g. digestive tract
- effect involuntary activities of body
  - → smooth muscle, glands & heart rate
- surrounded by layer of CT
  - → continous with CT layer of single neurons
- ANS
- neurons are multipolar
  - → irregular shaped cell bodies
- axons: non-myelinated
  - ↳ pass to blood vessels & sweat glands
- satellite cells surround each nerve
- use 2 neuron circuits
  - ↳ 1. pre-ganglionic fibre; located in CNS
    2. post-ganglionic fibre; located in peripheral ganglion system
- chemical mediator: acetylcholine

### Neurosecretory cells

- → large cell nucleus
- → large axon endings
- → large cell
- in the brain
- terminal ends are connected to capillaries
  - ↳ hormone secretion
- electric signals → chemical signals } secrete neurohormones

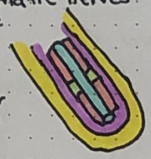
# Topic 12. Nerve fibres and their sheaths. Peripheral nerves

## Nerve fibers

- thread like extension of neuron
- axon covered by sheaths of glial cells
- larger axons = myelinated fibers (covered by a myelin sheath) ↳ specialized to faciliate the axonal function
- thinner axons = non-mydinated fibers (not covered)
- all nerve fibers have a neurolemma sheath
- in PNS = myelin & neurolemmal sheaths derived from Schwann cells

unmyelinated fibers:
- in CNS & PNS
- NO Ranvier nodes
- slower conduction
- group of small axons
  ↳ each invaginates a single Schwann cell

myelinated fibers:
- in CNS (oligodendrocytes) & PNS (Schwann cells)
- have Ranvier nodes
- faster conduction
- bulk of somatic nerves
- structure:



= Ranvier nodes

= axis cylinder

= myelin sheath

= neurolemma

= Endoneurium

## Sheaths

- derived from cells of ectodermal origin
  - Oligodendrocytes (CNS)
  - Schwann cells (PNS)

- myelination
  - takes 7 years
  - myelin forming cells: Schwann cells / oligodendrocytes
  - membrane: 70% lipids / 30% proteins (MBP)
- myelin sheath
  - major dense lines
  - intraperiod lines

## Peripheral nerves

- cranial nerves & spinal nerves
- each nerve consist of parallel bundles of nerve fibers:
  ↳ afferent or efferent
  ↳ myelinated or non-myelinated
- CT sheats support nerve fibers as well as the associated blood & lymph vessels
- derived into three groups (based on location & conduction speed)

Group A fibers:
- myelinated (heavy)
- somatic
- efferent or afferent
- 5 - 120 m/s
- 4 - 20 μm

the wider & more myelinated the neuron the faster it transmits electrical impulses

Group B fibers:
- myelinated (moderate)
- efferent
- preganglionic
- autonomic
- 3 - 15 m/s
- 1 - 4 μm

Group C fibers:
- unmyelinated
- afferent or efferent
- post ganglionic
- sympathetic fibers
- 0,2 - 1,5 μm
- 0,5 - 2,5 m/s

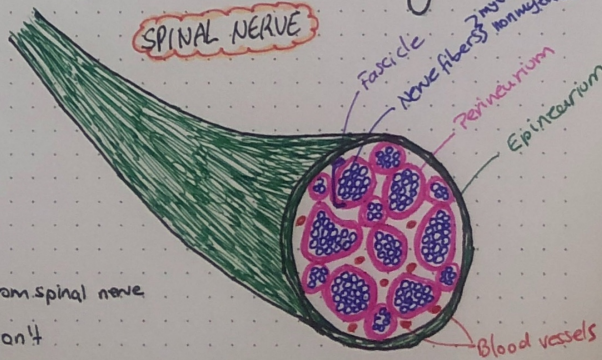
- Spinal nerves:
- 31 pairs leaving spinal cord
- connected to spinal cord by 2 roots:

(1) anterior root
→ away from CNS (signals)
→ efferent fibers

(2) posterior root
→ to CNS (signals)
→ afferent fibers
↳ sensoring fibers

- Cranial nerves:
- 12 pairs leaving the brain
- fibers are of diverse functional types
- differ in development & relation to the senses from spinal nerve
- attached to the brain → irregular intervals
- some have multiple ganglions, while other don't

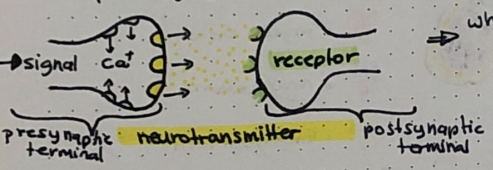
## SPINAL NERVE



# Topic 43. Synapses - principle of organization, types.

## Synapses

- nerve endings - connection site to another neuron
- strength & polarity are determind by the physical & neurochemical characteristics
- synaptic communication:
  - transmission of nerve signals (from one neuron to another)
  - unidirectional transmission
  - electrical signal → chemical signal
    (pre-synaptic cell) (post-synaptic cell)
  - release of neurotransmitter
    ↳ tiny molecules that bind to specific receptors
    ↳ function: opens or closes channels or initiates second messenger cascades
- 3 components:
  → pre-synaptic terminal (neurotransmitter)
  → synaptic cleft
  → post-synaptic terminal (receptor)




⇒ what happens:
(1) nerve impulse open $Ca^+$-ion channels
(2) promoting $Ca^+$-ion influx
(3) causes neurotransmitter release via exocytosis → from presynaptic terminal
(4) neurotransmitter diffuse over the synaptic cleft & binds to receptors (postsynaptic terminal)
(5) effect: excitatory or inhibitory
↳ Acetylcholine (ACh) ↳ γ-aminobutyric acid (GABA) or glycine

## Types:

- classification of synapses according to:

(1) ways of transmission < Electrical / Chemical

(2) contacting structures < Axosomatic / Axodendritic / Axoaxonic

(3) Morphology < Asymmetrical / symmetrical

(4) Functionality < Excitatory / Inhibitory

(5) Atypical synapses < Reciporal dendrodendritic / serial synapse

# Topic 44. Neuroglia - types & features

## Neuroglia

### General:

- support neuronal survival activities
  - ↳ more abundant in the brain
- origin → progenitor cells
- in CNS → surround neuronal cellbodies as well as the processes of axons & dendrites

### Function:

- → support nutrition
  - ↳ by satellites & macroglia
- → poison defence
  - ↳ e.g. support blood brain barrier
- → support electrical communication
  - ↳ by neuroglia
  - ↳ ion-regulation, build myelin sheath

### Types

- 6 types of glial cells
- divided into CNS & PNS glial cells

Central glial cells:
(1) Oligodendrocytes } macro-glia
(2) Astrocytes } macro-glia
(3) Ependymal cells
(4) Microglia

Peripheral glial cells:
(5) Schwann cells
(6) Satellite cells of ganglia

(1) Oligodendrocytes:
- produce myelin sheaths
- around axons in CNS
- predominant in white matter

(2) Astrocytes:
- many radiating processes
- unique to CNS
- most diverse → 2 types
  (1) fibrous astrocytes (WM)
  (2) protoplasmic astrocytes (GM)
- terminal branching is very extensive

(3) Ependymal cells:
- line ventricals (brain) & central canal (spinal cord)
  - ↳ columnar or cuboidal
  - ↳ sometimes has cilia at optical ends (facilitates movement of cerebrospinal fluid)

(4) Microglia
- small cells
- short & irregular processes (GM & WM)
- non-dividing
- involved in immune defense

(5) Schwann cells
- in PNS only
- from precursors
- interact with axons
- myelinate a single axon

(6) Satellite cells (ganglia)
- from embryonic neural crest
- form covering layer → cell bodies of neurons in ganglia of PNS
- support, insulate, nourish & regulate environments of neurons
  - ↳ e.g. regulate external chemical environment

# Topic 45. Receptor & effector endings - structure & functions

· 2 Types of nerve endings: (1) receptor & (2) effector

## receptor nerve endings

· transduce stimuli into signals in sensory nerves

← 2 Types →

unencapsulated (free) nerve terminal → detect touch & pressure

- most widely distributed
- most present in skin, mucous & serous membranes, muscle, deep fascia & visceral walls
- includes
  - → Merkel cells (light touch)
  - → free nerve endings (temperature & pain)
  - → root hair plexuses (detect movement of the hair)

encapsulated nerve terminals → detect touch & pressure

· phasic mechano receptors
↳ respond rapidly to stimuli on the skin

· 4 encapsulated receptors:
- → Meissner corpuscle (fingertips, palms & soles)
- → Pacianian corpuscle (touch & pressure)
- → Krause end bulbs (penis → pressure)
- → Ruffini corpuscle (pressure)

· 3 main groups of sensory receptors:
(1) Exteroceptors
(2) Proprioceptors
(3) Interoceptors

· Classification according to:
(1) Sensory modality
- chemoreceptors (chemical stimuli)
- mechanoreceptors (mechanical stress)
- noci receptors (perception of pain)
- thermoreceptors (temperature stimuli)
  ↳ heat, cold & both
- bar receptors (pressure respond)

(2) Location < cutaneous receptors / muscle spindles

(3) Morphology < free nerve endings / encapsulated nerve endings

(4) Kinds of touch sensations:
- light touch
- cold
- heat
- pain

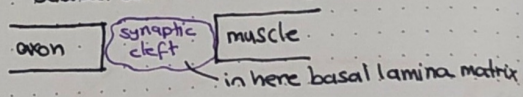
## effector nerve endings

· myoneural junction (motor end plate)
↳ for communication between nerve & muscle

· axon covered by Schwann cells
↳ contact with striated muscle fibers

· in axon terminal: many mitochondria & synaptic vesicles
↳ contains ACH

· between axon & muscle: synaptic cleft




· in sacroplasma of muscles there are many:
- nuclei
- mitochondria
- ribosomes &
- glycogen granules

· Autonomic effector endings
- → Sympathetic - adrenergic (NA)
- → Parasympathetic - cholinergic (ACh)
- → Purigenic - ATP & adenosine

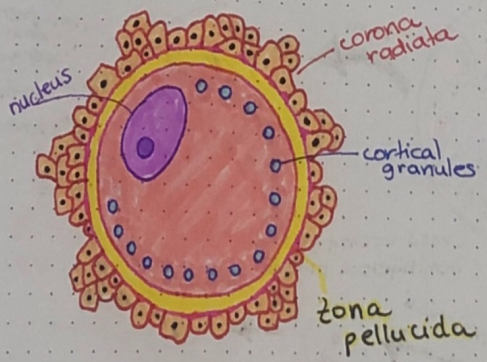
3

## Topic 96. Sex cells - female sex cells

- OVA (egg cells) or ovum (singular)
- known as gametes
  - ↳ reproductive cells
  - ↳ half the genetic informations = 23 chromosomes = haploid
- each gamete can differ from each other
  - ↳ depends on mix of chromosomes
- spherical in shape & ~120 μm in diameter
- not-motile
- does contain organelles & cytoplasm
  - ↳ developes new life
- only one per month produced
- process in which egg cells are produced is called oogenesis → takes place in ovary

### Structure

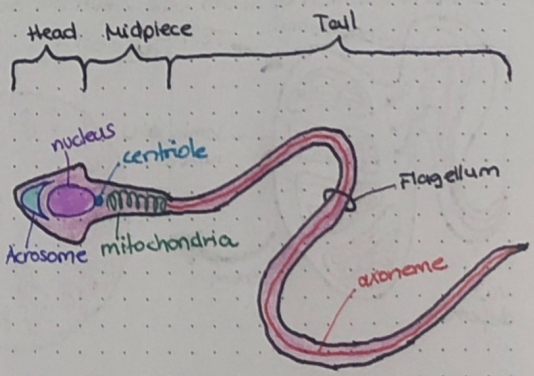
- Ovum is surrounded by two layers:
  - Zona pellucida: jelly coat; mediated sperm entry
  - Corona radiata: follicular cells that nourish the egg




## Topic 41. Sex cells - male sex cells

- Spermatozoa (sperm cells)
- known as gametes
  - ↳ reproductive cells
  - ↳ half the genetic information = 23 chromosomes = haploid
- each gamete can differ from each other
  - ↳ it depends on the mix of chromosomes
- much smaller than egg cells
  - ↳ 58-67 μm in diameter
- millions of sperm cells in each ejection
  - ↳ around 20 million
- motile
  - ↳ because of the tail
  - ↳ have a long way to the egg cell
- only one organelle: nucleus
- process in which sperm cells are produced is called spermatogenesis → takes place in testes

### Structure




- A spermatozoa consists of three main sections:
  - Head: contains nucleus, acrosome & centriole
  - Midpiece: contains mitochondria (ATP source)
  - Tail: Flagellum bends to faciliate movement

* the acrosome is a Golgi apparatus that is capable of releasing special digestive enzymes that are needed to penetrate the egg cell to produce the zygote

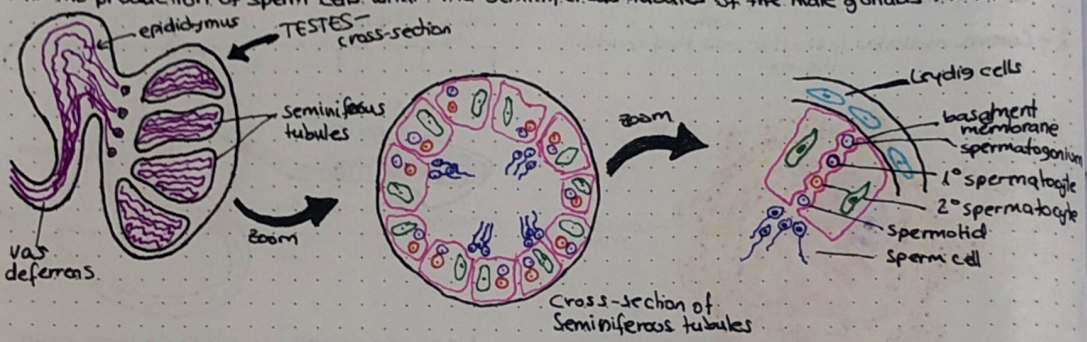
## Topic 48. Subject, tasks and methods of general embryology

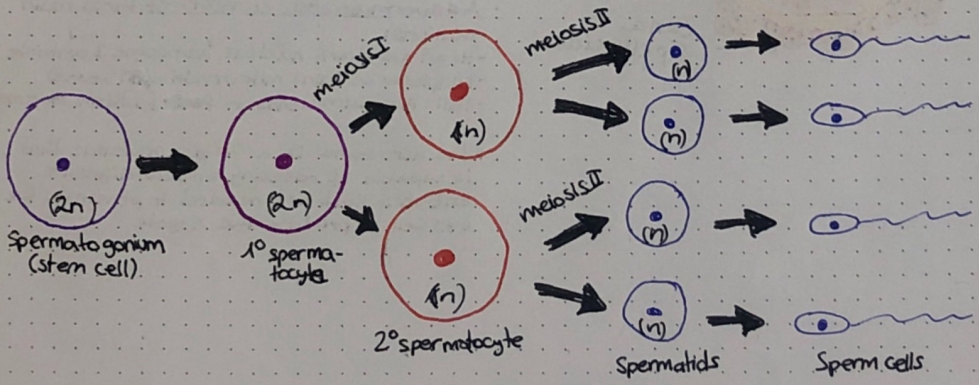
- general embryology = embryogenesis
- study of formation & development of an embryo from the moment of its inception to birth
- cells which carry out reproduction = located in sex organs/gonads
  - ↳ female = OVUM → location: ovary
  - ↳ male = SPERMATOZOA → location: testes
  - ↳ specialized organs involved in reproduction
- specialized cells (ovum & spermatozoa) are produced by gonads
- fused ovum & spermatozoa form zygote:
  - ↳ known as fertilized egg or fertilized ovum
  - ↳ begins as single cell, but rapidly divides in the days following fertilization
  - ↳ contains all of the 46 necessary chromosomes
    - ↳ 23 getting from sperm cell
    - ↳ 23 from egg cell
- development of the embryo begins when spermatozoon fuses with ovum
  - ↳ process known as fertilization

## Topic 49. Spermato- & ovogenesis. Ovulation

### Spermatogenesis

- is the production of sperm cells within the seminiferous tubules of the male gonads ⇒ testes



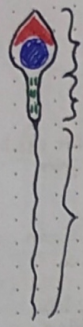




- within the walls of the seminiferous tubules are precursor stem cells called Spermatogonium
  - ↳ they are diploid & give rise to future sperm cells
- Leydig cells: found interstitium; release testosterone (hormone), which stimulates the stem cells to differentiate into the primary spermatocyte (diploid).
  - ↳ undergo meiosis I to produce secondary spermatocyte
- secondary spermatocyte then undergoes meiosis II to form the spermatid
  - ↳ ultimately matures into the sperm cell
- Another group of cells that play a role in spermatogenesis are Sertoli cells
  - ↳ they provide nutrients to the growing sperm cell & help remove the unwanted cytoplasm

## Epididymus

- once sperm cells are produced in the seminiferous tubules, they move into a region of highly - convoluted tubular, called the epididymus
  ↳ here the sperm cells are matured and stored until released

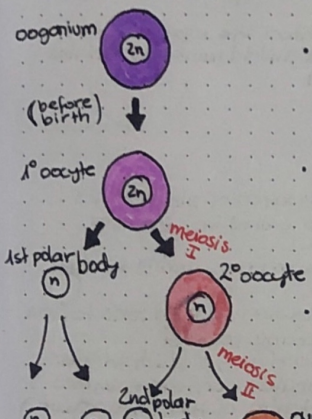
Structure of sperm cell



- Head: contains the haploid nucleus and acrosome
- Midpiece: contains many mitochondria
- Tail: composed of flagellum that helps in locomotion

## Ovogenesis

- is the process by which female gametes are produced in the ovaries.
- unlike in males, in females all the 1° oocytes are produced during fetal development




- the precursor stem cells in females are called oogonia (plural) & oogonium (singular)
- durin fetal development, all the oogonia differentiate into primary oocytes → remain in prophase I of meiosis
- when the female reaches puberty a cycle begins in which one 1° oocyte will undergo meiosis I to produce the secondary oocyte.
  ↳ will remain frozen in metaphase II of meiosis
- during fertilization the secondary oocyte will finish meiosis II to produce the mature ovum (egg cell)

## Ovulation

- is the process when the 2° oocyte frozen in metaphas II is popped out of the graffien follicle
- for this process special enzymes (proteases) are activated by

LH (Luteinizing hormone)
↳ these special enzymes are scissor-like-enzymes
↳ process is triggered by the LH surge

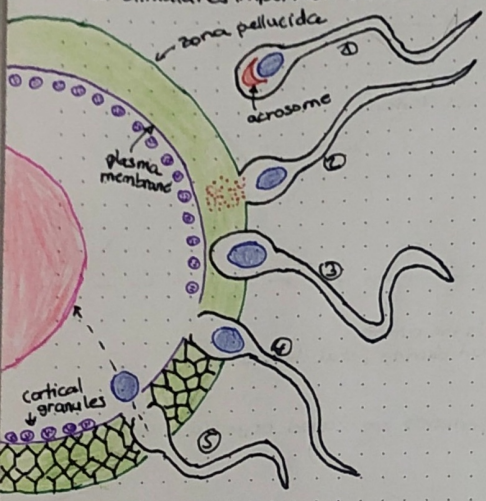
- scissor-like cause these proteases are eating away & breaking down specific tissue around the graffien follicle

- after the tissue is cut away from the proteolytic enzymes the 2° oocyte pops out
- summed up during ovulation the 2° oocyte is ejected, the fimbriae of the fallopian tube are going to become stiff & push the fluid towards the fimbrae, after that the fimbrae catches the 2° oocyte & keeps it in the ampulla until the sperm cell comes & tries to fertilize it
- this process occurs technically (assuming a normal cycle) about day 14 or 15

# Topic 50. Fertilization

- is the process by which a sperm cell fuses with the ovum to produce the zygote
- this process serves several important functions

(1) restores the diploid number of chromosomes
(2) activates the egg &
(3) stimulates important reactions that begin embryological development




① the sperm cell approaches the egg

② the sperm contacts the zona pellucida of the egg & the sperm starts releasing digestive enzymes from the acrosome

③ the digestive enzymes drill a hole until the sperm reaches the plasma membrane of the egg cell.

④ the membranes of the sperm & egg fuse; this initiates the cortical reaction in which cortical granules are released and change the composition of the zona pellucida
↳ this prevents any other sperm from fusing with the egg

⑤ the nucleus of the enters the egg & fusion of the two nuclei restores the diploid number & initiates embryological development

## Contact & Cortical Reaction

- when the sperm cell contacts the egg, it interacts first with a thick layer of glycoproteins called zona pellucida; the sperm cell contains a structure at its tip called the acrosome that releases enzymes that begin digesting hole in the zona pellucida
- during this process, two reactions take place that prevent other sperm from entering the egg:

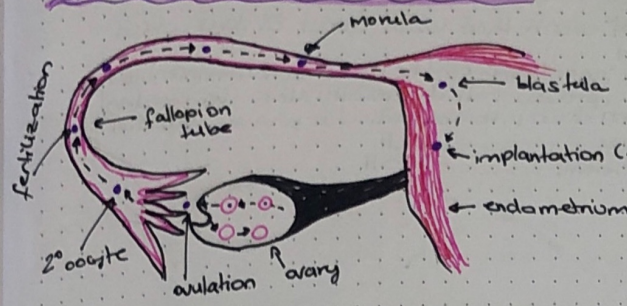
(1) ion channels in the membrane of the egg open, thereby allowing sodium ions to flow into the cell, this depolarizes the cell and changes the membrane polarity
(2) depolarization of membranes causes a movement of calcium ions which triggers the release of corticale granules via exocytosis; these granules contain enzymes that change the composition of the zona pellucida; the hardening of this extracellular layer prevents other sperm from entering; this is known as the cortical re

## Fertilization Activates the Egg

- fertilization causes the egg to undergo the remainder of meiosis II; once the nucleus of the sperm makes it way into the cytoplasm of the egg, it fuses with the eggs nucleus, forming a diploid cell

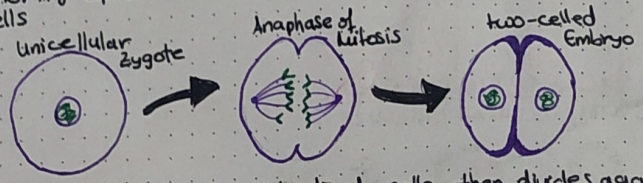
- the calcium released into the cytoplasm stimulates metabolic process, oxygen usage increases & protein synthesis is stimulated; the zygote ultimately begins dividing & embryological developement is initiated

# Topic 51. Segmentation & Blastogenesis

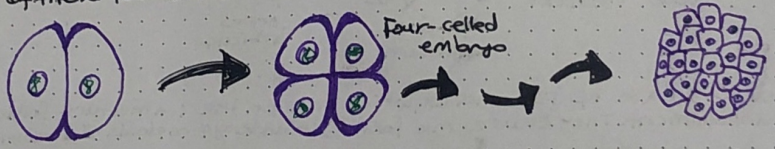



## Segmentation

- as soon as fertilization takes place in the fallopian tube, the influx of calcium ions into the zygote activates it & sets into motion many metabolic processes such as protein synthesis
- shortly afterwards it undergoes its first mitotic division to produce two identical cells



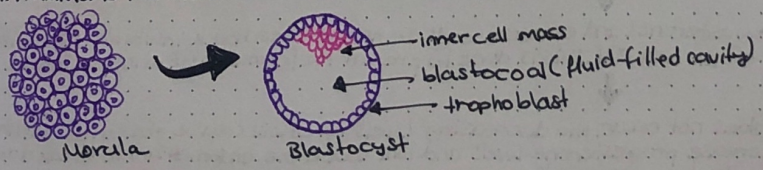

- each one of these two **identical** cells then divides again to produce a four-celled embryo.




- these cell divisions continue (mitosis) forming the 32-cell stage, called morula
- Collectively, these rapid mitotic divisions following fertilization are cleavage/segmentation
- during cleavage
  (1) cells do not grow so the final mass of cells is not larger than the initial zygote.
  (2) the zygote portions into many identical cells that will serve as the basic building blocks of the developing embryo.

## Blastulation

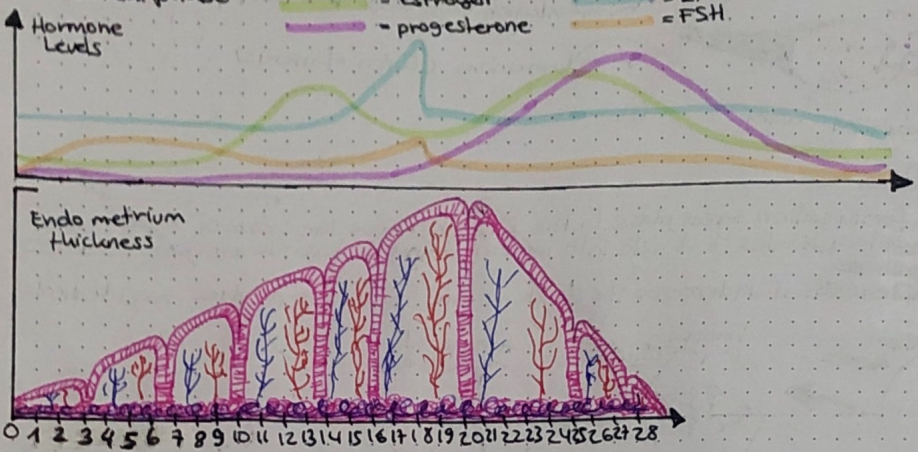
- the morula will continue dividing until it forms the blastula, a sphere of some hundred cells that cont a hollow cavity called blastocoal.
- in humans the blastula is called blastocyst.

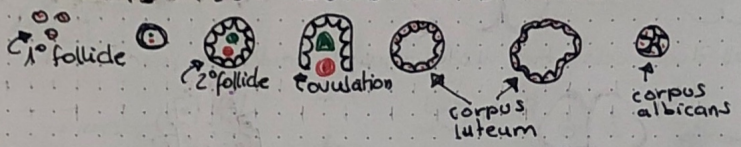



- the trophoblast gives rise to the chorion & placenta while the inner cell mass gives rise to the actual organism
- Cleavage & blastulation occurs as the zygote (and developing embryo) travels to the uterus
  ↳ for development to continue the embryo must implant itself into the endometrium

# Topic 52. Cyclic changes in uterine mucosa (the menstrual cycle)

- the menstrual cycle is a sequence of events that lasts about 28 days, which prepares the woman for pregnancy
- if fertilization does not occur the inner lining of the uterus (endometrium) along with the 2° oocyte is discharged in a process called menstruation (ie. bleeding)
- the menstrual cycle can be broken down into the follicular phase, ovulation & the luteal phase




GnRH causes release of FSH and LH, which acts on the immature follicle & stimulates it to begin development. They cause the follicle to undergo meiosis I & become the 2° follicle.

↓

The developing follicle begins begins to release estrogen, which stimulates the thickening and formation of the endometrium in preparation for implantation

↓

*After about 2 weeks, there is a rapid rise of LH (LH surge). This stimulates the mature 2° follide to rupture, releasing the 2° oocyte into the fallopian tube. This process is called ovulation

↓

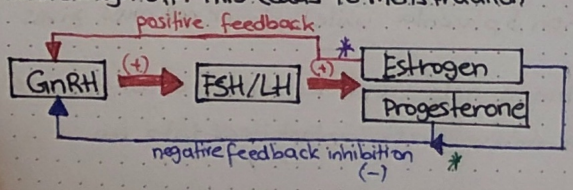
The continued release of LH stimulates the remaining portion of the 2° follicle to become the corpus lutem, which now begins releasing progesterone → thickens & maintains the endometrium

↓

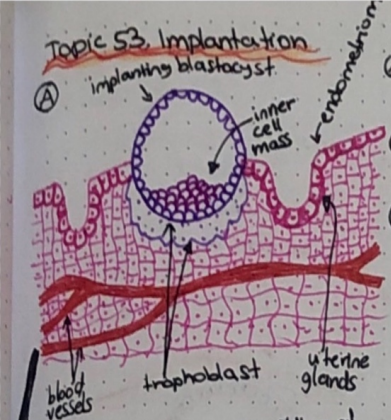
*The rising levels of progesterone (and estrogen) leads to negative feedback inhibition of GnRH, which decreases levels of LH and FSH. This is done to prevent the formation of another follicle.

↓

Eventually if fertilization does not occur, the decreasing levels of LH will cause the corpus luteum to worsen. This will decrease progesterone levels and will cause the endometrium to break down and slough off. This leads to menstruation



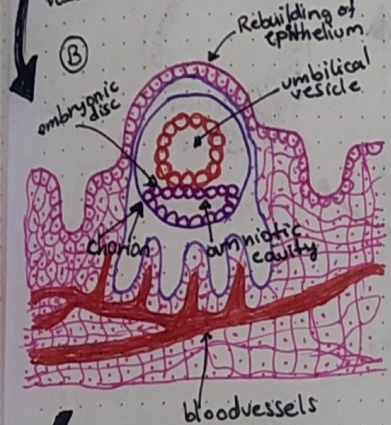
# Topic 53. Implantation




(1) On about the 7th day following fertilization the tiny embryo (blastocyst) begins implantation

(2) Cells of trophoblast release digestive enzymes that dig a hole large enough to accommodate the embryo

(3) Embryo begins to slowly make its way further into the vascular and connective tissue of endometrium

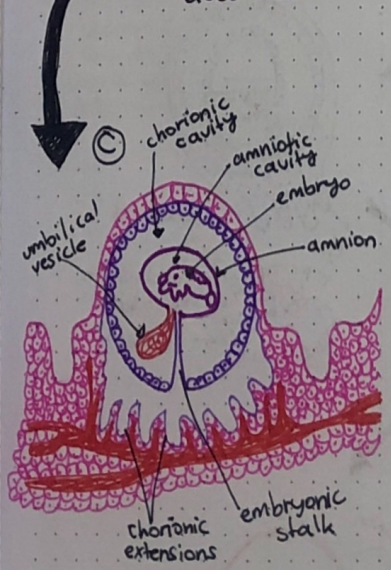



(4) On about the 10th day after fertilization, the trophoblast forms the chorion

(5) As the embryo digs deeper, the opening of the endometrium created by the implantation process is sealed off with new epithelial cells. Development continues entirely inside the new endometrium

(6) the digestive enzymes open up some of the maternal blood vessels, thereby creating a temporary source of oxygen & nutrients

(7) the amniotic cavity & the umbilical vesicle are formed




(8) After about 25 days following fertilization, a direct connection between the chorion and the uterine blood vessels exists. This will eventually become the placenta

(9) The embryonic stalk is formed. This will eventually form the umbilical cord

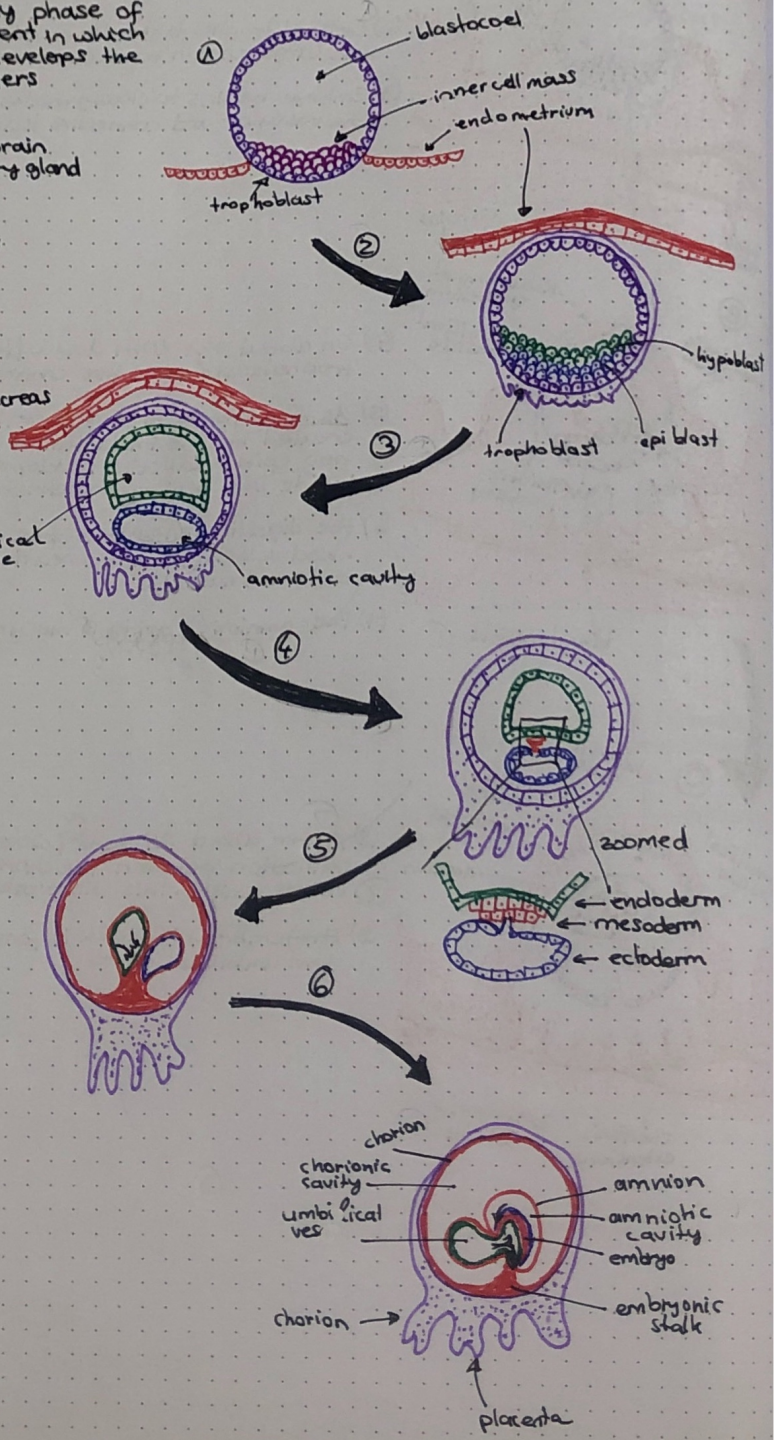
# Topic 54. Formation of germ layers & axial organs

Gastrulation - an early phase of embryological development in which the implanted blastula develops the three distinct germ layers

① Ectoderm (external)
Integumentary system, brain and spinal cord, pituitary gland

② Mesoderm (middle)
Musculoskeletal system, cardiovascular system, excretory system, reproductive system

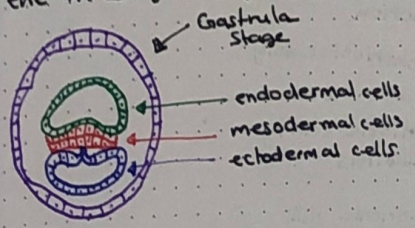
③ Endoderm (internal)
Epithelial layer of lungs, digestive system, liver, pancreas & bladder; also forms thyroid and parathyroid glands



# Topic 55. Derivatives of germ layers, Disturbances in the development - mutations

## Organogenesis

- is the process by which the three germ layers form the many organs and structures found in the adult individual
- the three germ layers include the endoderm, mesoderm & ectoderm




### 1) Endoderm (inner)

1. Epithelium of digestive tract (excluding mouth & anus)
2. Accessory Organs of Digestive
   - Liver
   - Pancreas
   - Gall bladder
3. Thyroid, Parathyroid & thymus gland
4. Epithelium of lungs
5. Epithelium of reproductive ducts, urethra & bladder

### 2) Mesoderm (middle)

1. Muscle
   - skeletal
   - cardiac
   - Smooth
2. Cardiovascular System
   - Heart
   - Blood & blood vessels
3. Skeletal system
   - Bone & bone marrow
   - Cartilage

(1–3: Musculoskeletal System)

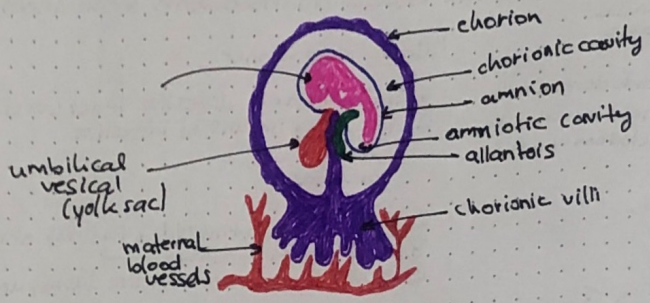
4. Lymphatic system
5. Excretory & reproductive Systems
   - kidneys & ureter
   - Gonads (testes & ovaries)
6. Dermis of skin
7. Adrenal cortex

### 3) Ectoderm (outer)

1. Integumentary system
   - outer layer of the skin (epidermis)
   - hair, nails, sebaceous glands, melanocytes
2. Nervous system
   - CNS (brain & spinal cord)
   - PNS (ganglia)
3. Sensory organs
   - Lens & cornea of the eye
4. Epithelium of mouth & anus
5. Epithelium of pituitary & pineal gland
6. Adrenal medulla
7. Tooth enamel

# Topic 56. Formation and development of embryonic envelopes

- during embryonic development, the embryo forms four extra embryonic membranes that are ultimately discharged following birth
- these membranes include the chorion, allantois, umbilical vesicle (yolk sac) & the amnion




## Chorion

- is formed from cells that come from the trophoblast and the mesodermal germ layer
- functions in several important ways:

① it contains a fluid that can absorb shock that the embryo experiences due to some outside force → thereby protecting the embryo
② the chorionic villi extend into the endometrium, eventually helping form the placenta
→ therefore they create a structure that is involved in providing the developing embryo with nutrients & oxygen

## Amnion

- this structure directly surrounds the developing embryo. It consists of an inner layer that comes from the ectoderm and an outer layer that comes from the mesoderm. The cells of the amnion secrete a watery fluid that fills the amniotic cavity
- the amnion has a similar set of functions as the chorion

① creates a protective environment that absorbs shocks & cushions the embryo
② prevents the embryo from drying out
③ enables the embryo some freedom of movement

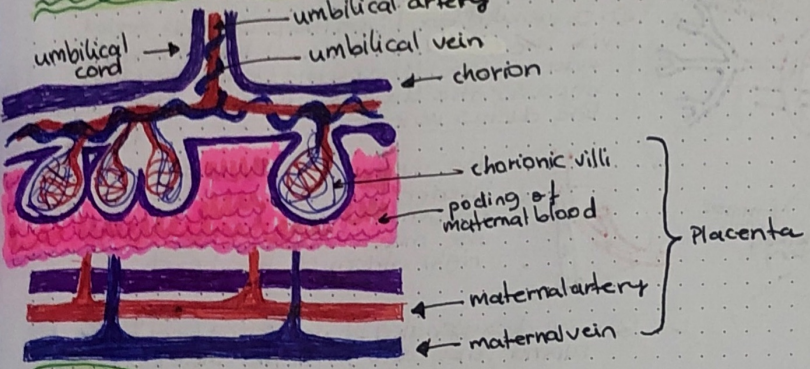
## Umbilical vesicle (yolk sac)

- the yolk sac contains nutrients needed for development; In humans however, the yolk sac does not actually contain any nutrients and is called the umbilical vesicle; it helps form blood during early development

## Allantois

- in humans, the allantois is a small outgrowth of the developing digestive tract and it is mainly non-functional; it does however contribute to the formation of blood vessels that make up the umbilical

# Topic 51. Placentation. Structure of placenta. Umbilical cord.




## Placenta

- the human placenta is an organ of exchange between the mother and the fetus
- it has several important functions
  1. provides nutrients and exchanges gas
  2. wast product removal
  3. Endocrine gland
  4. Immune protection

- How does the placenta form?

A) during implantation, the embryo releases enzymes that digest the endometrium & form tiny extensions that become the chorionic villi

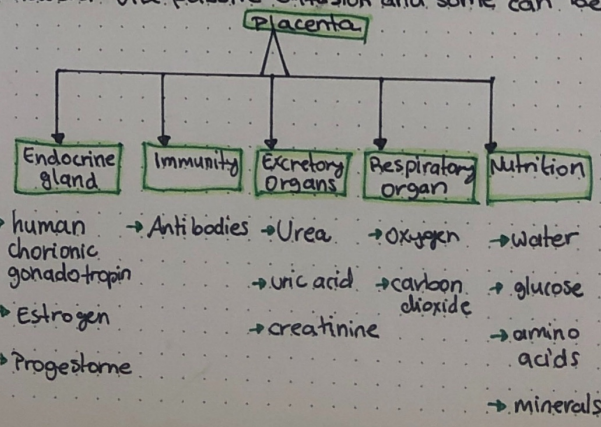
B) as the circulatory system of the embryo develops, these chorionic villi become populated with the embryo's blood vessels; these blood vessels connect with the umbilical vein & artery

C) the digestive enzymes also partially digest maternal blood vessels, causing the maternal blood to ooze out and invade the area around the chorionic villi

D) as the embryo develops, the umbilical cord forms; it encloses the umbilical veins and umbilical artery that connect to the chorionic villi.

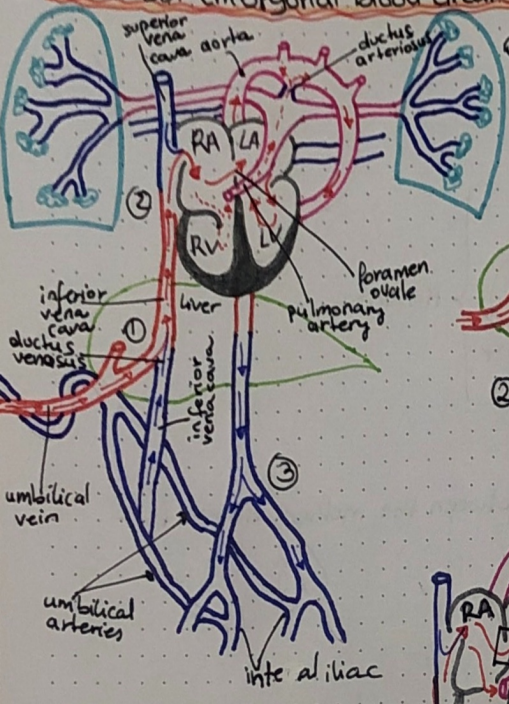
- therefore we see that the placenta consits of the chorion that forms the villi and the surrounding uterine tissue that contains the maternal blood vessels

- the maternal and fetal blood do not actually mix in the poding area; the plarental membrane creates a semipermeable membrane that acts as a barrier for relatively large substances such as red blood cells, small molecules can move however via passive diffusion and some can be pumped activel

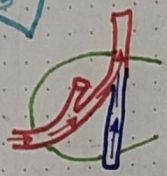



- towards the end of pregnancy, the placenta release corticotropic-releasing (CRH) that stimulates the pituitary gland to release ACTH.
- ACTH then stimulates the adrenal glands to produce a precursor molecule that is used by the placenta to form more estrogen.
- Risirg level of estrogen ultimately causes the smooth muscles of uterus contract

# Topic 58. Embryonal blood circulation

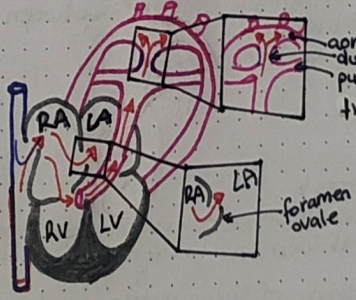



① • Oxygenated blood from the placenta is carried via the umbilical vein; as it travels past the underdeveloped liver of the fetus, the blood bypasses the liver via a blood duct called the ductus venosus



• the ductus venosus connects with the inferior vena cava, which mixes the oxygenated with deoxygenated blood; the mixed blood then travels to the right atrium of the heart

② • the deoxygenated blood coming from the superior vena cava is further mixed with the oxygenated blood coming from the inferior vena cava before it enters the right atrium




• since the fetal lungs are filled with fluid, they contain a high resistance and high pressure; As a result, the blood is rerouted and moves to the lower-pressure left atrium via the foramen ovale

• some blood however does move into the right ventricle and into the pulmonary trunk; however most of this blood is rerouted once more via the ductus arteriosus, which connects the pulmonary trunk to the aorta

③ • the partially oxygenated blood then travels from the aorta to the developing organs of the fetus.
• the deoxygenated blood is eventually returned back to the placenta via the internal iliac arteries that connect with the umbilical arteries

# Topic 59. Teratology - teratogenic factors

| Teratogenic drugs | & their Effect in fetus |
|---|---|
| T → Thalidomide | → Phocomelia (Seal like limbs) |
| E → Ethanol | → fetal alcohol syndrome |
| R → Retinoids ↳ Isotreonine | → cerebrofacial, heart defect |
| A → ACE Inhibitor | → Renal Damage |
| T → Tetracycline | → Teeth and Bone defect |
| O → Oral hypoglycemic Agent ↳ sulfonyl ureas | → Prolonged Severe hypoglycemia |
| Causes (C) → Carbamazepine | → Neural tube defect |
| Very (V) → Valproic Acid | → Cardiac & limb malformation |
| Weak (W) → Warfarin | → depressed nose, eye & hand defect |
| L → Lithium | → foetal gauter |
| I → Iodide | → foetal hypothyroidism |
| P → Phenytoin | → foetal hydantoin syndrome |

# ER function and structure detailed

Rough ER [ protein synthesis]

1. in nucleus of cell is DNA which can be translated to RNA by transcription but the mRNA is send away to bind on the ribosomes of the rough ER
2. The rough ER can with the help of the mRNA build a good structure of a protein
3. The protein has to go trough the ER but is has to be modified
4. Modification: a sugar binds to a specific amino acid of the protein ( which is called Asparangen) — —> protein is modified and ready to leave the rough ER
5. This process is also called N– linked Glycolorasation
6. Modified Protein ( Glycoprotein) is embedded into a vesicle that leaves the ER
7. Some proteins called Cap II Tag on the vesicle to show the directions or where the vesicle has to go
8. The protein leaves the ER and goes straight to the Golgi apparatus
9. the proteins enters through the cis face of the Golgi apparatus and is modified even more
10. Protein will be packed and exits through trans face of Golgi apparatus and is send away to one of three locations :

- goes to the cell Membrane and works as a channel protein or membrane protein
- fused with the membrane and is released out of the cell ( f.e as a hormone or a transmitter) — —> also called a secretory protein
- packed in a vesicle and specialized as a lysosome ( which is helpful in breaking down certain things in the cell)

What types of cells in the body are rich with RER ?

1. pancreas cells ( Exucrine) —> Digestive enzymes are needed to break down the food that we eat
2. Plasma cells —> pump out Anti bodies which are Glycoproteins
3. Goblet cells —> in stomach area and they produce a lot of Mucin
4. Neuron cells—> pump out Neurotransmitter ( Nissl bodies are needed)

Smooth ER [ lipid synthesis]

1. Acetyl Coa ( molecule) can be taken up by the ER and goes through many enzymatic steps
2. can be linked with carbon chains and form an fatty acid ( fatty acid synthesis) so it can be broken down to form ATP
3. or synthesis phospholipids