EMBRYOLOGY

LEARNING OBJECTIVES

- Gametogenesis (quickly revise)
- Fertilization
- Blastocyst formation + Embryo Hatching
- Implantation
- Bilaminar Disc
- Gastrulation + Tri Laminar Disc
- Formation of Notochord
- Derivatives of the 3 germ layers
- Pharyngeal Arches

Timeline:

Event	Time
Fertilisation	Week 1 day 1
Morula (16 cell embryo)	Week 1 day 3
Blastocyst entrance into uterine cavity	Week 1 day 4
Hatching (ZP discarded)	Week 1 day 5
Implantation	Week 1 day 6
Differentiation of trophoblasts into cytotrophoblasts and syncitiotrophoblasts	Week 1-2
Embryo completes implantation	Week 2
Formation of bilaminar disc	Week 2 day 7/8
Gastrulation (formation of trilaminar disc)	Week 3 day 13-17
Neuralation	Week 3 -formed by the end
Primordial heart starts pumping	Week 4
Limb Buds appear	Week 4
Embryo shows spontaneous movement	Week 6
Embryo heart can be seen with ultrasound	Week 6
Embryo heart can be detected by auscultation	Week 20

GAMETOGENESIS

- **Process where gametes are produced for sexual reproduction**
- **2 types – oogenesis and spermatogenesis**

	Spermatogenesis	Oogenesis
Process		
Location	Occurs *entirely* in testes	Occurs *mostly* in ovaries
Meiotic divisions	Equal division of cells	Unequal division of cytoplasm
Germ line epithelium	Is involved in gamete production	Is not involved in gamete production
Gametes		
Number produced	Four	One (plus 2 – 3 polar bodies)
Size of gametes	Sperm smaller than spermatocytes	Ova larger than oocytes
Timing		
Duration	Uninterrupted process	In arrested stages
Onset	Begins at puberty	Begins in foetus (pre-natal)
Release	Continuous	Monthly from puberty (menstrual cycle)
End	Lifelong (but reduces with age)	Terminates with menopause

OOGENESIS

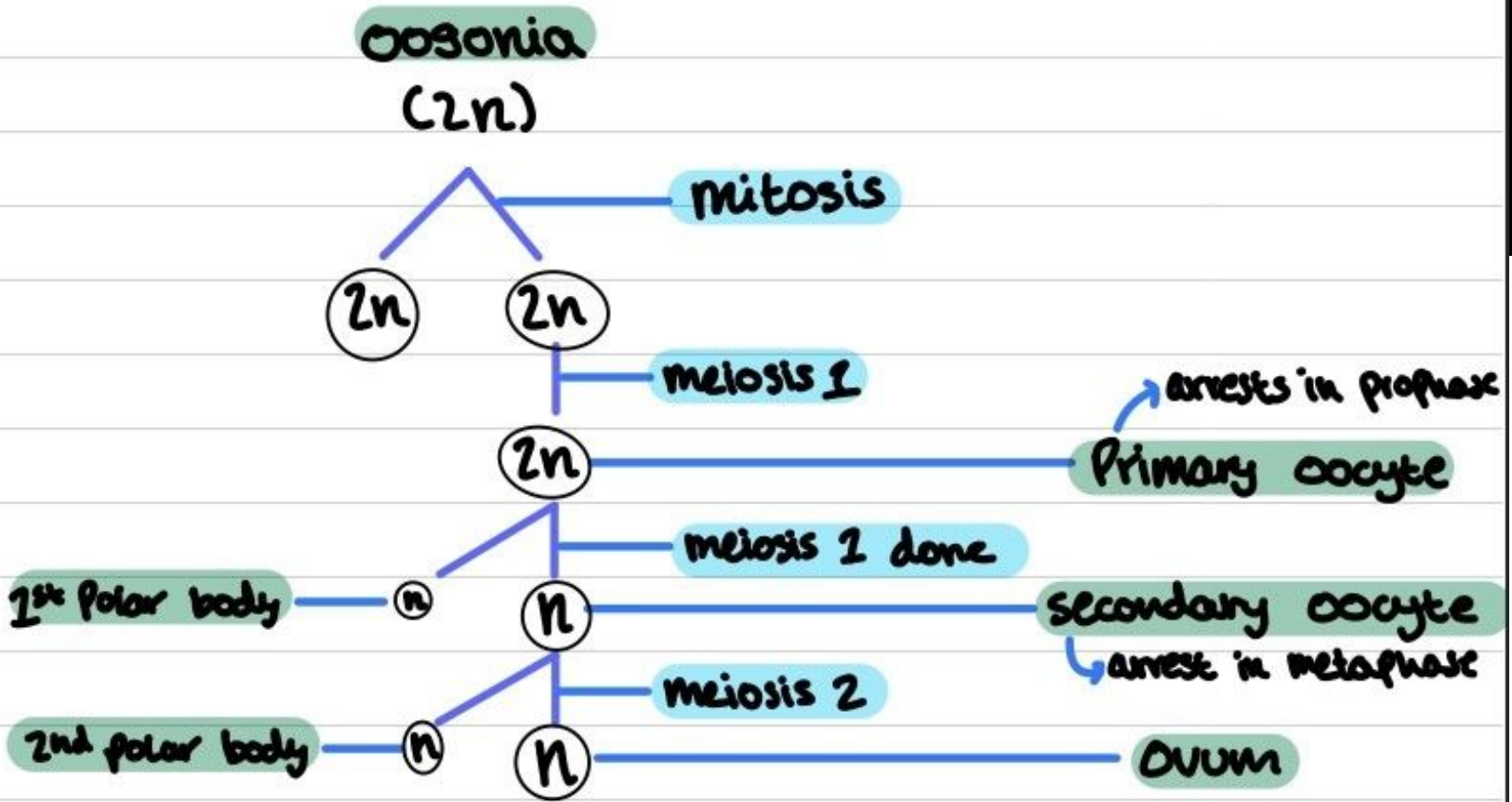
- Asymmetrical division
- Primary oocyte > secondary oocyte > ovum
- Produces polar bodies – they are small non-functional cells

1) Oogonia undergoes mitosis – primary oocyte (2n)
2) Cell undergoes meiosis 1 – secondary oocyte (n) and polar body
3) Cell undergoes meiosis 2 – ovum (n) and polar body

- Primary oocyte – arrested in prophase 1 until menstrual cycle
- Secondary oocyte – arrested in metaphase 2 until fertilisation

Oogenesis:

↑ asymmetrical division



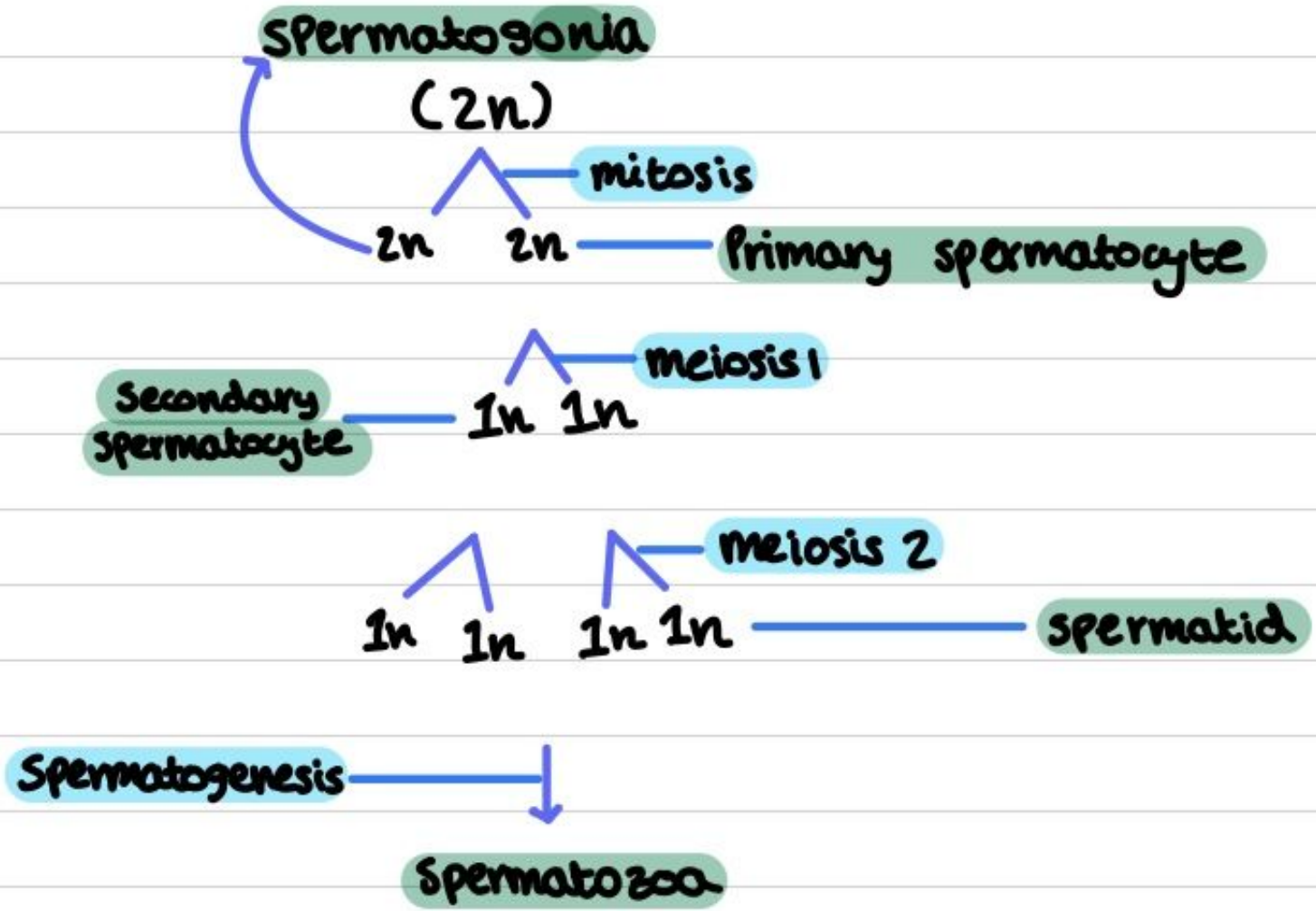
* arrest in prophase 1 until menstrual cycle
* arrest in metaphase 2 until fertilisation

SPERMATOGENESIS

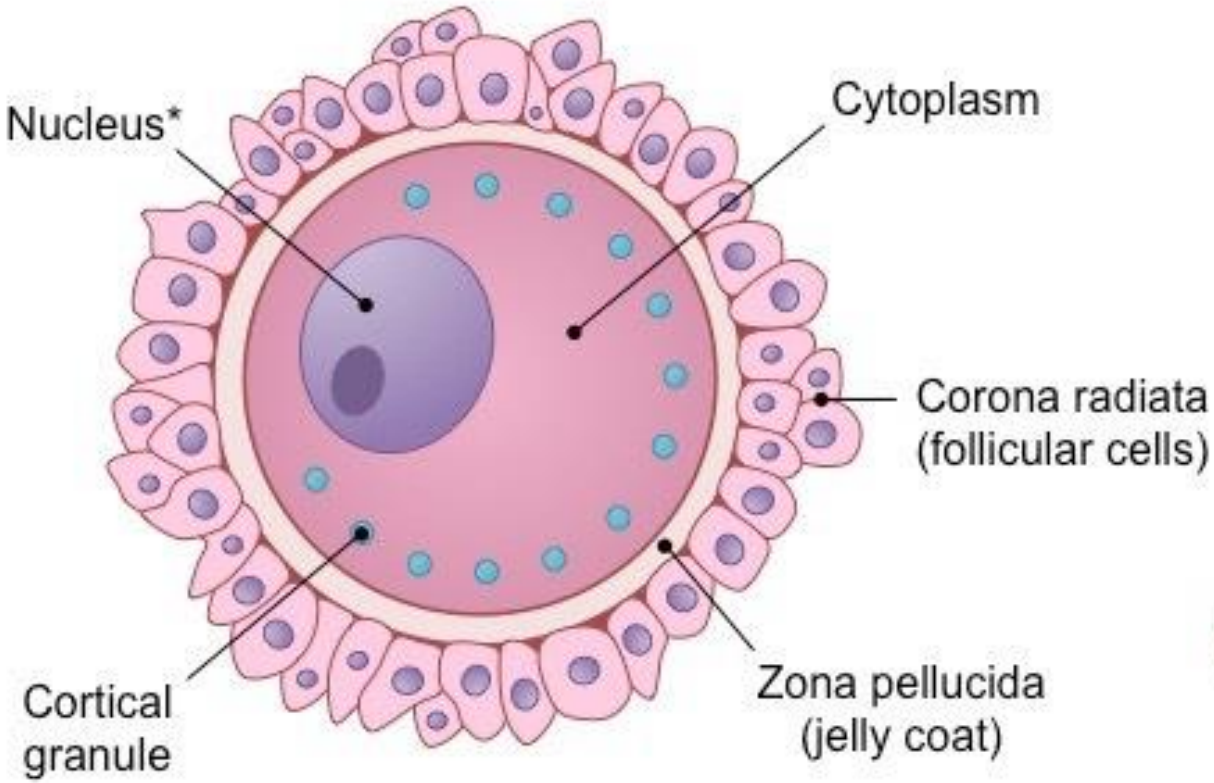
- Formation of spermatozoa from spermatogonia
- Spermatogonia > primary spermatocyte > secondary spermatocyte > spermatid > spermatozoa (spermatozoon – singular)

1) Spermatogonia undergo mitosis – primary spermatocyte (2n)
2) primary spermatocyte undergoes meiosis 1 – secondary spermatocyte (n)
3) Secondary spermatocyte undergoes meiosis 2 – spermatid
4) Spermatid undergoes spermatogenesis - spermatozoa

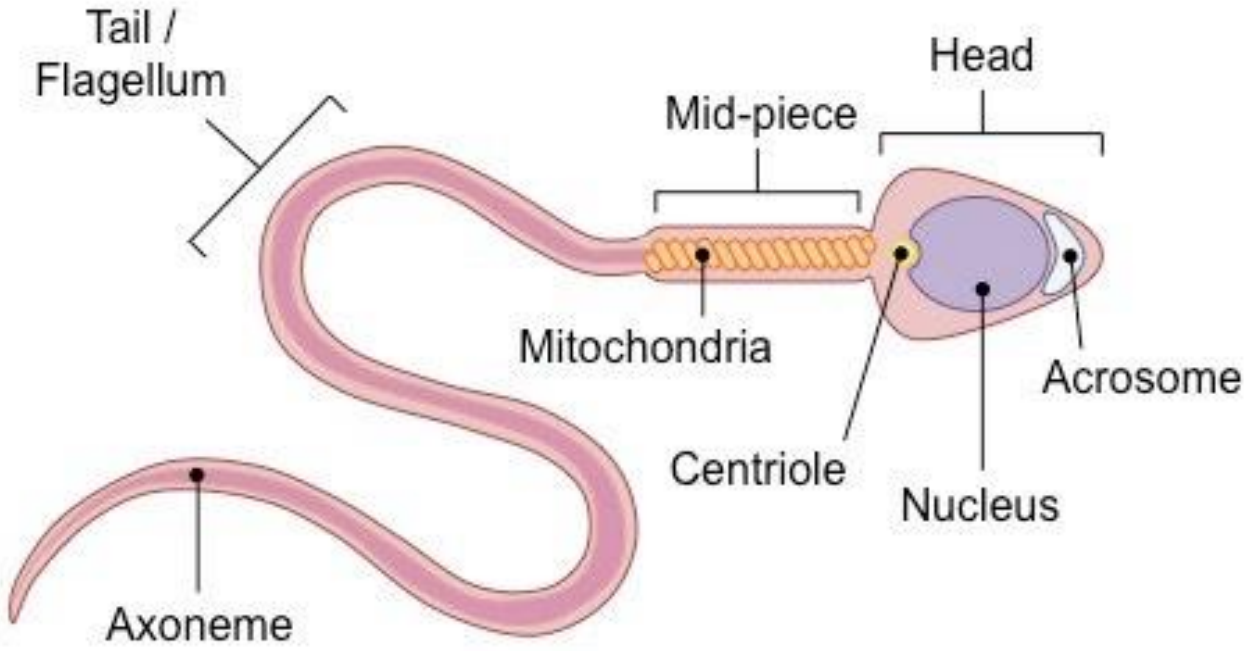
Spermatogenesis :



Human Egg (Ovum)



Human Sperm (Spermatozoa)



***NB:** Mature human ova are arrested in metaphase II until fertilization and hence do not actually possess a condensed nucleus However, nuclei are typically included in biological drawings of egg cells to represent the presence of haploid DNA material

FERTILISATION

- Fertilisation is the complex sequence of coordinated molecular events, that results in the fusion of male and female gametes into a zygote.
- Haploid sperm fuses with haploid ovum to form diploid zygote

This happens in 3 phases:

1) Penetration of corona radiata and zona pellucida
2) Fusion of plasma cell membranes
3) Fusion of pro nuclei to form a zygote

- Takes place in the ampulla of the fallopian tube – week 1, day 1

PROCESS OF FERTILISATION

Capacitation of sperm

- Removal of cholesterol, glycoproteins from plasma membrane around the acrosomal region of sperm
- Induces hypermotility – sperm can ‘swim’ through hyaluronic acid and granulosa cells to reach zona pellucida

Penetration of corona radiata

- Hyaluronidase (enzyme) is released from acrosome – causes dispersal of granulosa cells

Penetration of zona pellucida

- Sperm binds to ZP3 receptors – Ca^{2+} influx which causes an acrosomal reaction where acrosin is released to penetrate zona pellucida

CONTINUED...

Egg = polyspermy, can allow multiple sperm to enter

fast block

- Sperm binds to membrane of secondary oocyte – influx of Na^+ into egg – creates positive charge across membrane – prevents polyspermy

Slow block – cortical reaction

- Sperm binds to membrane – Ca^{2+} influx – triggers cortical granules to release enzymes to harden the cell membrane – inactivates ZP3 – prevents polyspermy

Why might we want to prevent polyspermy?


sperm
capacitation = removal of proteins of acrosome membrane
hyaluronidase
corona radiata
acrosin
zona pellicuda
egg = polyspermy
'hatching'
fast block
slow block
ovum
2nd meitotic division complete
=
zygote
rapid mitosis
2 blastomeres
morula
16 cells

ZYGOTE CLEAVAGE – WEEK 1

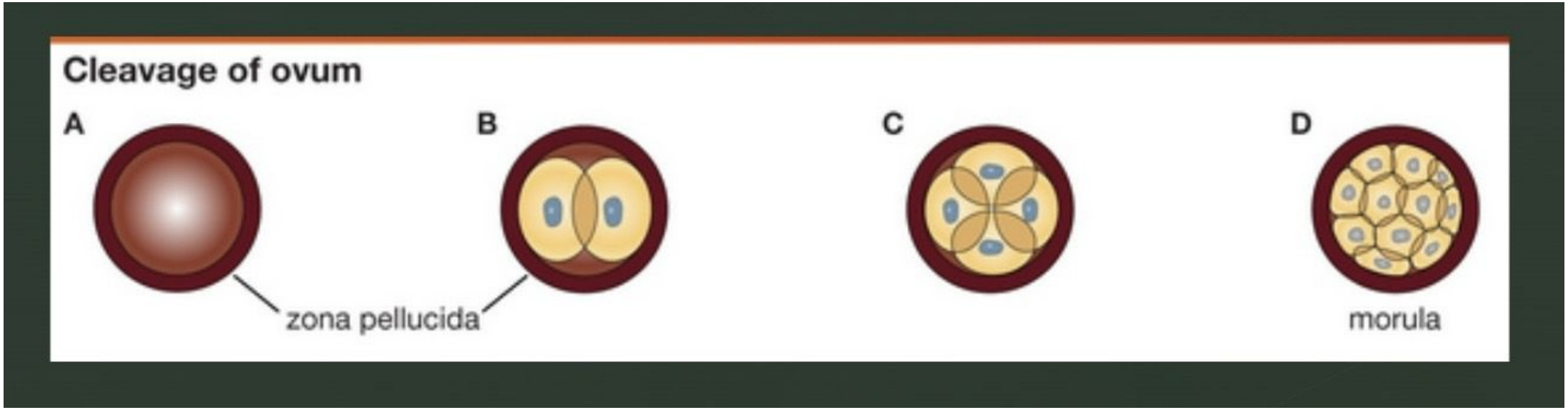
- 12-24 hours after fertilisation – rapid mitotic cell division of zygote into 2 blastomeres

Day 3

- Forms morula – 16 cells

The cell grows without an increase in its size!!

Zygote > 2 blastomeres > morula



Zygote Cleavage:

↑ rapid **mitosis** of **zygote** → **2 blastomeres** —(72 hrs)→ **morula (16 cells)**

blastocyst

FORMATION OF THE BLASTOCYSTS (DAY 4-5)

- Morula – divides and travels down fallopian tube towards uterus

Blastocyst – 32 cells

- Blastocyst divides into 2 – embryoblast (inner cell mass) and trophoblast (outer cell mass)
- Blastocele – blastocyst cavity – filled with fluid to form primitive yolk sac

Embryoblast

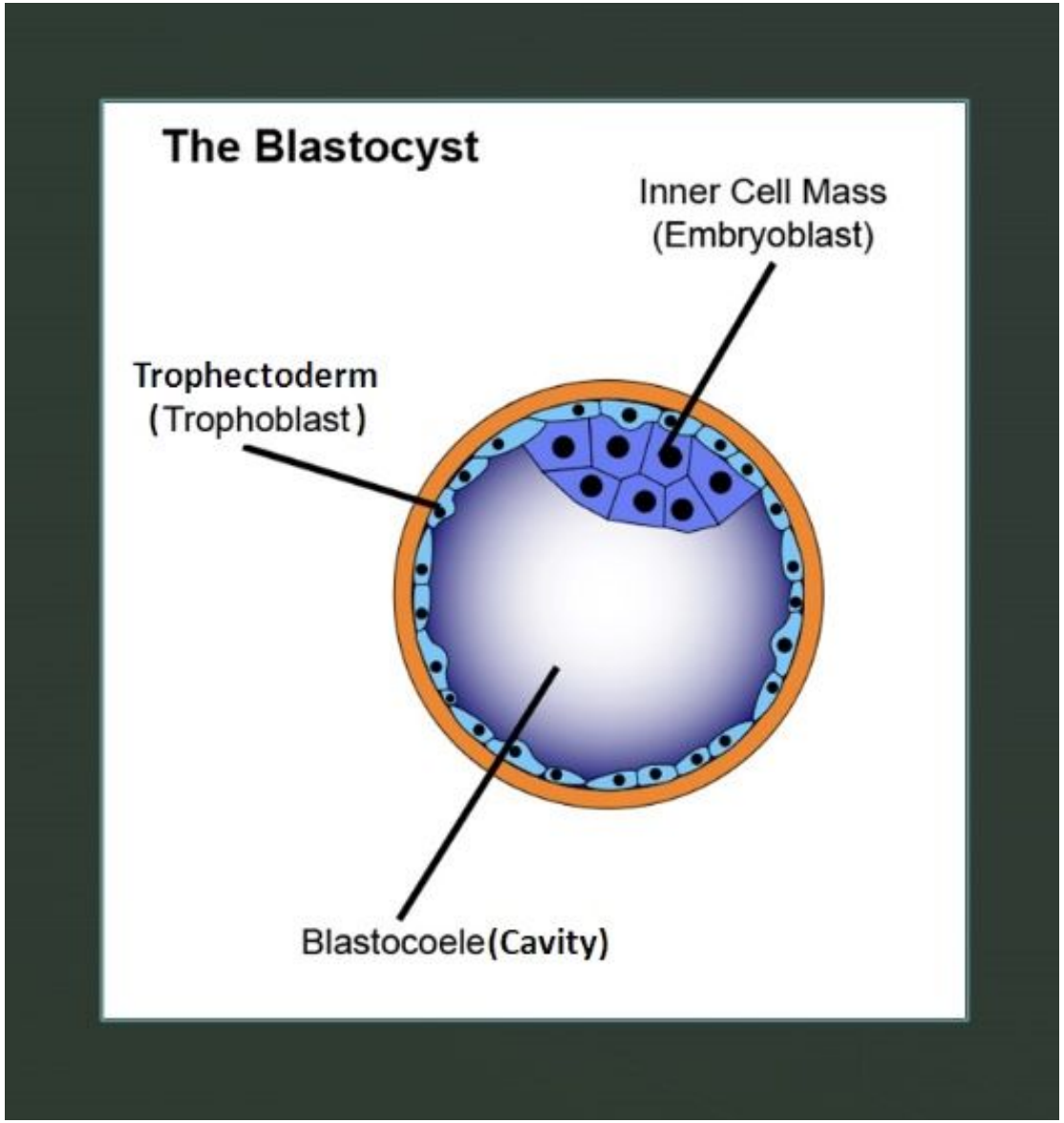
- Forms embryo

Trophoblast

- In contact with endometrium
- Facilitate implantation and placenta formation

Day 5 - hatching

- Blastocyst hatches – digests a hole into zona pellucida and squeezes through


The Blastocyst
Inner Cell Mass
(Embryoblast)
Trophectoderm
(Trophoblast)
Blastocoele(Cavity)

IMPLANTATION – DAY 6, ENDS IN WEEK 2

- Hatched blastocyst attaches to endometrial epithelium after 6 days
- Interaction between trophoblasts and endometrium causes trophoblasts to proliferate and differentiate into cytotrophoblasts and synctiotrophoblasts

Cytotrophoblasts

- Inner layer

Synctiotrophoblasts

- Outer layer
- Produce proteolytic enzymes – digest maternal tissues from embryo burrowing

BI-LAMINAR DISC – WEEK 2

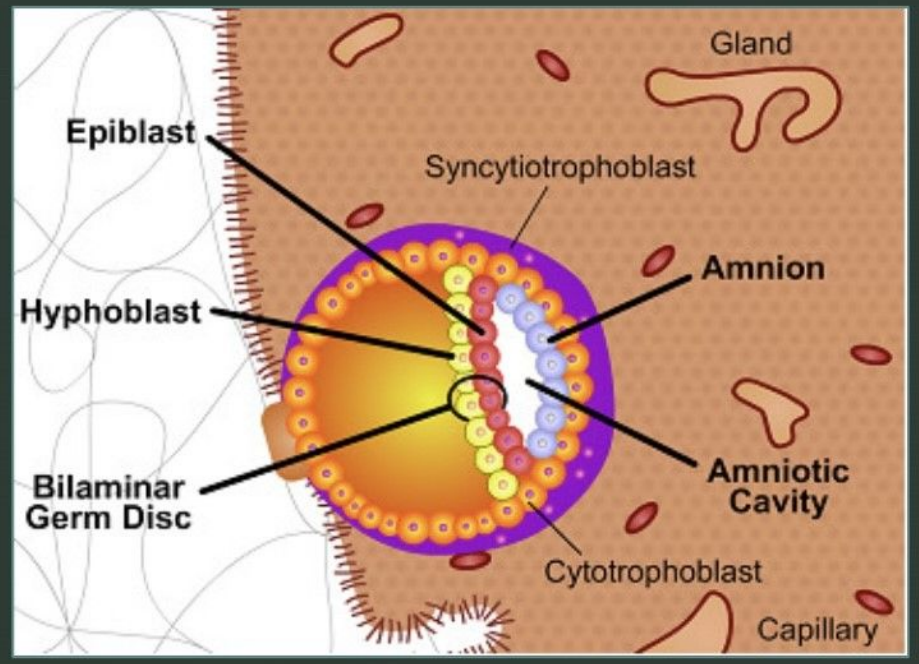
Embryoblasts divide into 2 – day 8

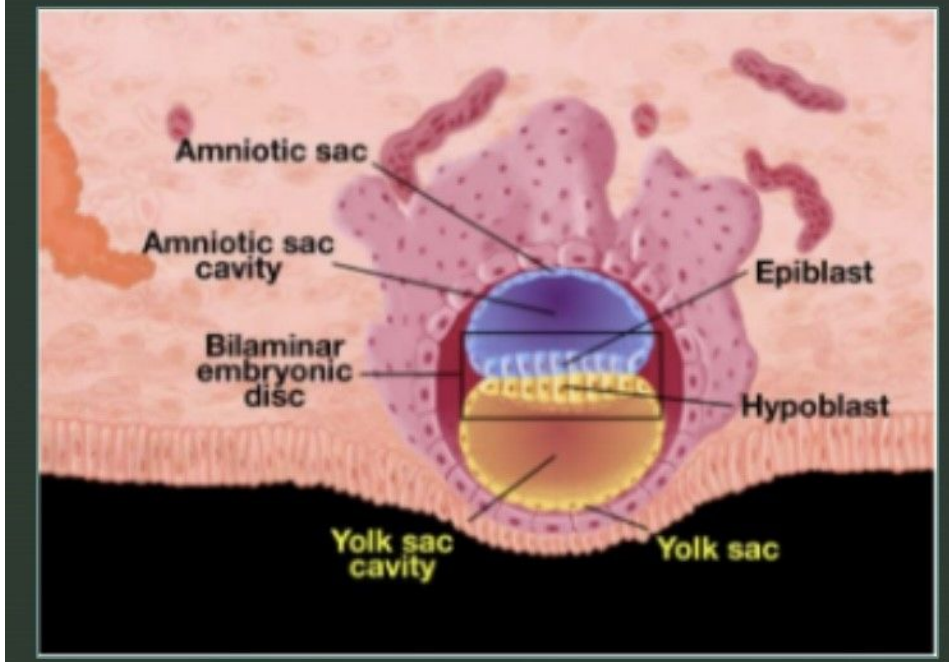
- Epiblast – form embryo
- Hypoblast – form yolk sac, placenta

Both form bi-laminar disc

Day 9-10

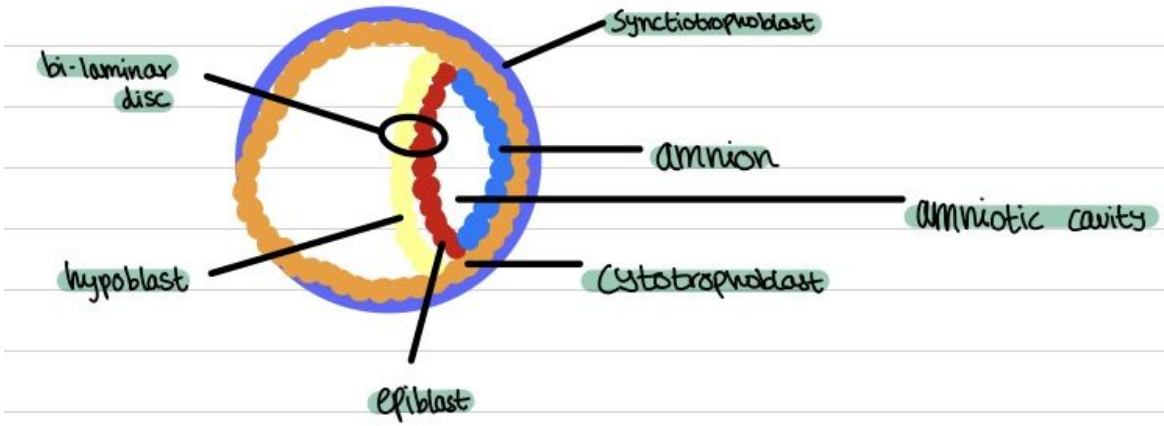
- Blastocele develops into yolk sac
- Bi-laminar disc is positioned between amniotic cavity and yolk sac





day 9-10:

↑ blastocyst cavity → yolk sac (hypoblast side)



GASTRULATION: FORMATION OF TRI-LAMINAR DISC – WEEK 3, DAY 13-17

Bi laminar disc > tri laminar disc – 3 germ layers

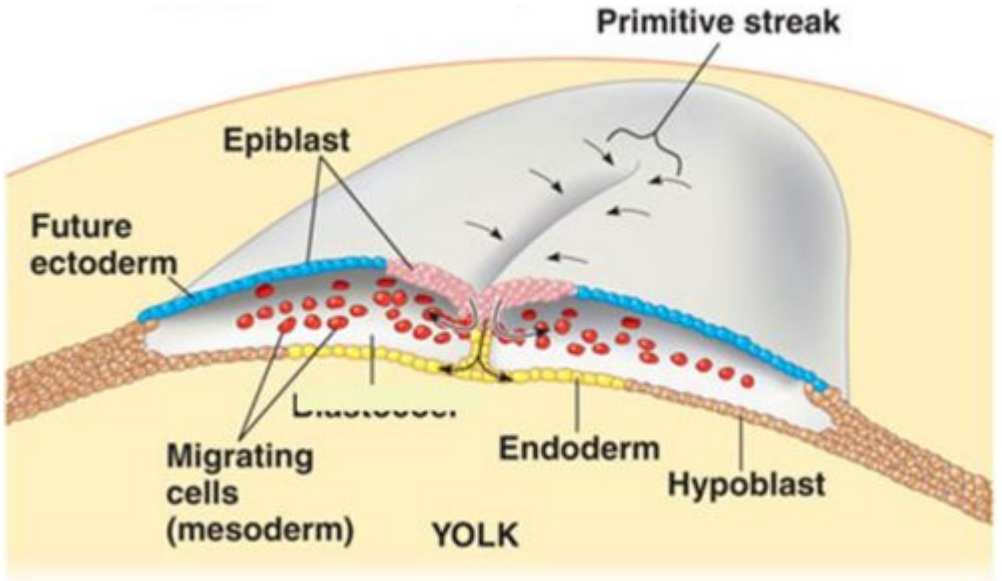
1) Epiblasts invaginate between bi-laminar disc > primitive streak (groove in midline of epiblast > primitive node > primitive pit

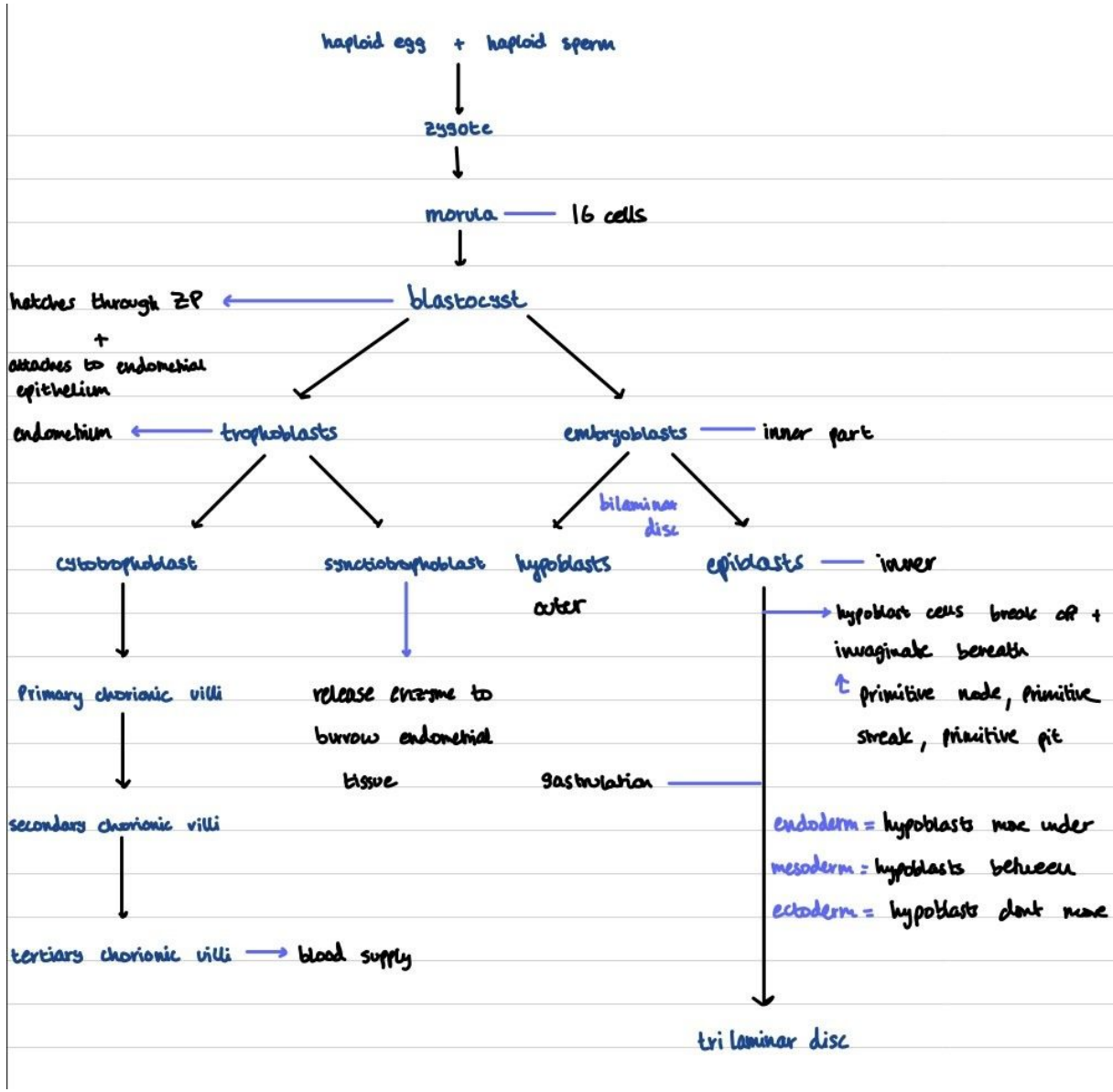
2) Cells break off the epiblast layer and travel through primitive streak – pit to fill space between epiblast and hypoblast

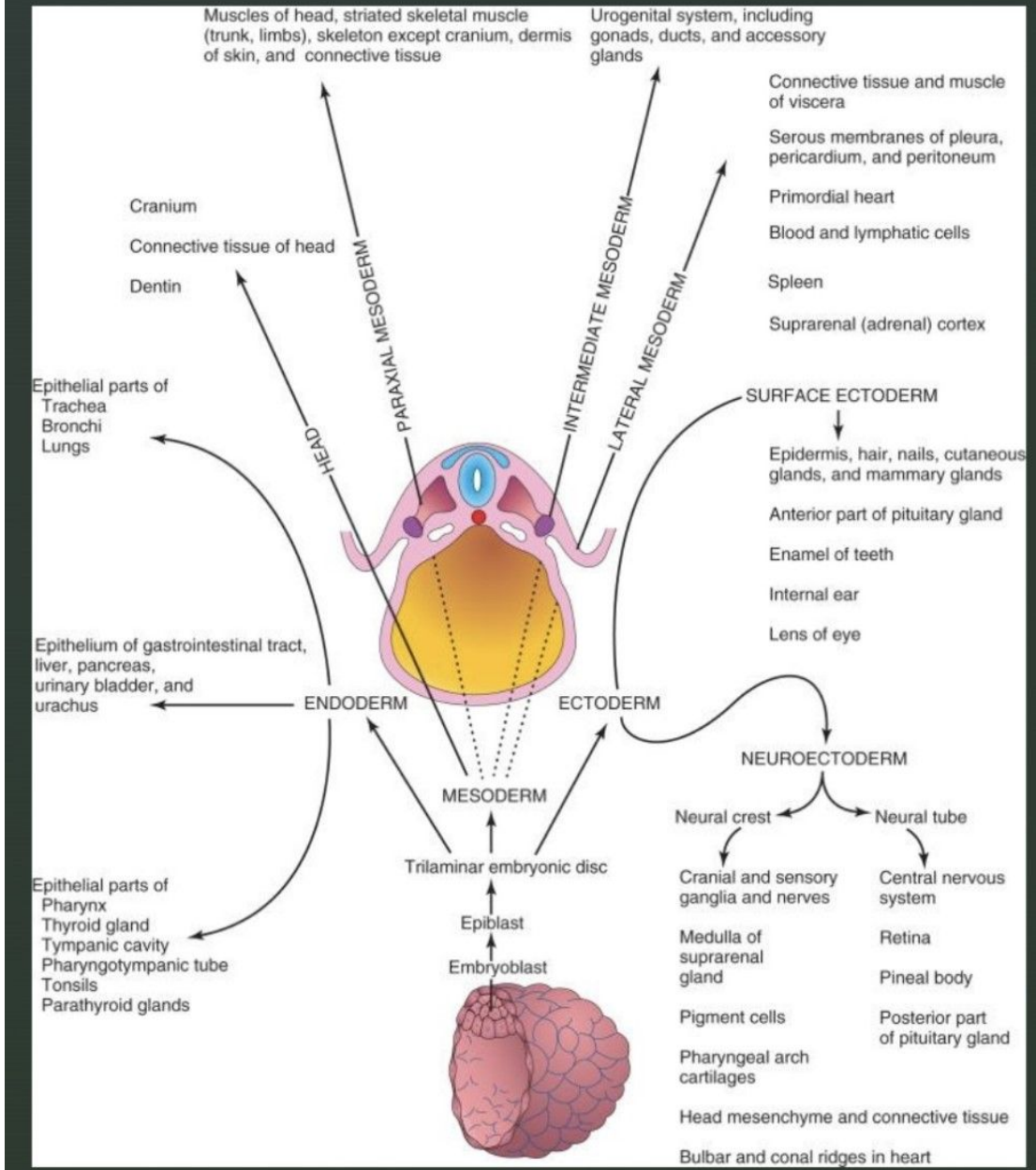
Endoderm – epiblasts replace hypoblasts

Mesoderm – epiblasts between epiblast layer and endoderm

Ectoderm – epiblasts that **did not** migrate




haploid egg + haploid sperm
zygote
morula — 16 cells
blastocyst
hatches through ZP
+
attaches to endometrial epithelium
endometrium
trophoblasts
embryoblasts — inner part
bilaminar disc
cytotrophoblast
syncitiotrophoblast
hypoblasts
outer
epiblasts — inner
hypoblast cells break off + invaginate beneath
primitive node, primitive streak, primitive pit
Primary chorionic villi
release enzyme to burrow endometrial tissue
gastrulation
secondary chorionic villi
endoderm = hypoblasts now under
mesoderm = hypoblasts between
ectoderm = hypoblasts don't move
tertiary chorionic villi → blood supply
trilaminar disc



Ectoderm	Mesoderm	Endoderm
Skin	Musculoskeletal System	GI Tract – Epithelial lining
Nails	Cardiovascular System	Lungs
Hair	Excretory System	Liver
CNS- Brain + Spinal Cord	Reproductive System	Pancreas
		Bladder
		Thyroid/ Parathyroid glands
		Thymus

NEURULATION – WEEK4, DAY16-21

Day 16-21

- mesodermal cells from the primitive node migrate toward the rostral end (head end) of the embryo and form a hollow tube of cells in the midline – the notochordal process
- The notochordal process cells will proliferate and detach from the endoderm to form a solid chord of cells = **Notochord**
- Notochord cells cannot extend past the prechordal plate as the ectoderm and endoderm there are firmly adherent to each other. This area is now called the oropharyngeal membrane. • A similar area on the other side of the primitive streak is the cloacal membrane.
- The notochord will eventually form the intervertebral discs
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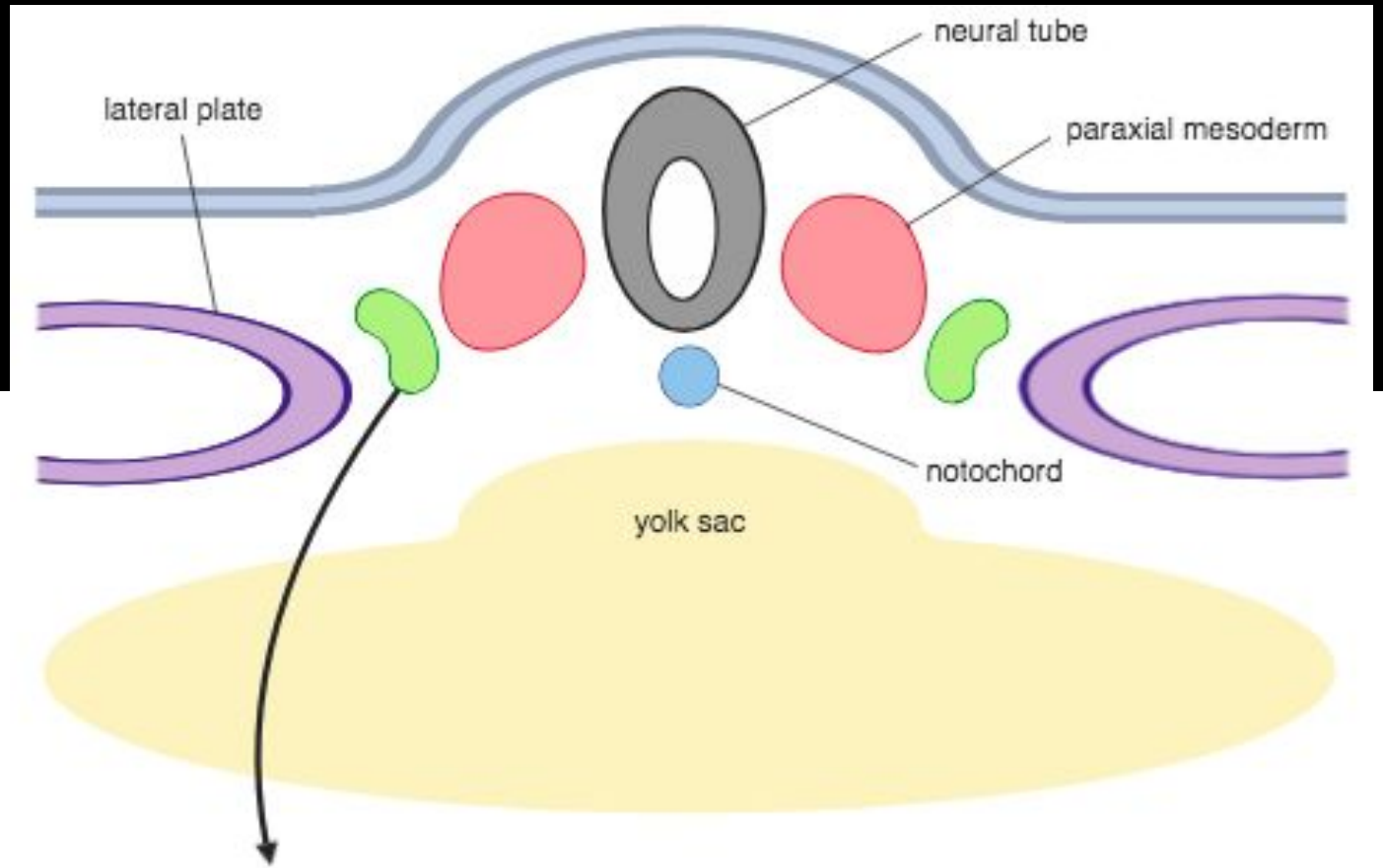
The notochord signals for the mesoderm to further differentiate into:

- Paraxial mesoderm – skeleton and muscles
- Intermediate mesoderm – gonads and kidneys

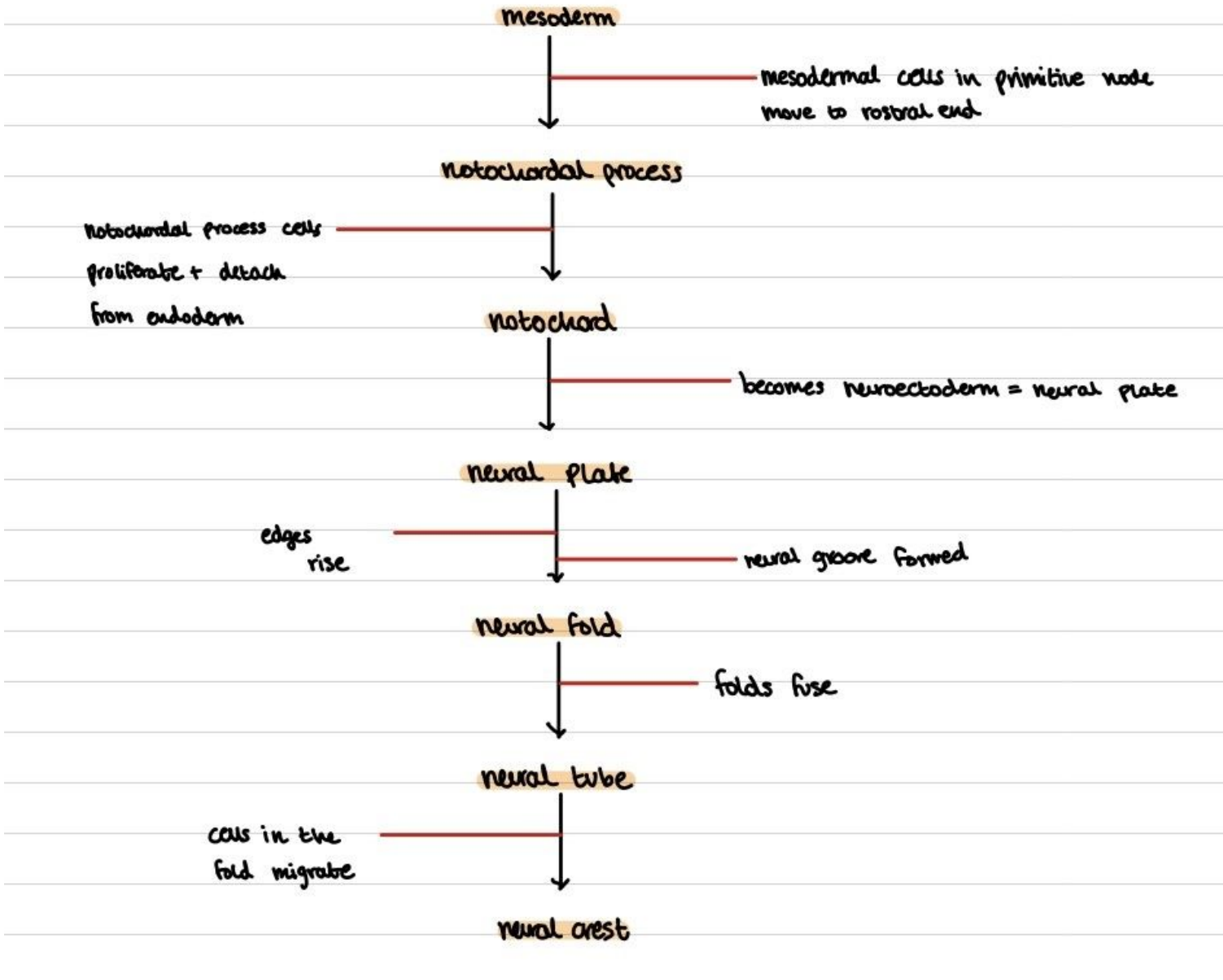


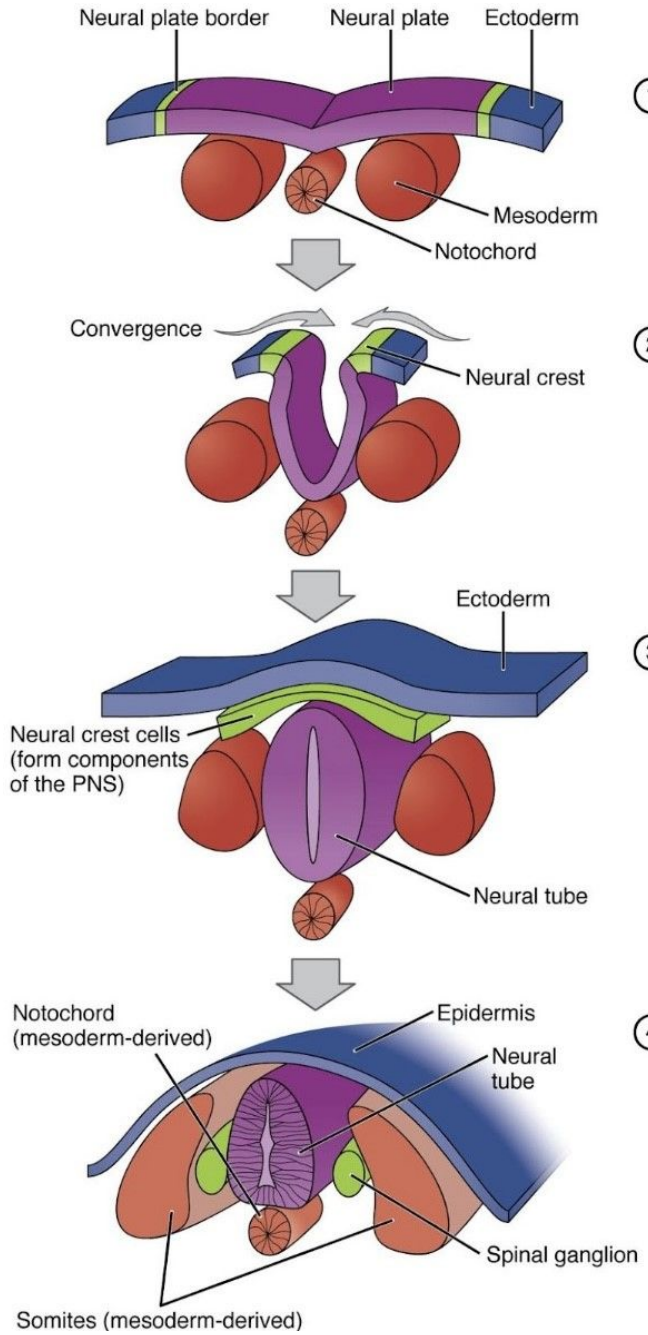
Intermediate Mesoderm → pronephros

pronephros → mesonephros → metanephros

mesonephros → gonads

metanephros → kidneys


mesoderm
mesodermal cells in primitive node move to rostral end
notochordal process
notochordal process cells proliferate + detach from endoderm
notochord
becomes neuroectoderm = neural plate
neural plate
edges rise
neural groove formed
neural fold
folds fuse
neural tube
cells in the fold migrate
neural crest



1. Neuroectodermal tissues differentiate from the ectoderm and thicken into the neural plate. The neural plate border separates the ectoderm from the neural plate.

2. The neural plate bends dorsally, with the two ends eventually joining at the neural plate borders, which are now referred to as the neural crest.

3. The closure of the neural tube disconnects the neural crest from the epidermis. Neural crest cells differentiate to form most of the peripheral nervous system.

4. The notochord degenerates and only persists as the nucleus pulposus of the intervertebral discs. Other mesoderm cells differentiate into the somites, the precursors of the axial skeleton and skeletal muscle.

PHARYNGEAL ARCHES

- Mesenchymal tissue – growth in cranial region in weeks 4-5
- Formation of pharyngeal arches and clefts
- 6 pharyngeal arches – 5^{th} one regresses soon after forming, PA 1, 2, 3, 4 and 6
- PA 4 and 6 fuse

Table 1. Structures Derived from Branchial Arch Components

Arch	Nerve	Muscle	Skeletal structure	Ligaments
First (mandibular)	Trigeminal (V)	Muscle of mastication Mylohyoid and anterior belly of digastric Tensor tympani Tensor veli palatini	Malleus Incus	Anterior ligament of malleus Sphenomandibular ligament
Second (hyoid)	Facial (VII)	Muscle of facial expression Stapedius Stylohyoid Posterior belly of digastric	Stapes Styloid process Lesser cornu of hyoid Upper part of body of the hyoid bone	Stylohyoid ligament
Third	Glossopharyngeus (IX)	Stylopharygeus	Greater cornu of hyoid Lower part of body of the hyoid bone	
Fourth to sixth	Superior larygeal branch of the vagus (X) Recurrent larygeal branch of the vagus (X)	Cricohyoid Levator veli palatini Constrictor of pharynx Intrinsic muscle of larynx Striated muscle of the esophagus	Thyroid cartilage Cricoid cartilage Arytenoid cartilage Corniculate cartilage Cuneiform cartilage	

QUESTION TIME!!! (EXPECTING 100%)

1. what week and what day is hatching
   a. week 1 day 6
   b. week 1 day 5
   c. week 2 day 1
   d. week 2 day 5

2. what undergoes spermatogenesis to form a spermatozoa
1. spermatid
2. spermatocyte
3. spermatogonia
4. zygote

3. what enzyme is released from acrosome to cause dispersion of granulosa cells?
1. progesterone
2. hyaluronic acid
3. acrosin
4. hyaluronidase

4. which ion enters the egg to prevent polyspermy?
1. Mg^{2+}
2. Ca^{2+}
3. Na^{+}
4. K^{+}

CONTINUED

5.how many cells is a morula?

1.16

2.32

3.15

4.48

6. what hormone is produced by placenta?

1.oestrogen

2.fsh

3.progesterone

4.lh

7. pancreas is derived from what germ layer?

1.ectoderm
2.mesoderm
3.endoderm
4.hypoblast

ANSWERS 😊

1) Week 1, day 5
2) Spermatid
3) Hyaluronidase
4) Na+
5) 16
6) Progesterone
7) endoderm

THANKS FOR LISTENING