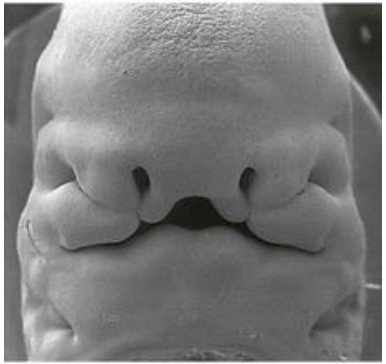


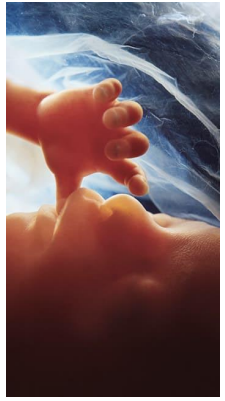
Basic embryology for Dentistry

Dr Gosia Wiench
m.d.wiench@bham.ac.uk

To understand the embryological development of the oral tissues, the dental care professional needs to have a basic knowledge of the process of embryo formation, and the significance of the origins of various body tissues and organs to help understand how congenital defects, pathology and disease processes occur.

Embryology - study of prenatal development

division



Embryo

Fertilization (zygote) to ~4 weeks — cell proliferation and migration

4 to 8 weeks — morphogenesis (differentiation and formation of all body structures)

Most congenital defects develop

Fetus

9 weeks to birth — growth and maturation

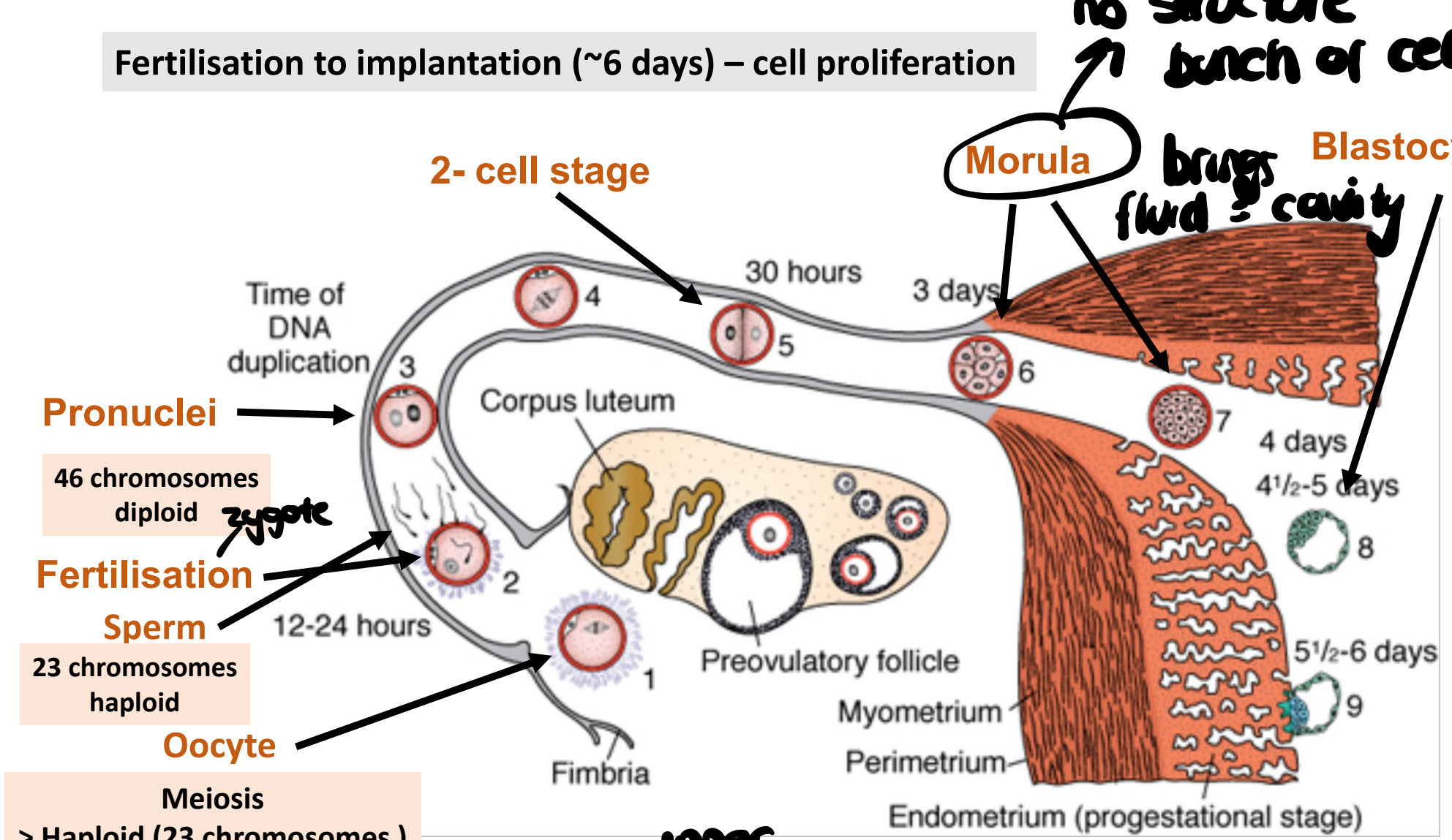
if serious then embryo dies

Oral embryology - study of the development of the oral cavity, and the structures within it.

Lecture highlights:

- Early development from fertilisation to implantation
- The formation of a two and then three layered embryo, derivatives of ectoderm, mesoderm and endoderm
- The beginnings of nervous system formation
- Folding of the embryo
- Neural crest cells and their migration
- Regulation of embryonic development

Fertilisation to implantation (~6 days) – cell proliferation



Pronuclei

46 chromosomes
diploid

Fertilisation

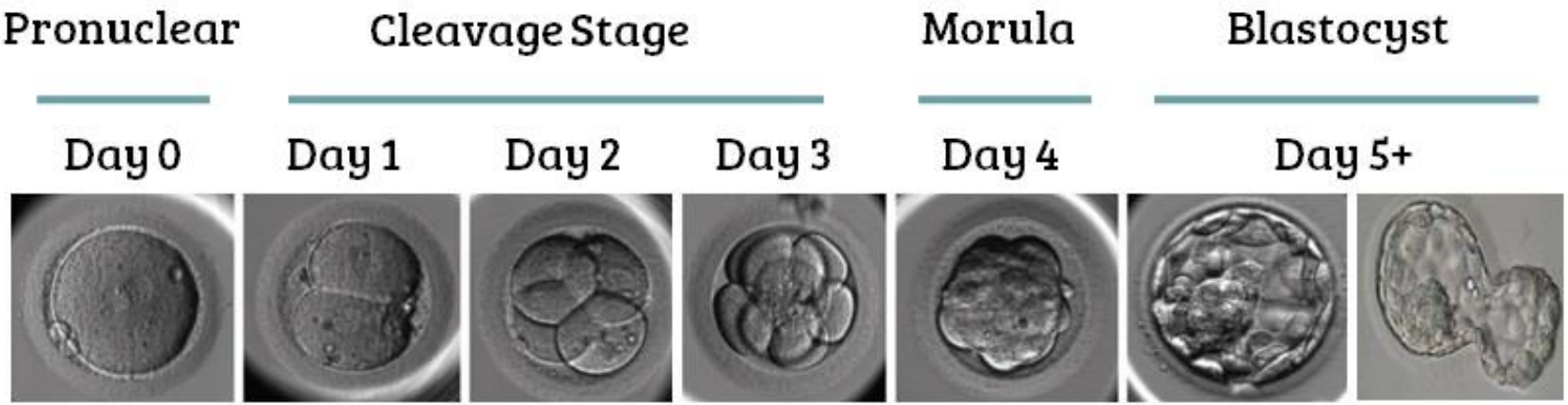
Sperm

23 chromosomes
haploid

Oocyte

Meiosis
> Haploid (23 chromosomes)

Blastocyst formation

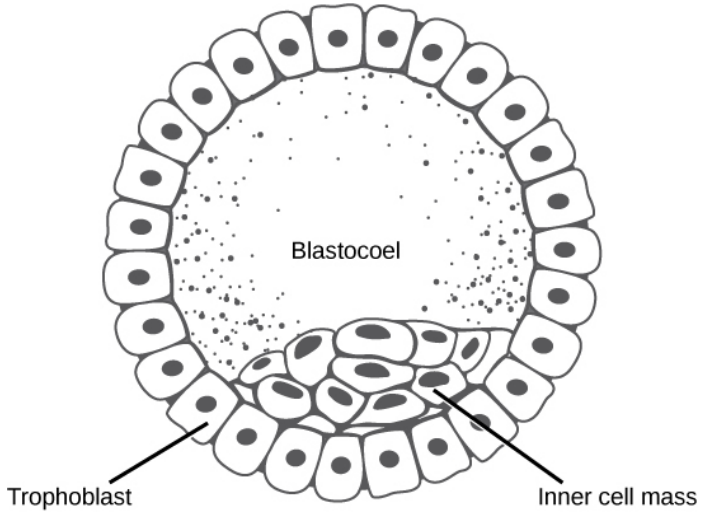


Two distinct cell populations:

Inner cell mass (embryoblast) > > embryo

Source of embryonic stem cells

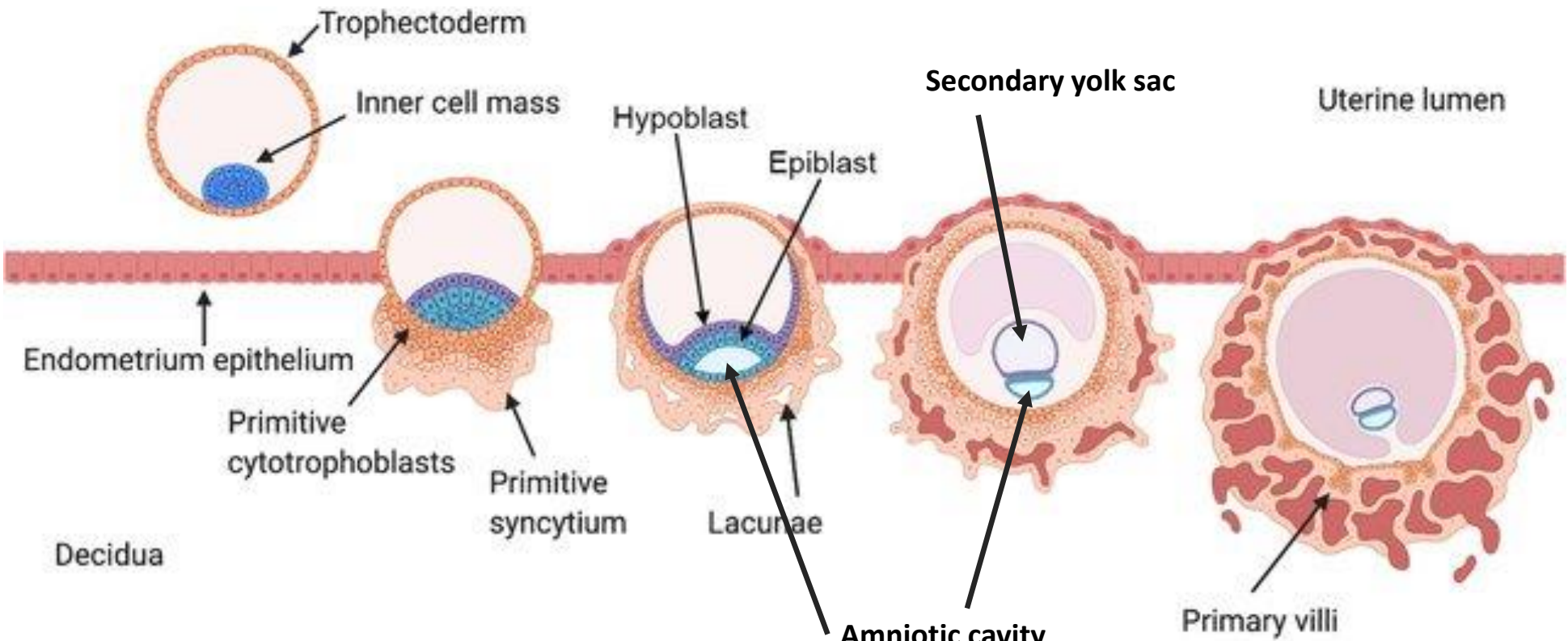
Trophoblast > > aids implantation and placenta development



Implantation and formation of bilaminar germ disc

epiblast forms embryo

Hypoblast & Epiblast



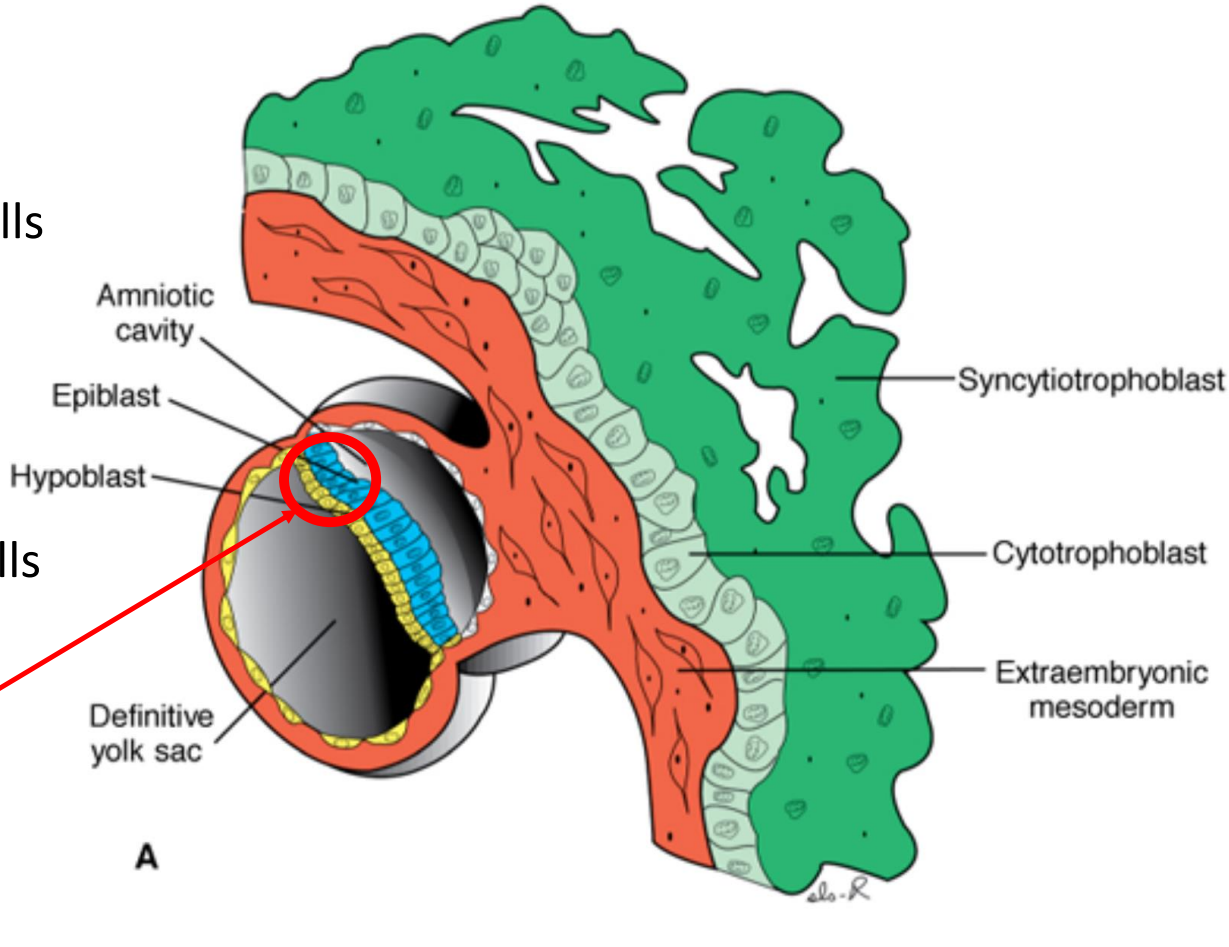
James, J.L. et al., Modelling human placental villous development: designing cultures that reflect anatomy. *Cell. Mol. Life Sci.* **79**, 384 (2022)

Bilaminar germ disc at 2 weeks

<u>Dorsal aspect:</u>
-Ectodermal layer with columnar cells
-Amniotic cavity formed

<u>Ventral aspect:</u>
-Endodermal layer with cuboidal cells
-Definitive yolk sac formed

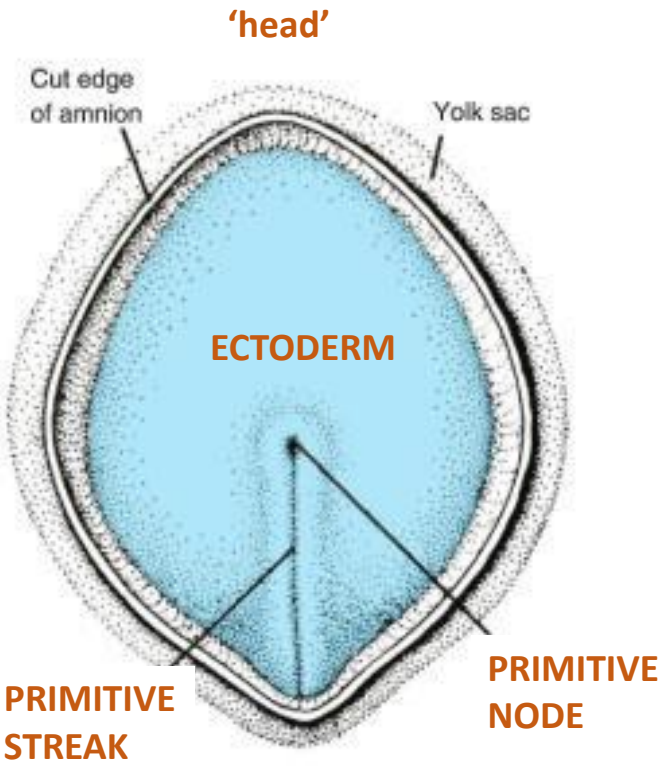
<u>Prochordal plate</u>
(rostral (head) end)

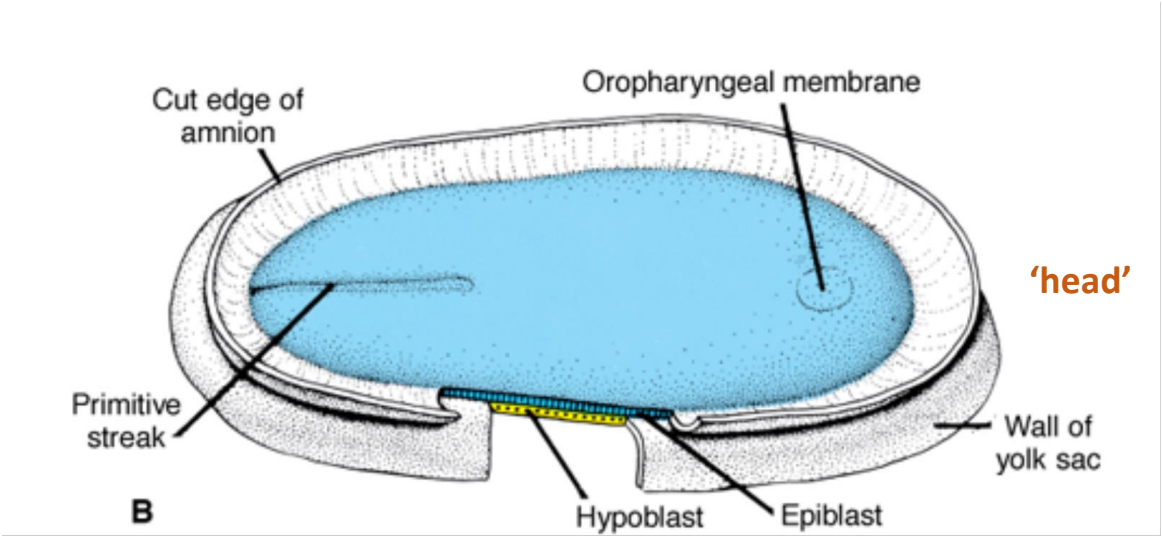


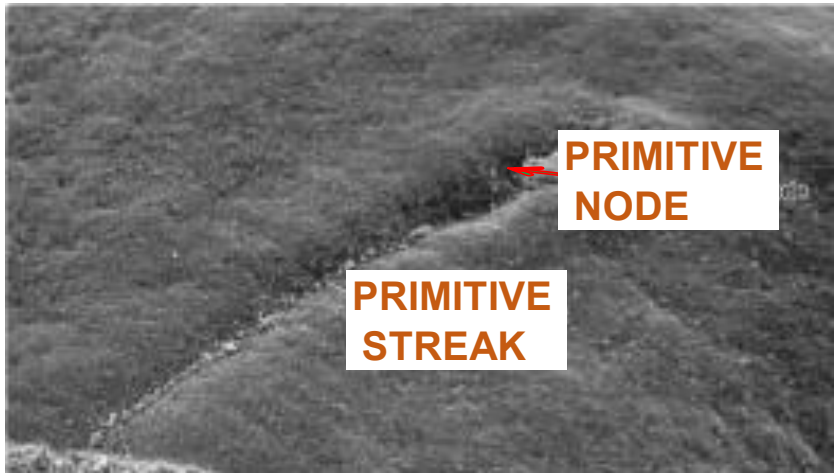
Gastrulation & formation of trilaminar germ disc at 2-3 weeks

•Disc of cells becomes pear shaped and develops a **head end** and a **tail end**

•Embryo now has two symmetrical halves – **left and right**

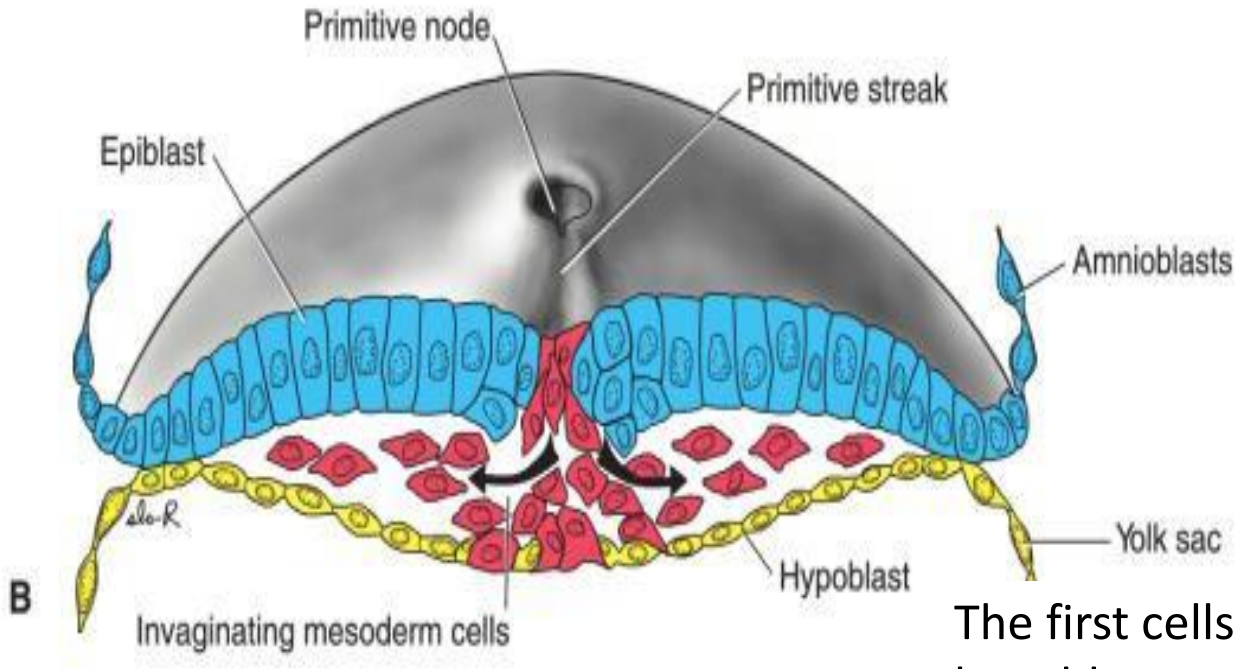






Formation of mesodermal layer

Cells of the **Epiblast** migrate towards the primitive streak and slip beneath it.



They then migrate either ***BETWEEN*** the **Epiblast** and **Hypoblast**
or ***DISPLACE*** the cells of the **Hypoblast** to form two new layers

The first cells to move inward displacing the hypoblast create the **definitive endoderm**
The cells above form the **definitive Mesoderm**
Remaining cells of the epiblast form **Ectoderm**

Nervous System, tooth enamel, epidermis…

Connective tissue (mesenchyme), cardiovascular system, muscle, blood cells

Most GI tract, respiratory system, part of urinary system

EXTRAEMBRYONIC ENDODERM

ECTODERM

MESODERM

ENDODERM

HYPOBLAST

PLACENTA

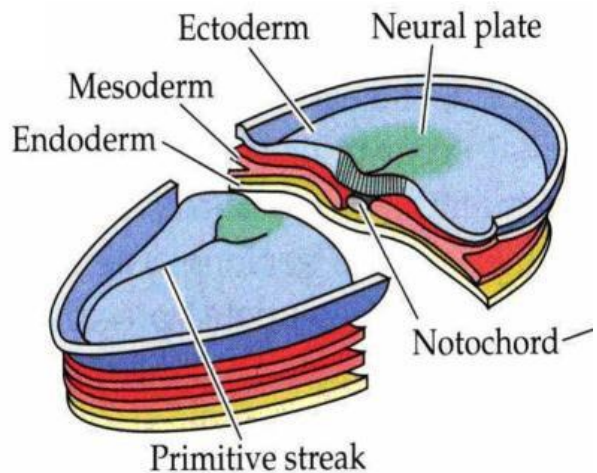
EPIBLAST

differentiation

TROPHOBLAST

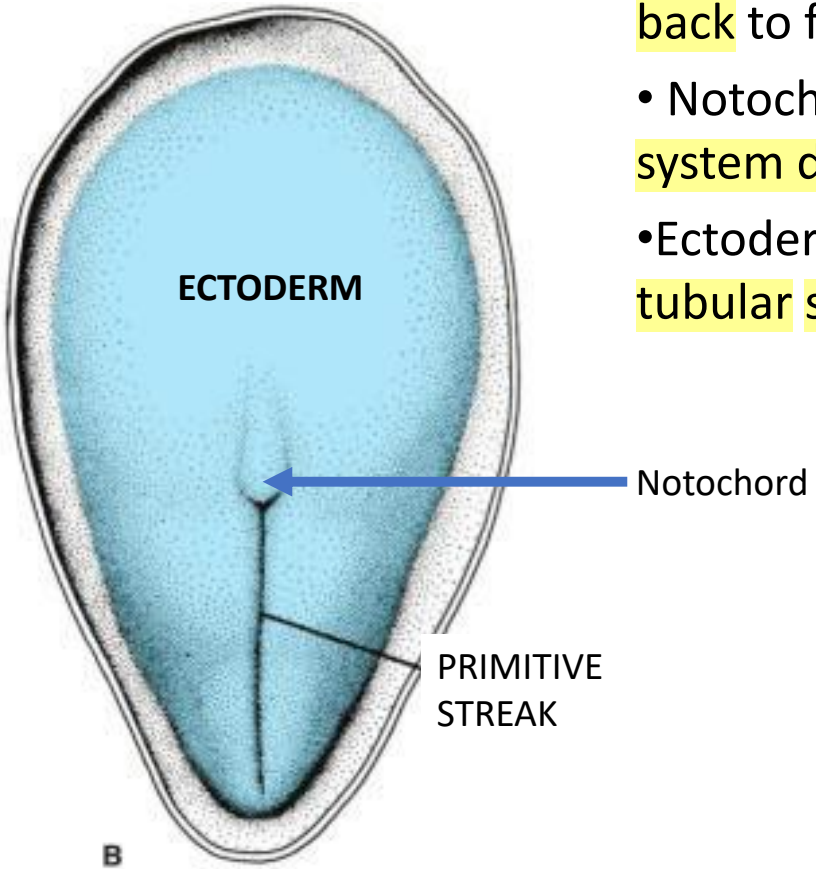
INNER CELL MASS

ZYGOTE



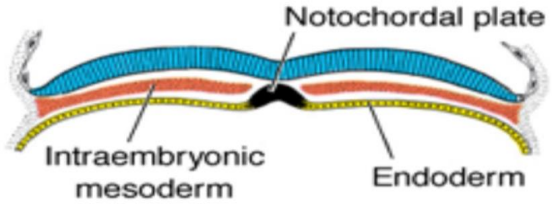
Formation of notochord – the start of nervous system development

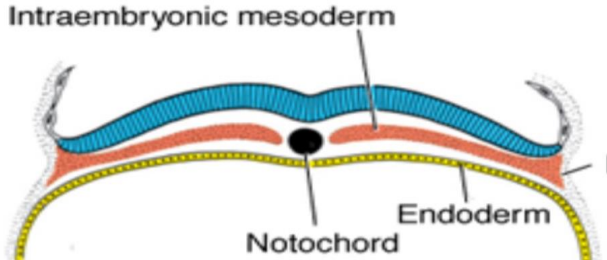
Cranial (head) end



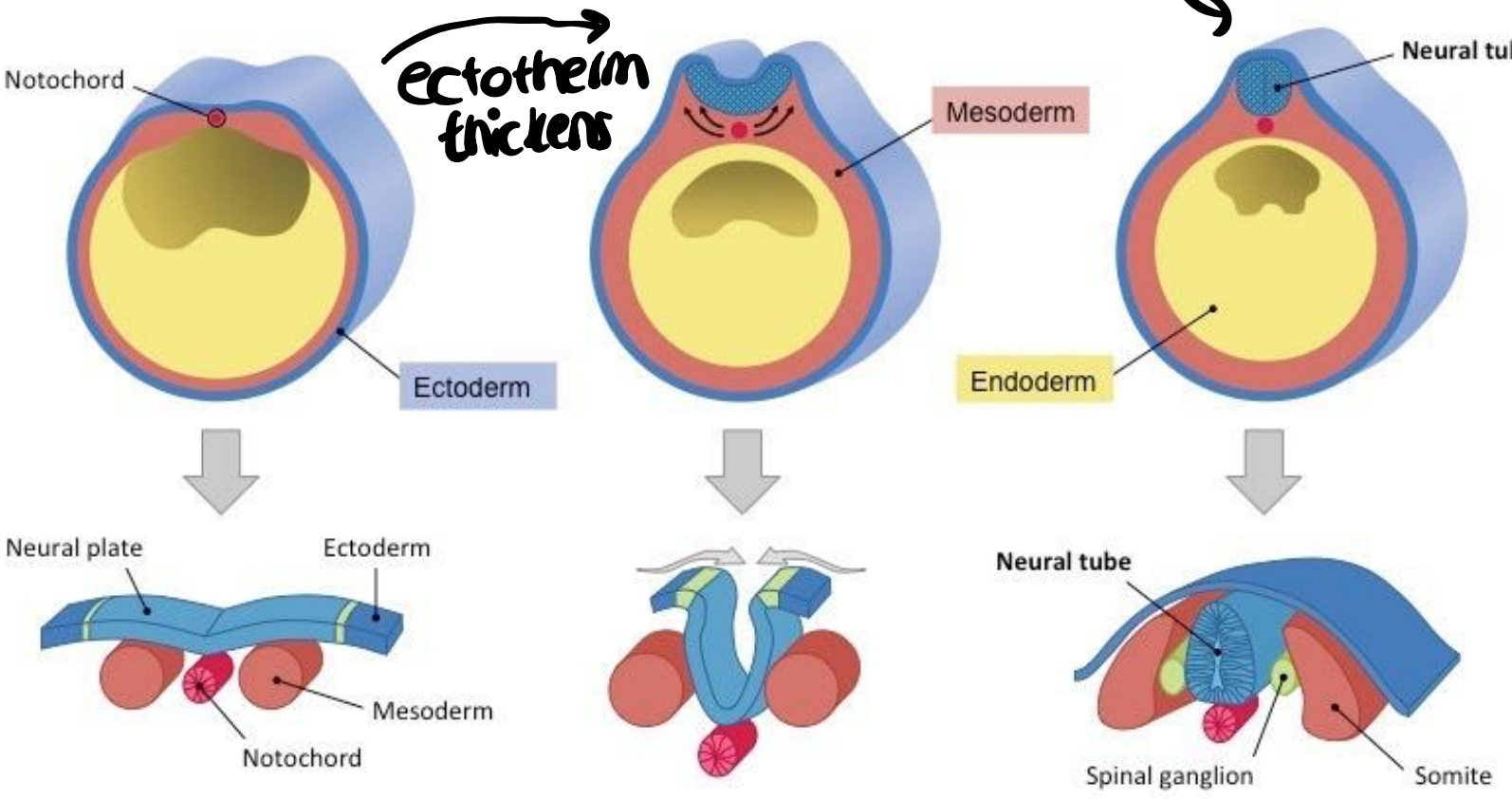
Caudal (tail) end

- Rod of cells develops from the primitive node and along the back to form the **notochord** (later spine)
- Notochord is an important site of signal secretion for nervous system development
- Ectoderm above notochord thickens and rolls to form a tubular structure (**neural tube**, later brain and spinal cord)





Formation of neural tube



1. Notochord forms from mesoderm cells soon after gastrulation is complete

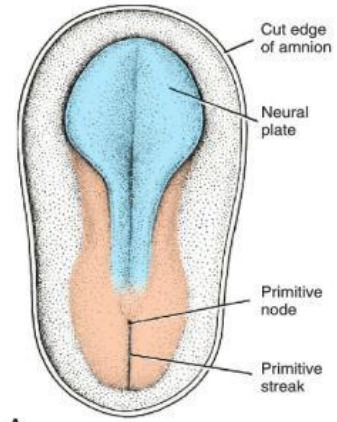
2. Signals from notochord cause inward folding of ectoderm at the neural plate

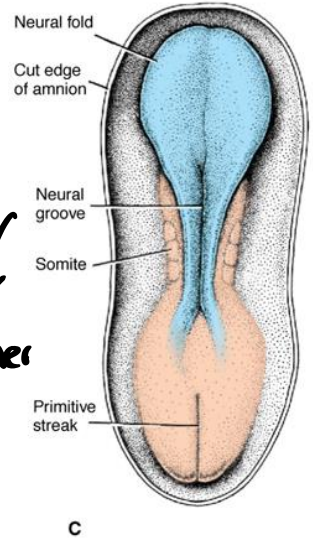
3. Ends of neural plate fuse and disconnect to form an autonomous neural tube

- The nervous system develops as a thickening within the ectoderm giving **neural plate** (at cranial end)
- **Neural** plate **folds** to form **neural groove**
- Neural groove fuses to form **neural tube**
- Neural tube gives rise to brain and spinal cord
- **Neural crest cells** separate and start migrating
- **Mesoderm** differentiates

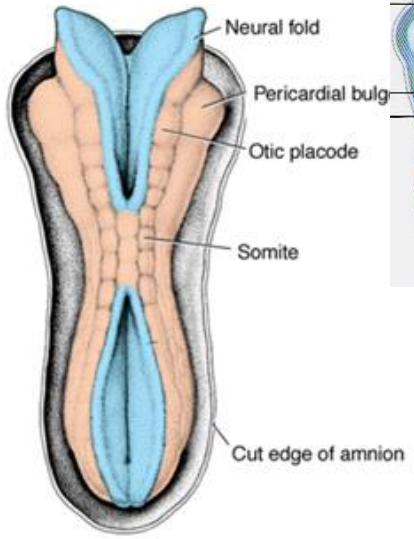
Formation of neural tube

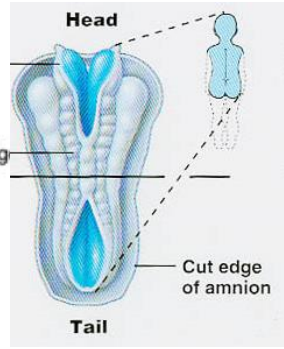
thickening





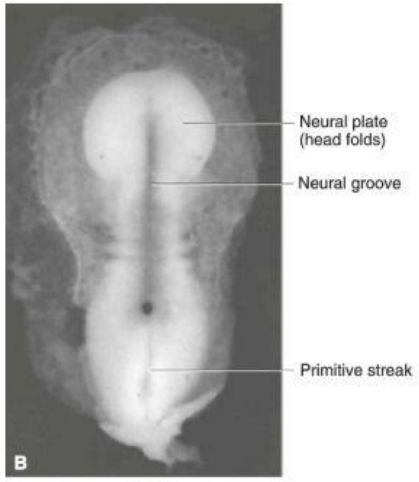
fuses together

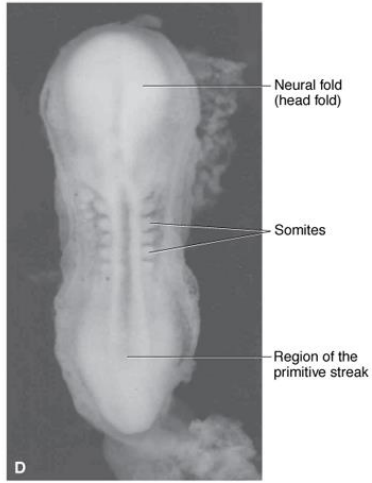


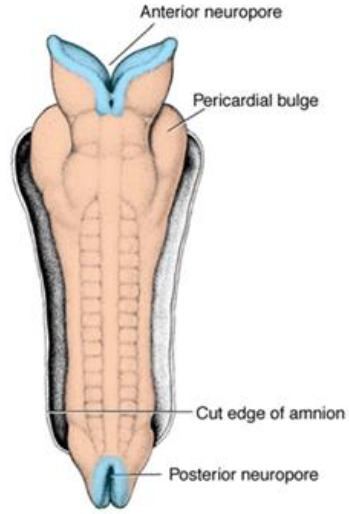


22 days after fertilisation

The cephalic and caudal ends of the neural tube communicate with the amniotic cavity by way of the **anterior (cranial)** and **posterior (caudal) neuropores**

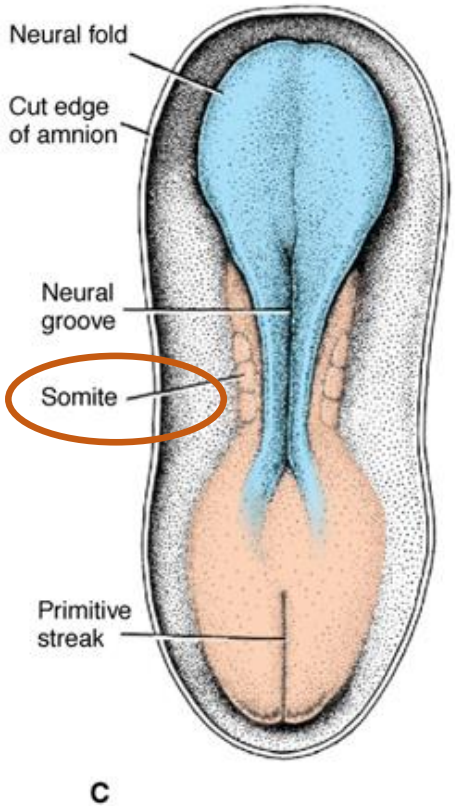






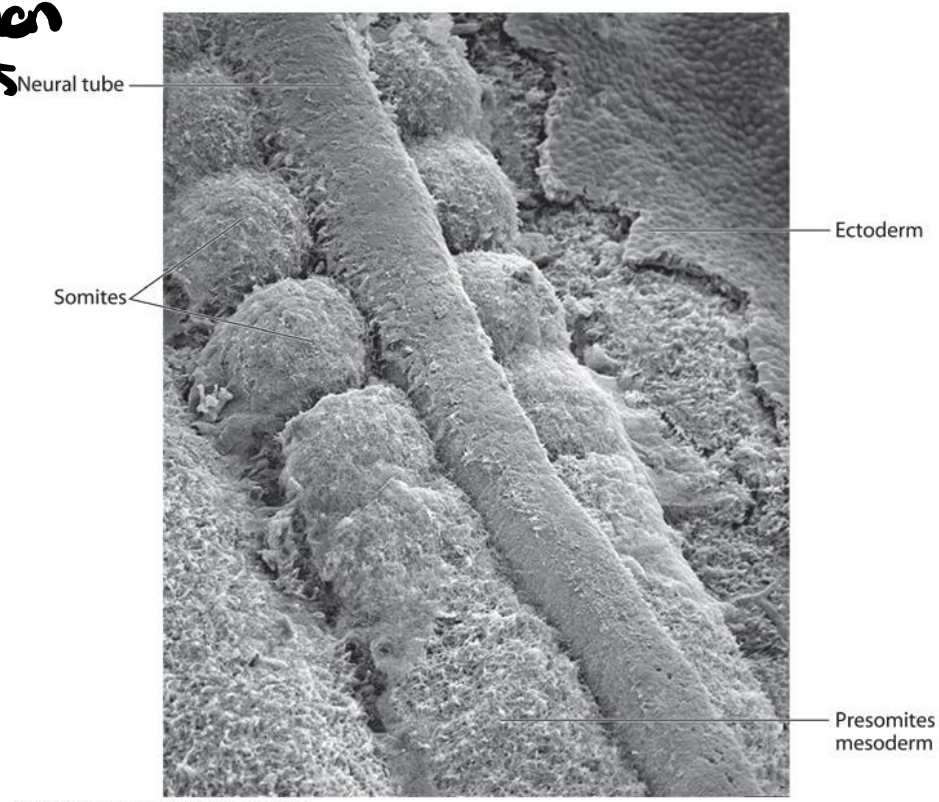
Formation and differentiation of mesoderm

↳ first process is differentiation of somites



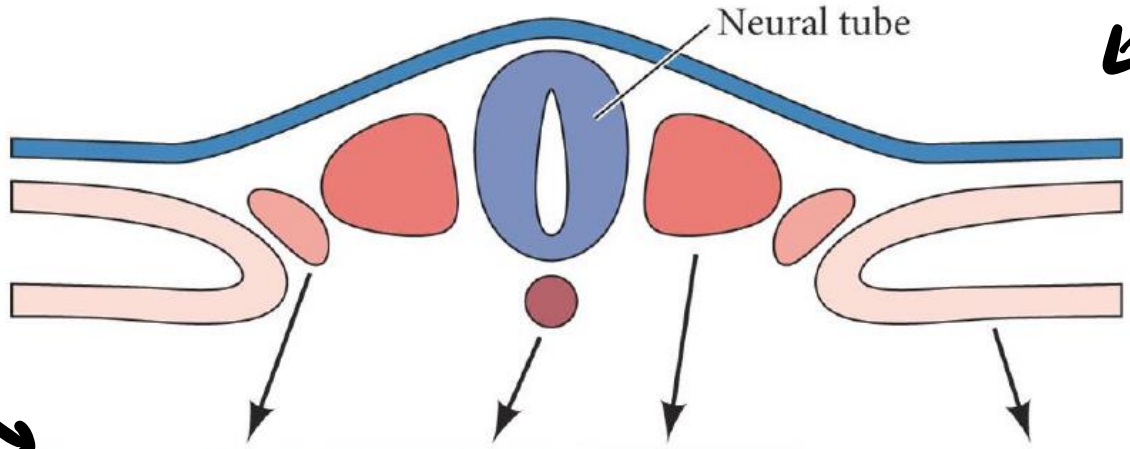
- The first phase in the differentiation of **somites** is a process of periodisation or ***segmentation***.

- Segmented blocks of **somites** appear progressively from the anterior (cranial) end.



Formation and differentiation of mesoderm

different segments

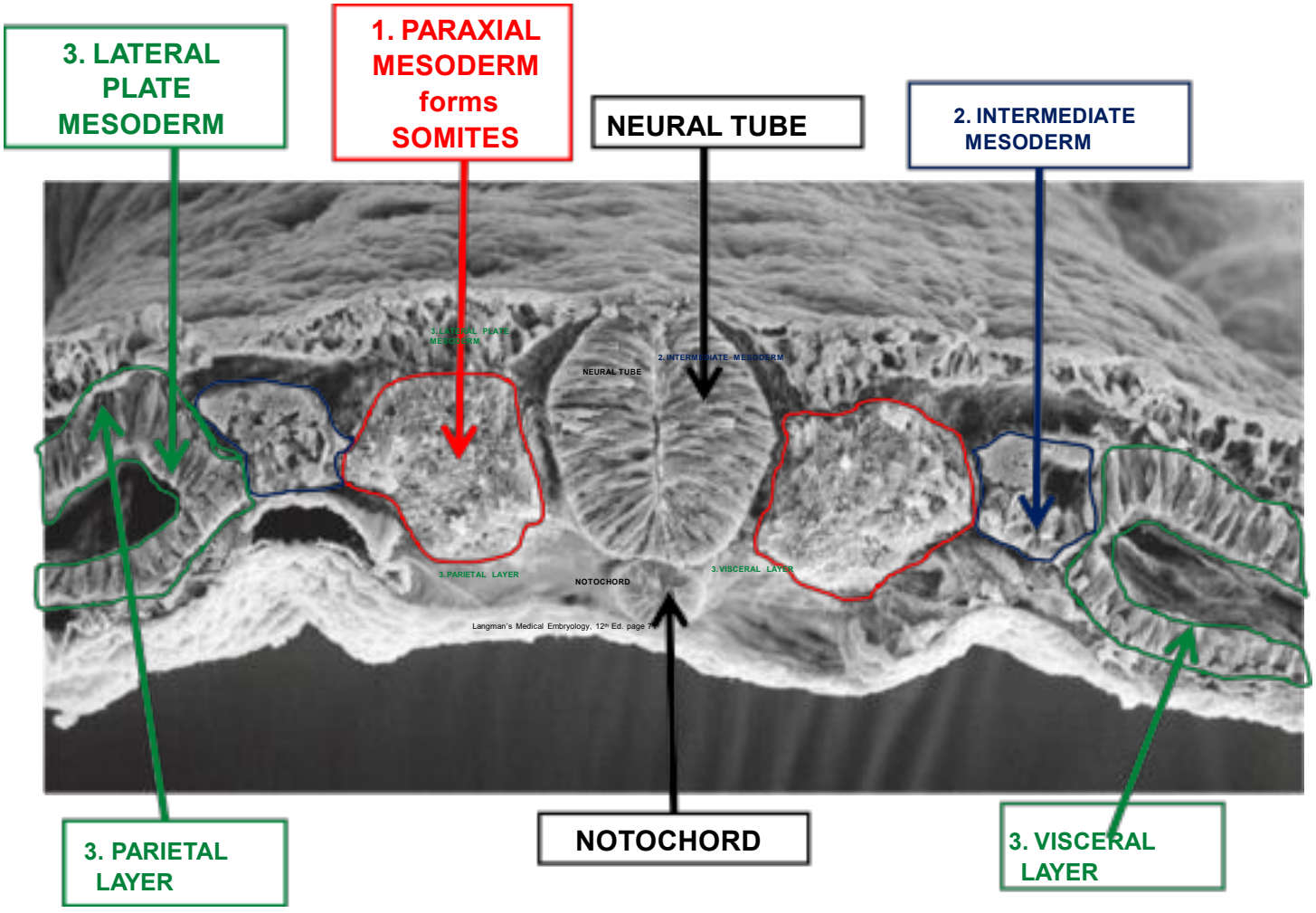


thin

thicker

- **Intermediate mesoderm**
  - Kidney
  - Gonads
  - **Urogenital system**
- **Chorda-mesoderm**
  - Notochord
- **Paraxial mesoderm**
  - Head
  - Somite
    - Sclerotome
    - Myotome
    - Dermatome
- **Lateral plate mesoderm**
  - Splanchnic
    - **Visceral**
    - Wall of gut tube
  - Somatic
    - **Parietal**
    - Dermis of body walls and limbs, bones, connective tissue, sternum
  - Extra-embryonic

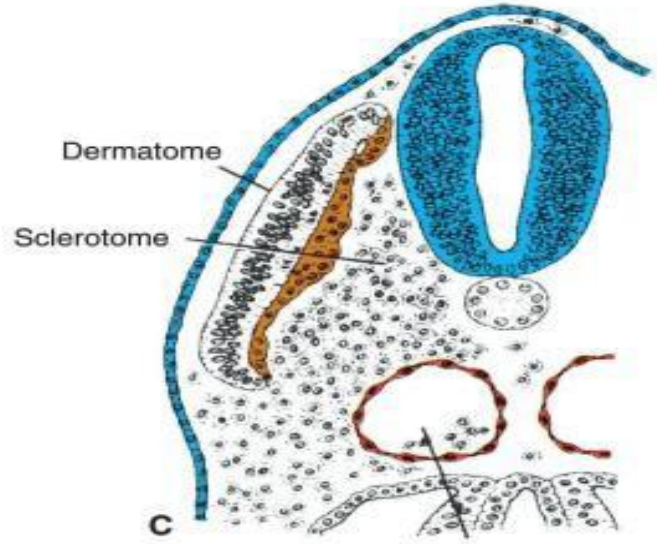
Organization of mesoderm

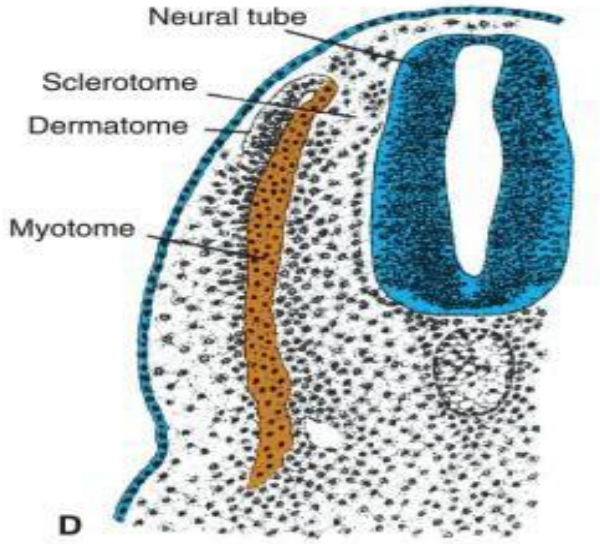


Somite differentiation

Supportive structure

SOMITE →
- **DERMATOME** → dermis
- **SCLEROTOME** → tendon, cartilage, bone (vertebrae –ribs)
- **MYOTOME** → muscle

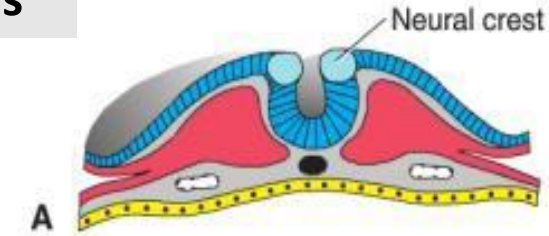


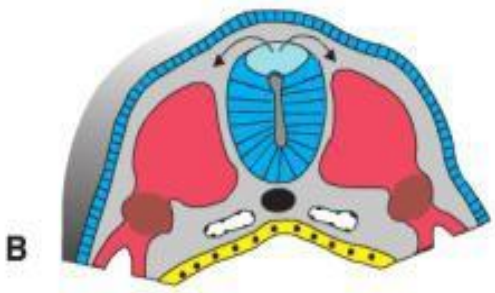


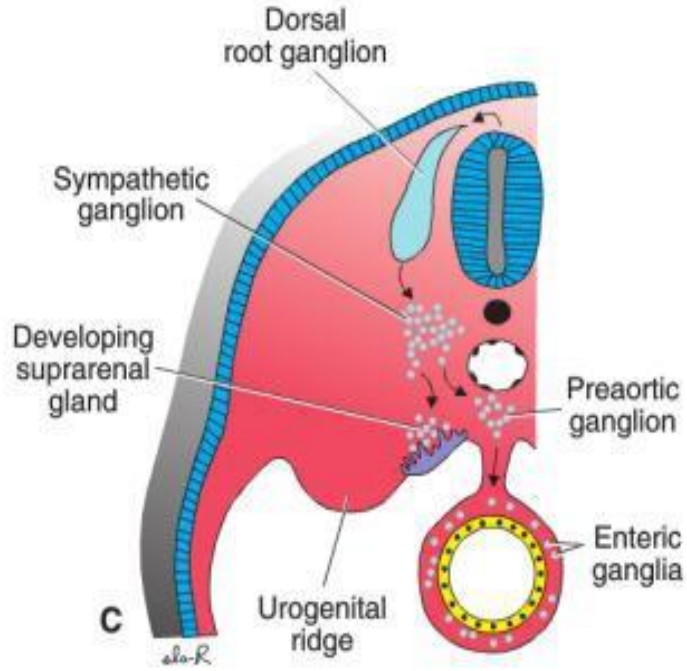
Migration of neural crest cells

Neural crest cells – early cells with major role in development

Form at dorsal/lateral aspects of neural folds







They have **capacity to migrate and differentiate** into many cells and structures:

To ectoderm → melanocytes

To mesoderm → connective tissue and bones of face and skull; cranial nerve ganglia; odontoblasts, dermis in face and neck; dorsal root ganglia; sympathetic ganglia, adrenal medulla; glial cells…

In head region most of connective tissues are derived from neural crest cells, hence – **ectomesenchyme** (neuroectodermal origins)
In the rest of the body – from mesenchyme

difference between head + rest of body

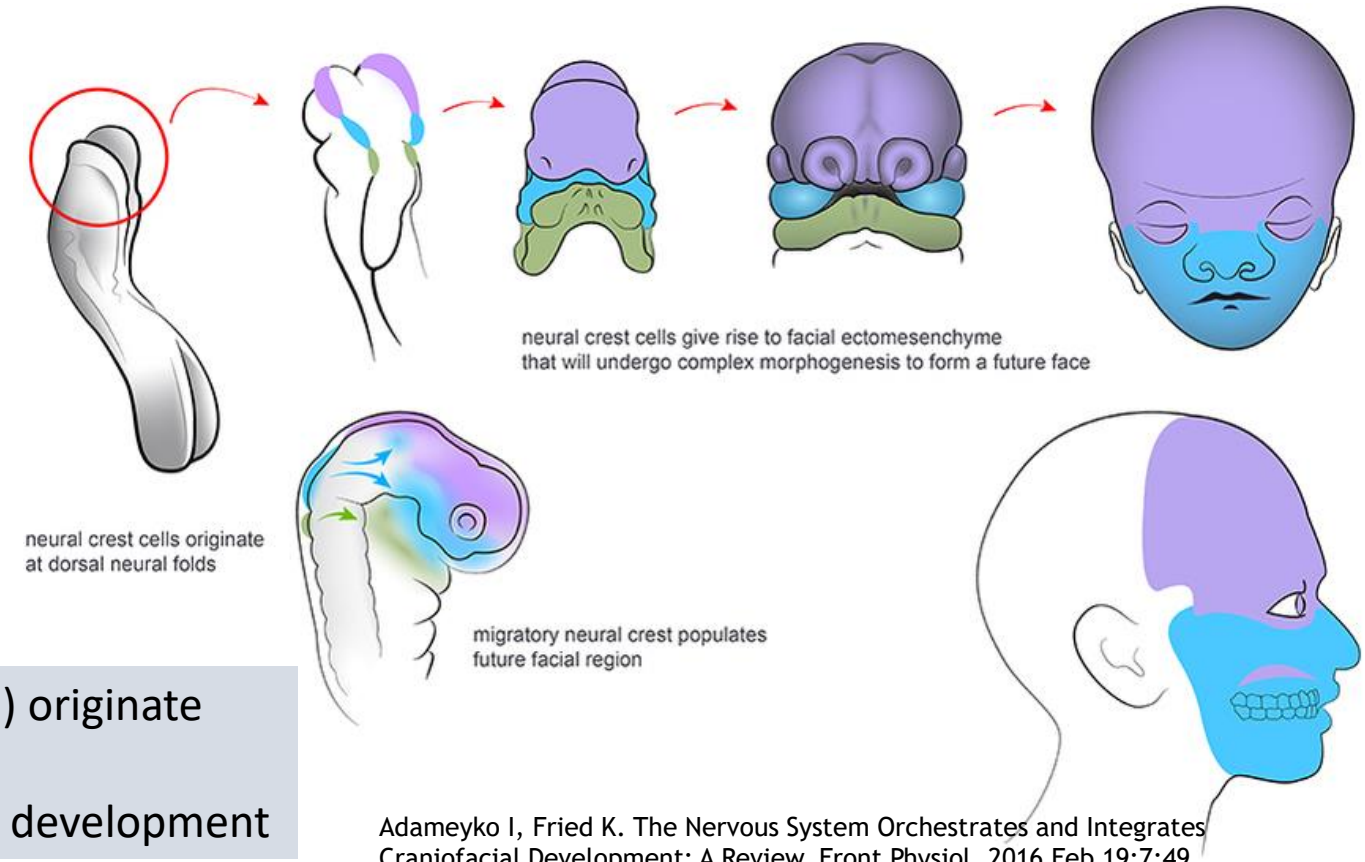
Cranial neural crest cells – development of oral tissues

formation of facial features

Proper migration of neural crest cells is key for the development of the face and the teeth

- Cranial and sensory ganglia and nerves
- Adrenal medulla
- Ectomesenchyme bones and skull
- Dentin
- Periodontal ligament
- Alveolar bone

Treacher Collins syndrome- failure of NCCs to migrate properly to facial region

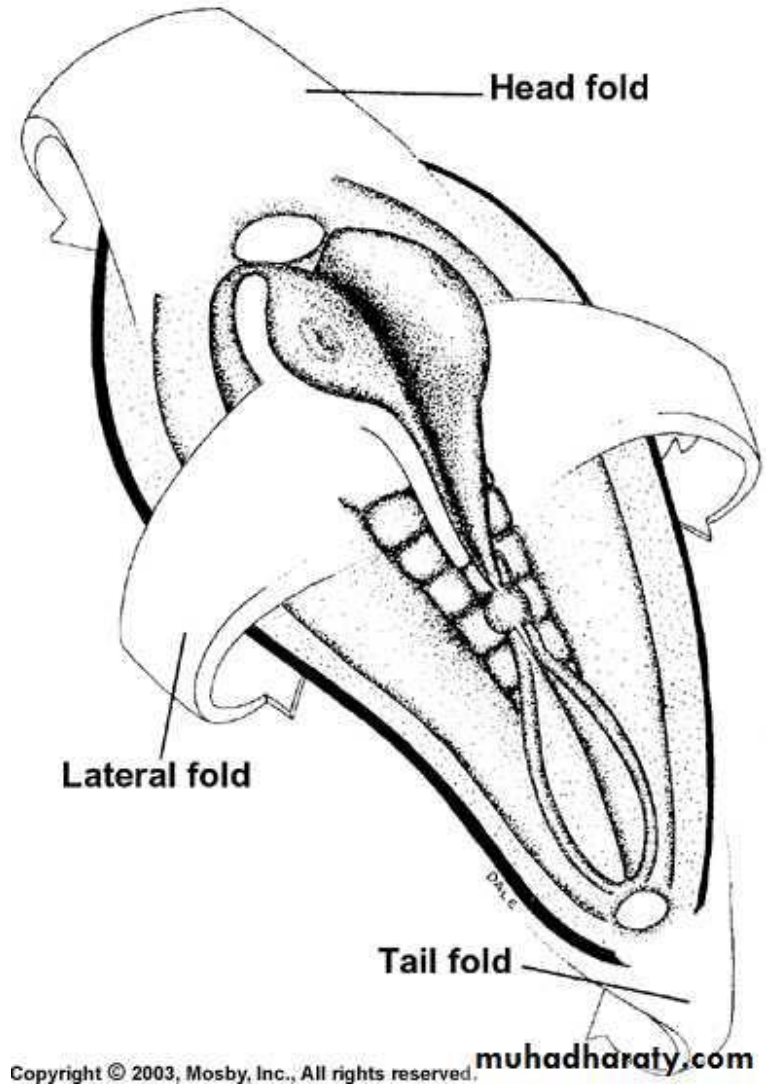


All teeth tissues (apart from enamel) originate directly from NCCs
NCCs are required for proper dental development

Adameyko I, Fried K. The Nervous System Orchestrates and Integrates Craniofacial Development: A Review. Front Physiol. 2016 Feb 19;7:49.

Folding of the embryo

Week 4-5



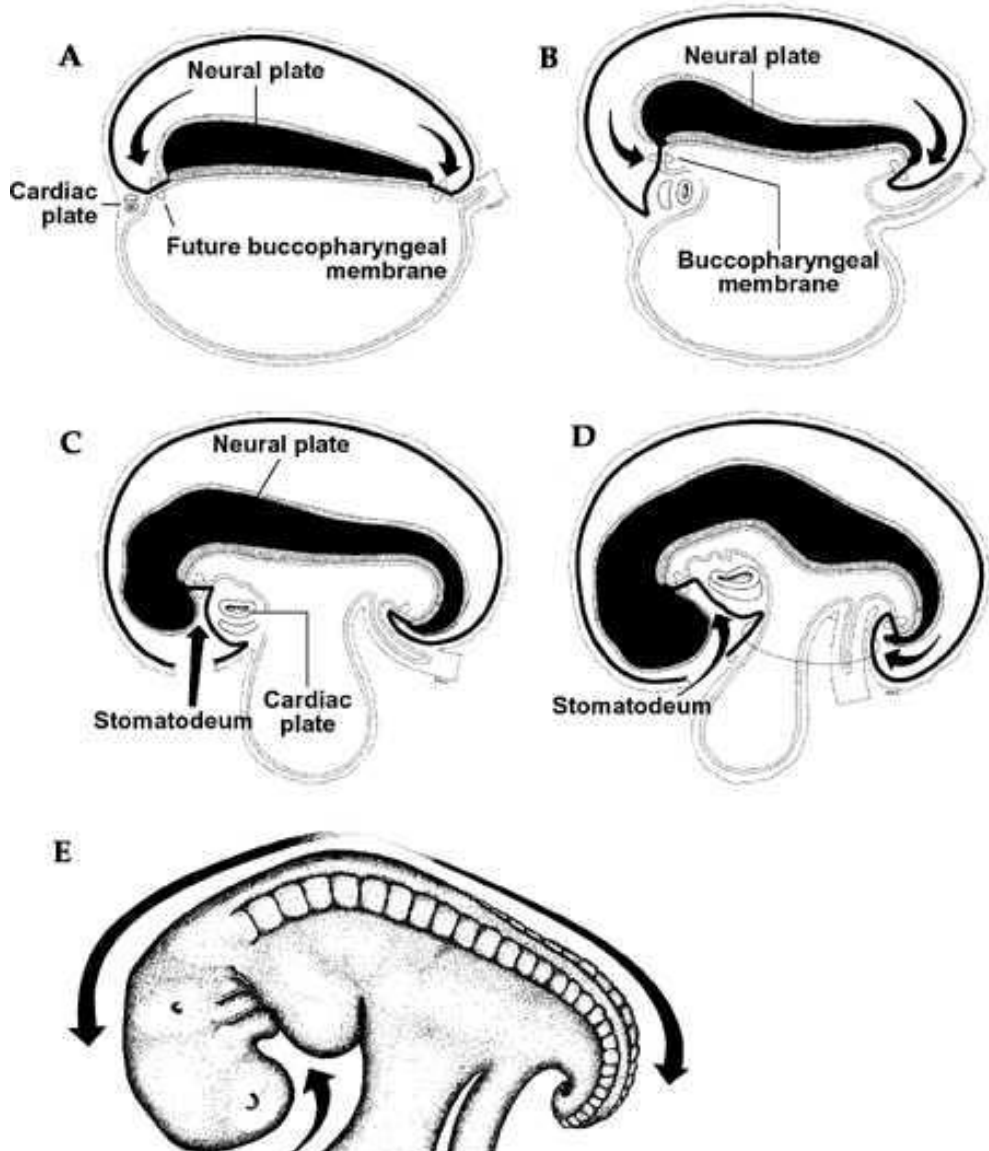
how embryo fol

Craniocaudal folding

Head fold leads to formation of **stomatodeum** (later – oral cavity)

Ectoderm comes to line with stomatodeum separated from the gut by **buccopharyngeal membrane**

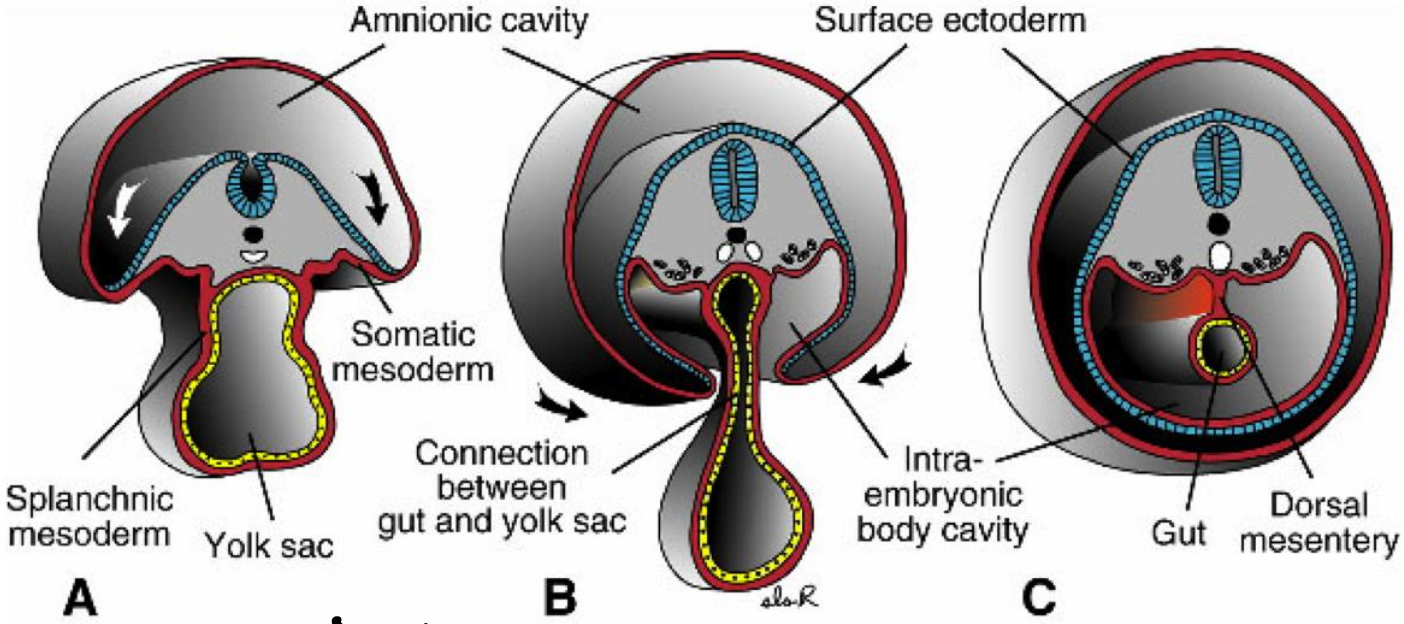
- oral cavity all ectoderm



Lateral folding

-the lateral edges of the embryonic disc move ventrally constricting the neck of the yolk sac

-the ecto- , meso- and endodermal layers from each side fuse together



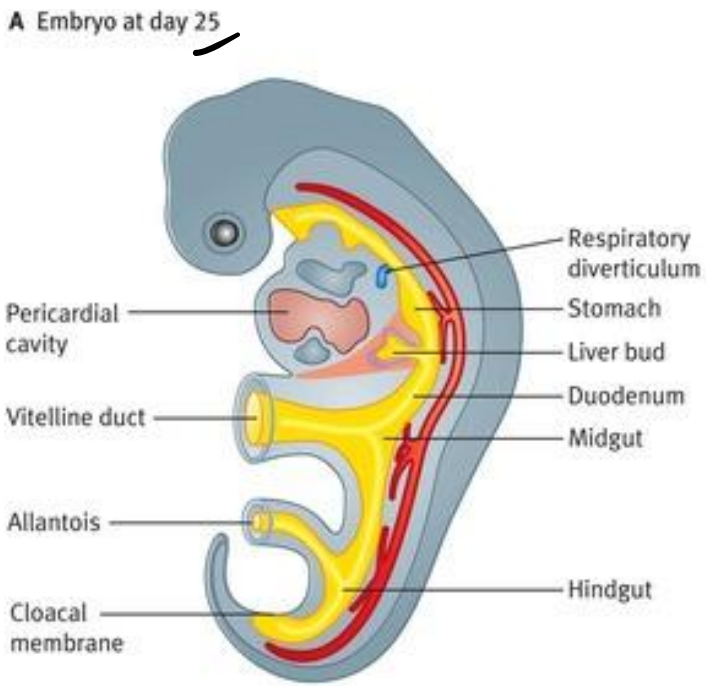
edges move

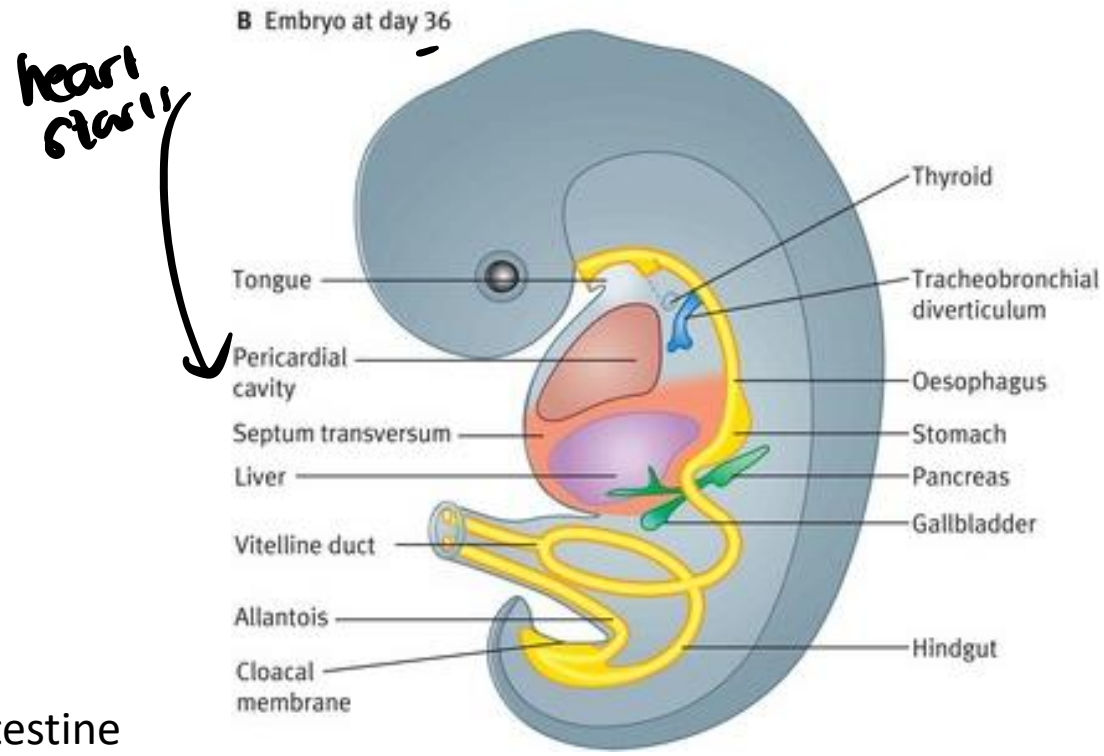
1. Ectoderm of the floor of the amniotic cavity encapsulates the embryo and covers the entire surface of the embryo (**surface ectoderm**)

2. Mesoderm disposition:

- The splanchnic mesoderm lines the visceral organs
- Somatic mesoderm forms the body wall and eventually the limb skeleton

Derivatives of the endoderm





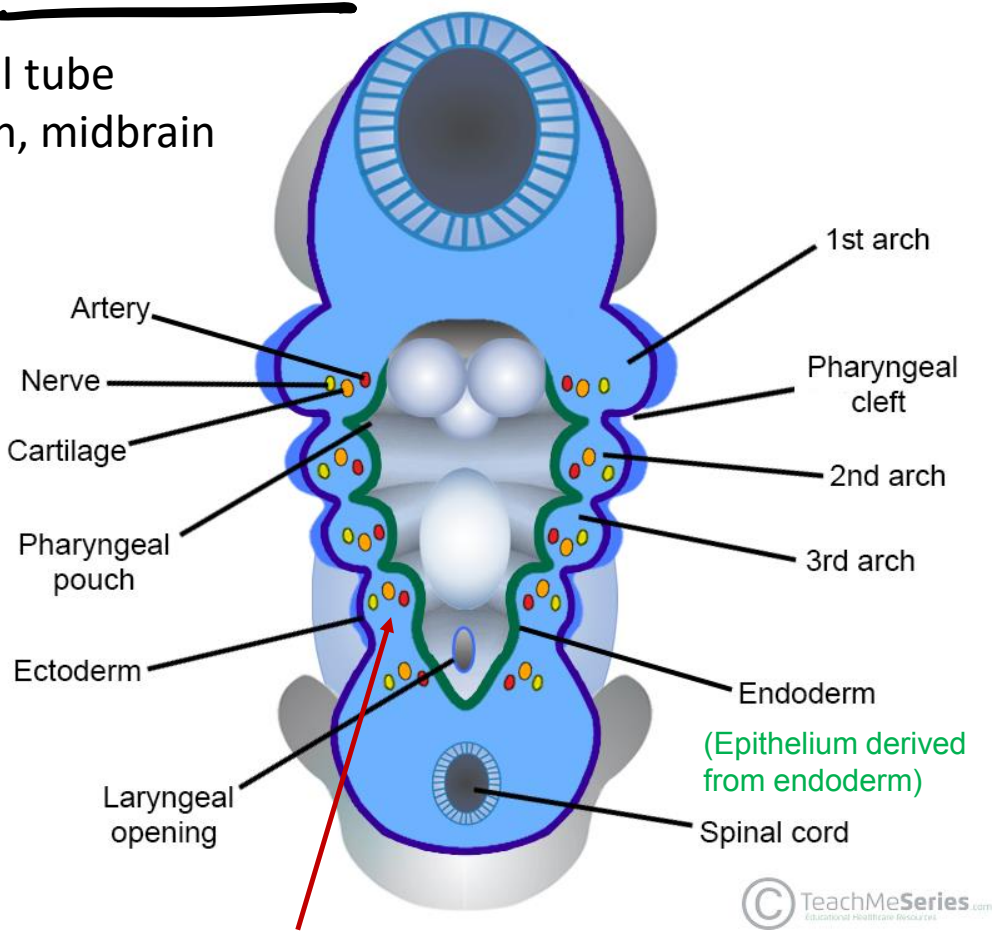
- Esophagus, stomach, small and large intestine
- Epithelium of respiratory tract
- Components of thyroid, parathyroids, liver and pancreas
- Epithelial lining of urinary bladder

Embryology. (2016). In A. Fiander & B. Thilaganathan (Eds.), *MRCOG Part One: Your Essential Revision Guide* (pp. 149-200). Cambridge: Cambridge University Press.

Development of the head and neck

In the head region: neural tube expands to form forebrain, midbrain and hindbrain

Growth of mesenchymal tissue (connective tissue) in the cranial region of the embryo results in the formation of arches, separated by clefts. These are the **pharyngeal arches** & **pharyngeal clefts**.



Simultaneously, a number of out-pocketings appear on the lateral wall of the pharynx – the **pharyngeal pouches**.

The pouches separate the arches on the internal (endodermal, future pharyngeal) surface whilst the clefts separate the arches on the external (ectodermal, future skin) surface.

Core: derived from **paraxial** and **lateral mesoderm** (muscle) and **neural crest cells** (skeletal elements)

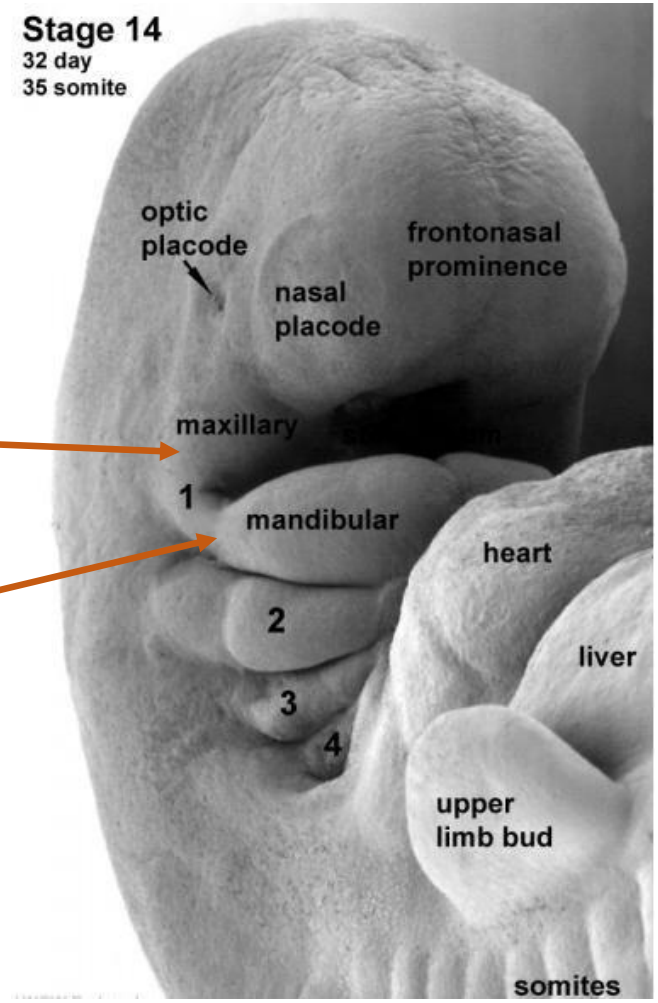
Pharyngeal arches

There are **SIX** pharyngeal arches – however, the 5th regresses soon after forming.

In the adult, each pharyngeal arch is associated with specific structures within the head and neck.

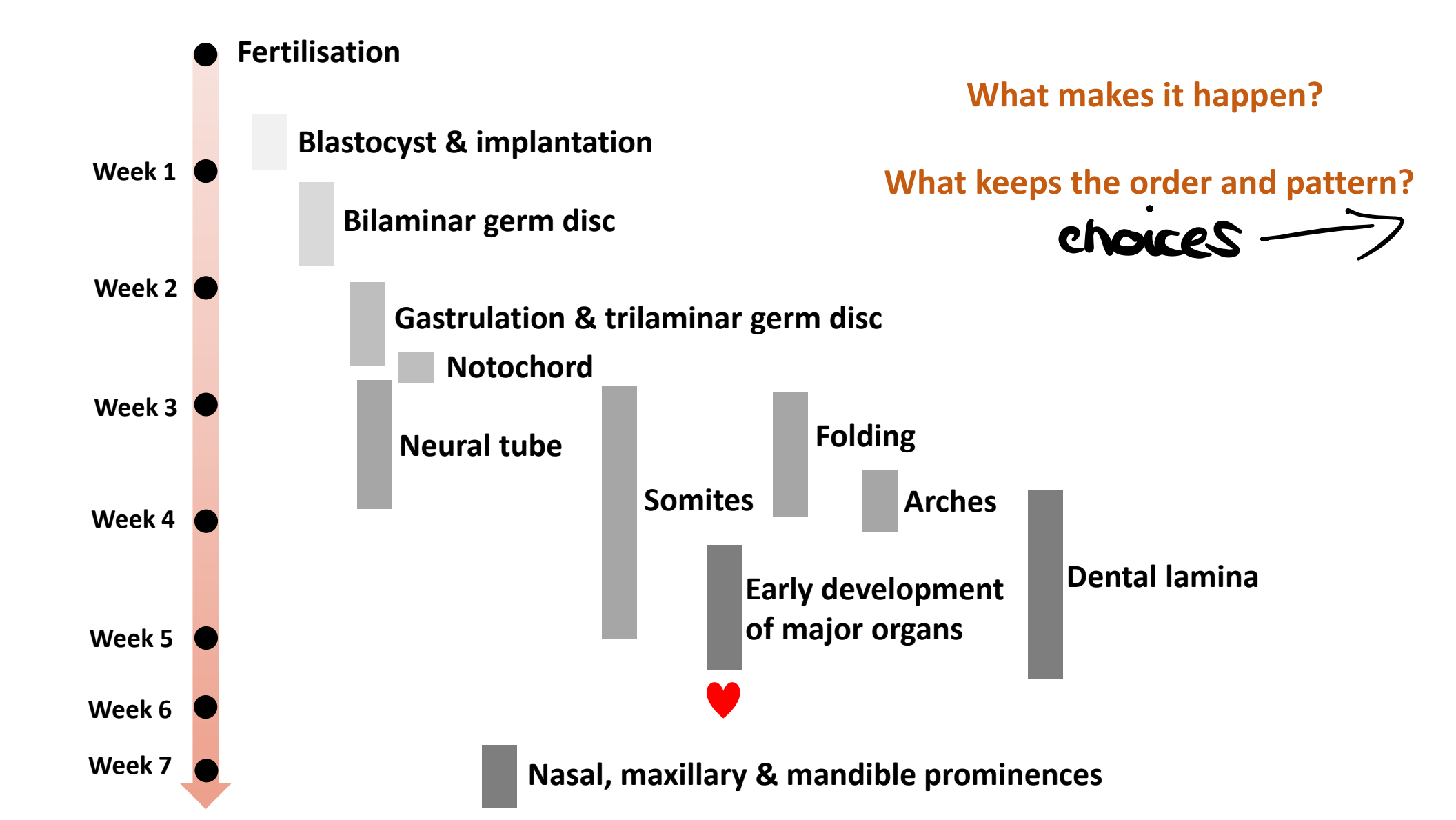
1st pharyngeal arch:

- **Maxillary prominence** (dorsal portion) – becomes the future maxilla.
- **Mandibular prominence** (ventral portion) – becomes the future mandible.

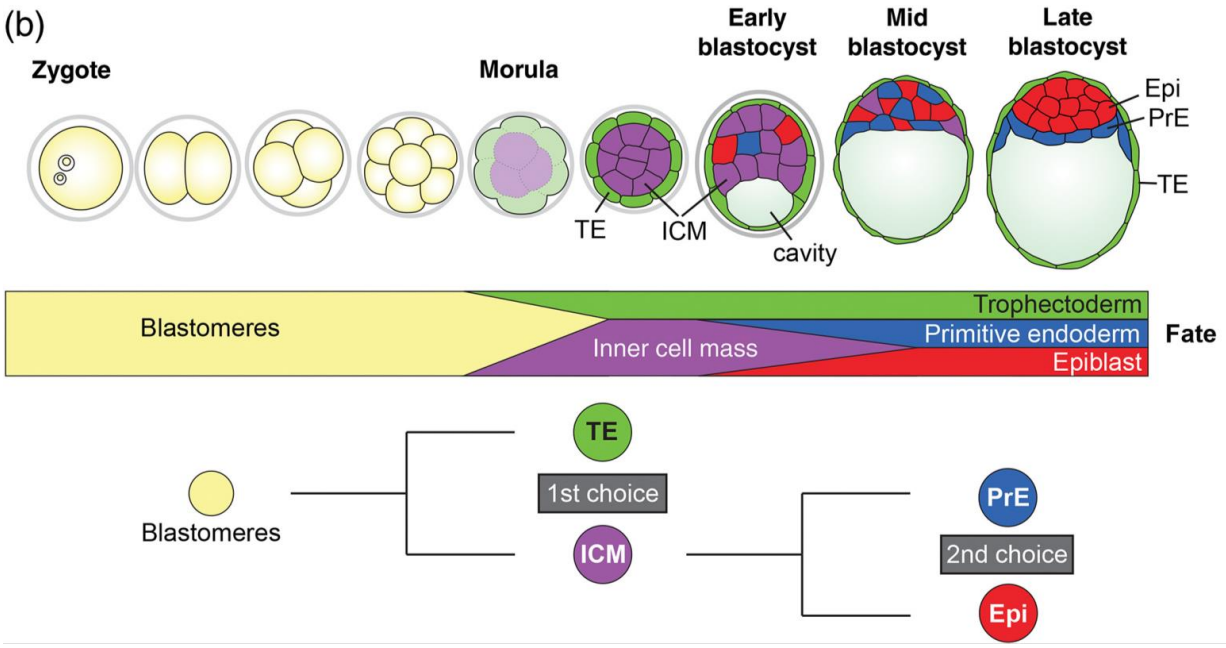


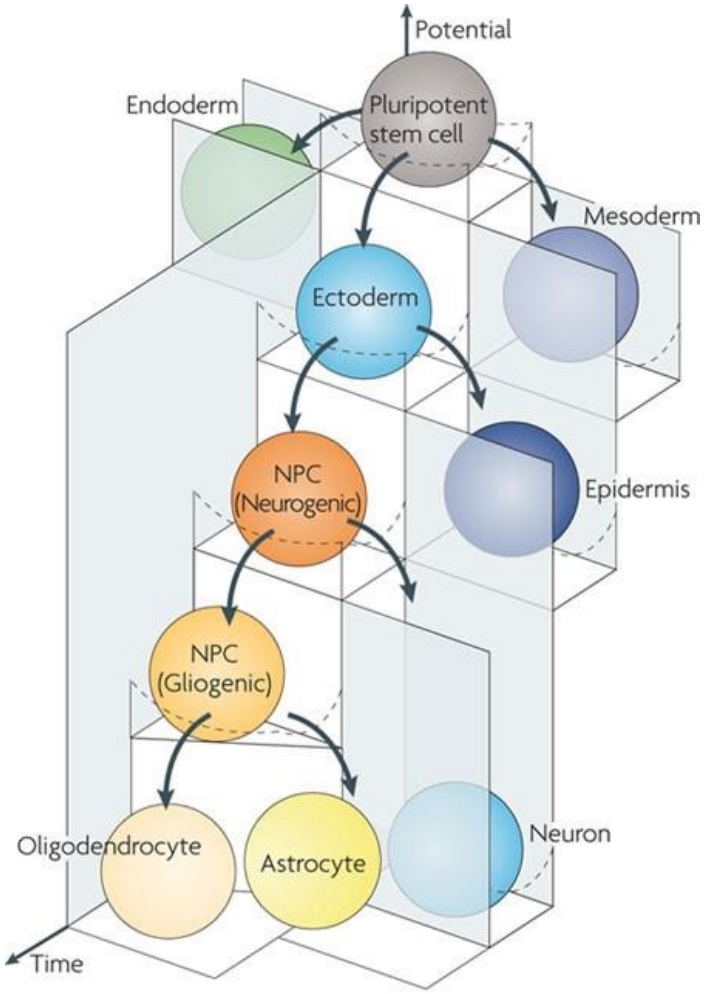
Trigeminal nerve

Sensory field of the skin of the face, the lining of the mouth and nose, and general sensation to the anterior 2/3 of the tongue.


Fertilisation
Blastocyst & implantation
Week 1
Bilaminar germ disc
Week 2
Gastrulation & trilaminar germ disc
Notochord
Week 3
Neural tube
Somites
Folding
Arches
Week 4
Early development
of major organs
Dental lamina
Week 5
Week 6
Week 7
Nasal, maxillary & mandible prominences
What makes it happen?
What keeps the order and pattern?
choices

Regulation of embryogenesis - all about making choices





Nature Reviews | Neuroscience

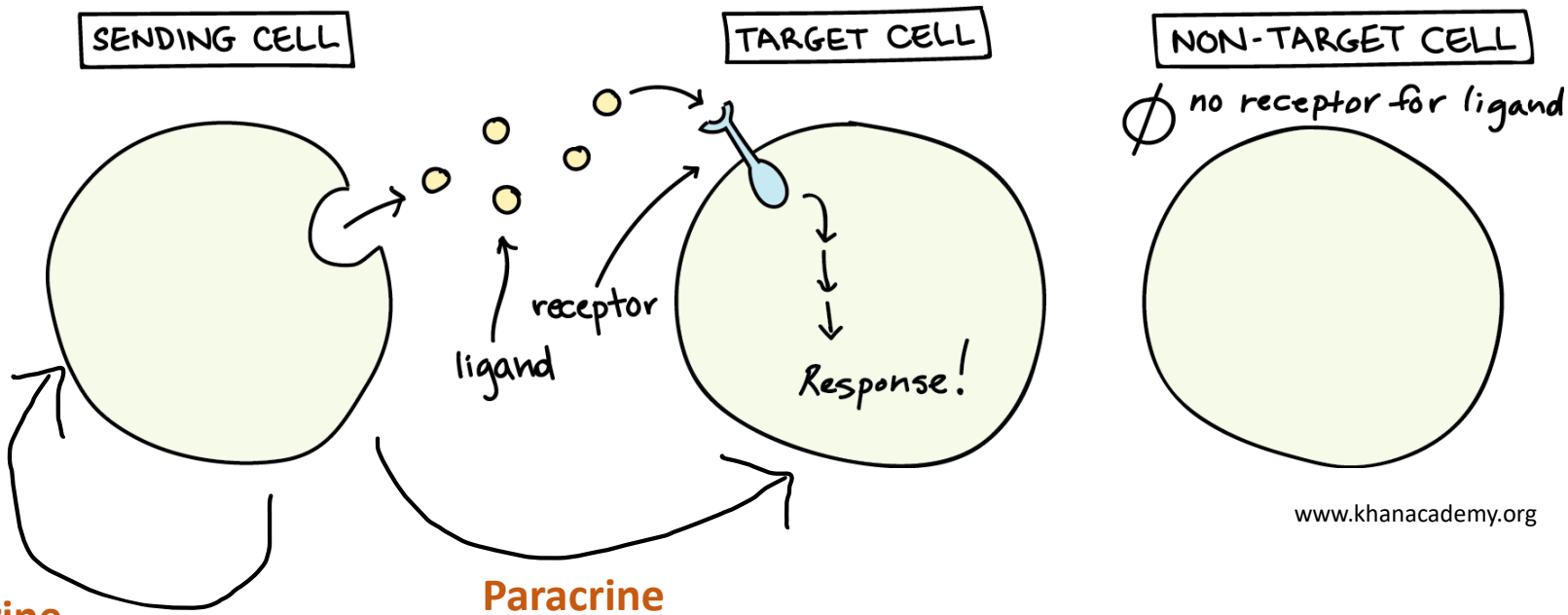
Regulation of embryogenesis = regulation of gene expression

choices made on

1 – **Signals**: autocrine & paracrine (growth factors, cytokines) pressure ... .

one cell produces signals that other cells receive

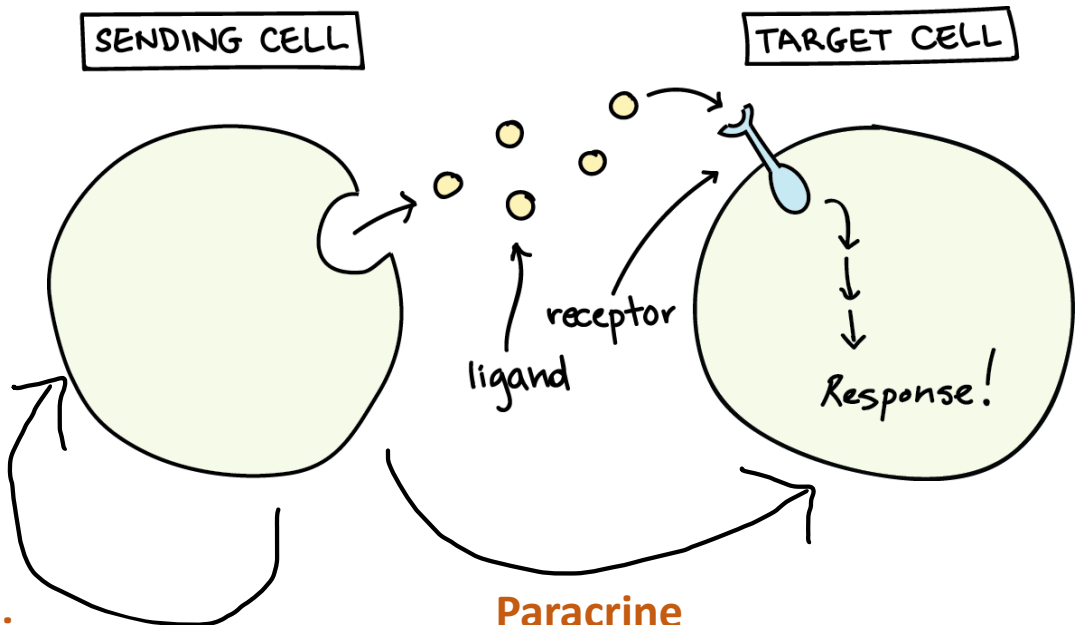
2 – **Receivers**: receptor & transcription factors (regulate expression of other genes)



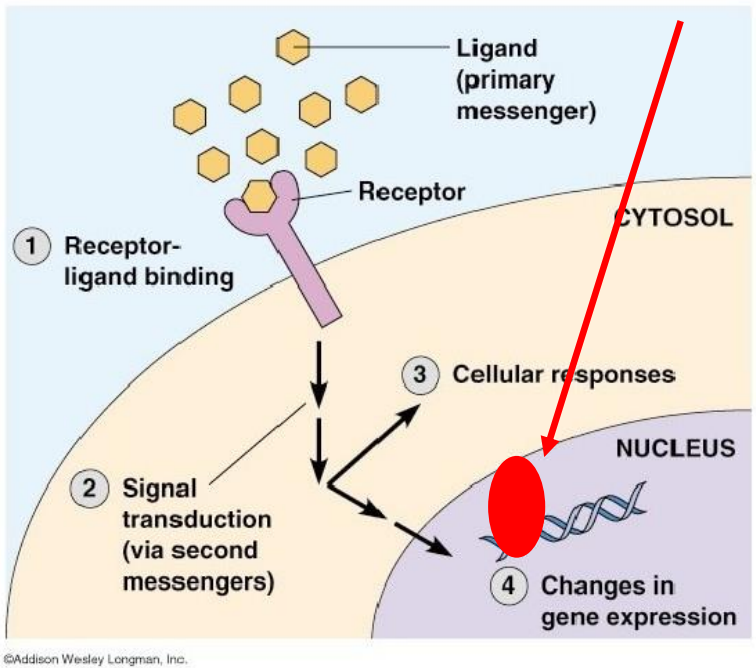
Regulation of embryogenesis = regulation of gene expression

1 – **Signals**: autocrine & paracrine (growth factors, cytokines)

2 – **Receivers**: receptor & transcription factors (regulate expression of other genes)



Transcription factor



Regulation of embryogenesis = regulation of gene expression

1 – **Signals**: autocrine & paracrine (growth factors, cytokines)

2 – **Receivers**: transcription factors (regulate expression of other genes)

3 – **Outputs**: gene expression & eventually cell fate or phenotype

- death
- survival
- proliferation
- differentiation

e.g structures between fingers

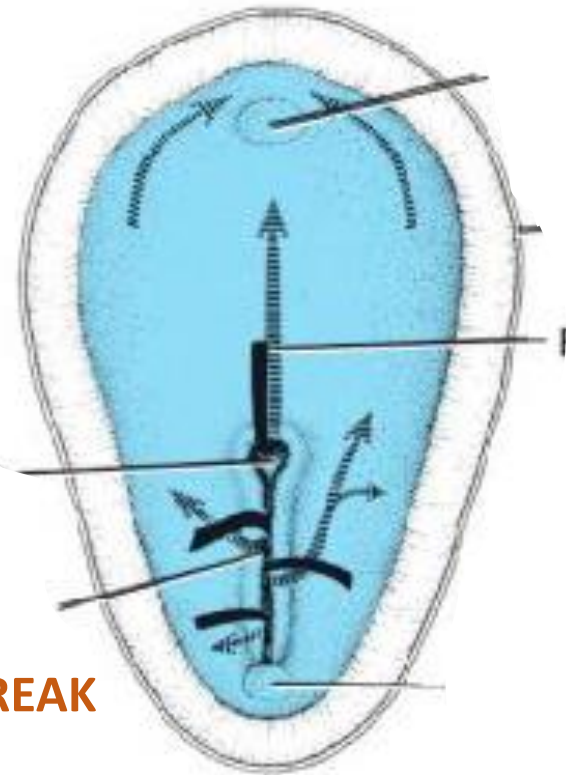
↳ specialisation

Patterning (head-to-tail, segmentation, dentition, etc) – spatiotemporal events

Regulation of embryogenesis – signals from primitive node and streak

Primitive Node releases signalling molecules that determine body axis and cell fate.

Cell migration and specification are controlled by fibroblast growth factor 8, **FGF8**, synthesized by the primitive streak cells.



NODAL: maintains primitive streak; upregulates many developmental genes, including:

Bone Morphogenetic Protein 4 (BMP4) (e.g. stimulates formation of **skin** from the ectoderm)

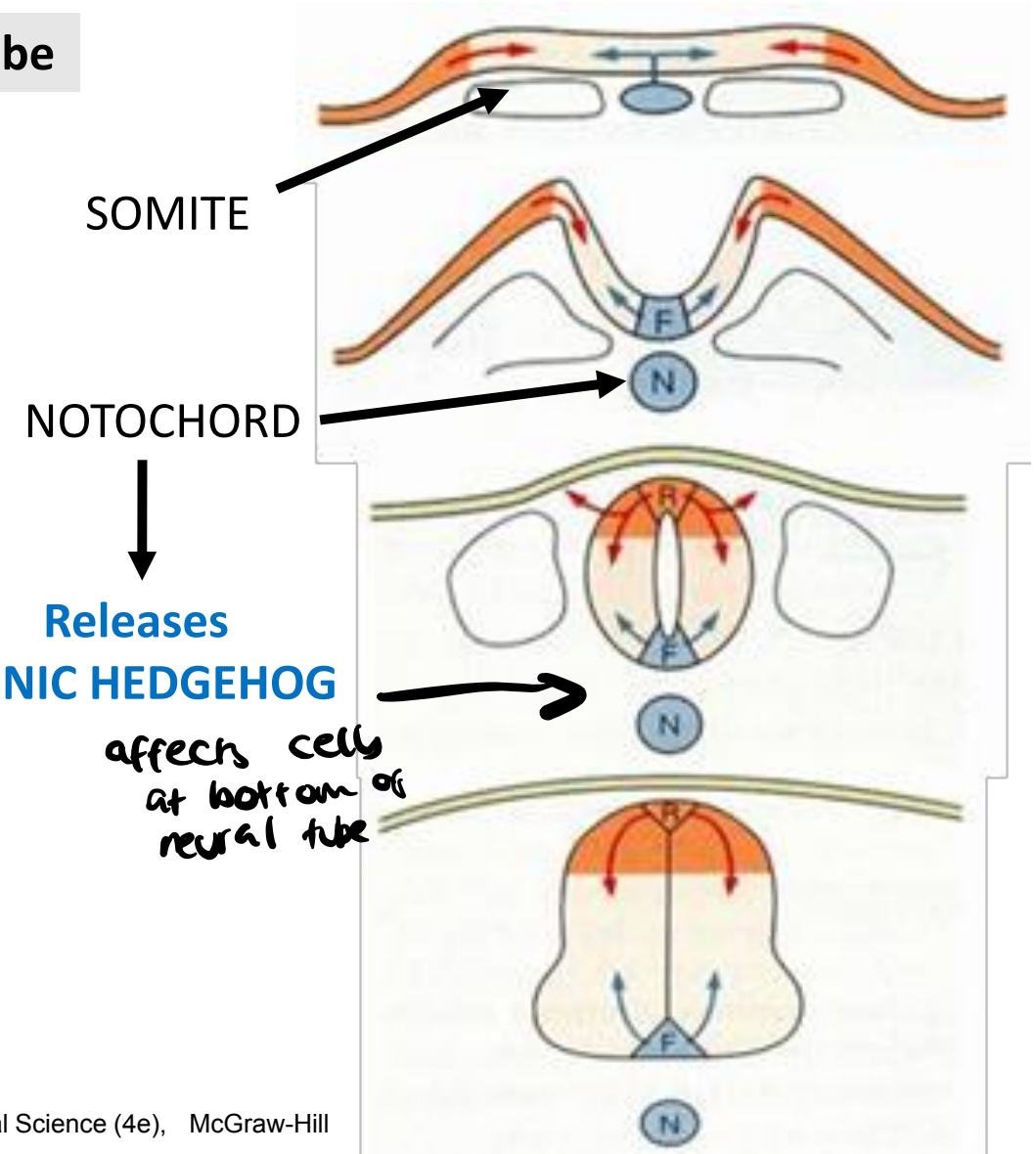
Chordin, Noggin → block action of BMP4, stimulate formation of **nervous system** and **cranial structures**

Regulation of embryogenesis – neural tube

Sonic Hedgehog (SHH)
Patterns the **ventral** neural tube
(**F** = *floor plate cells)*

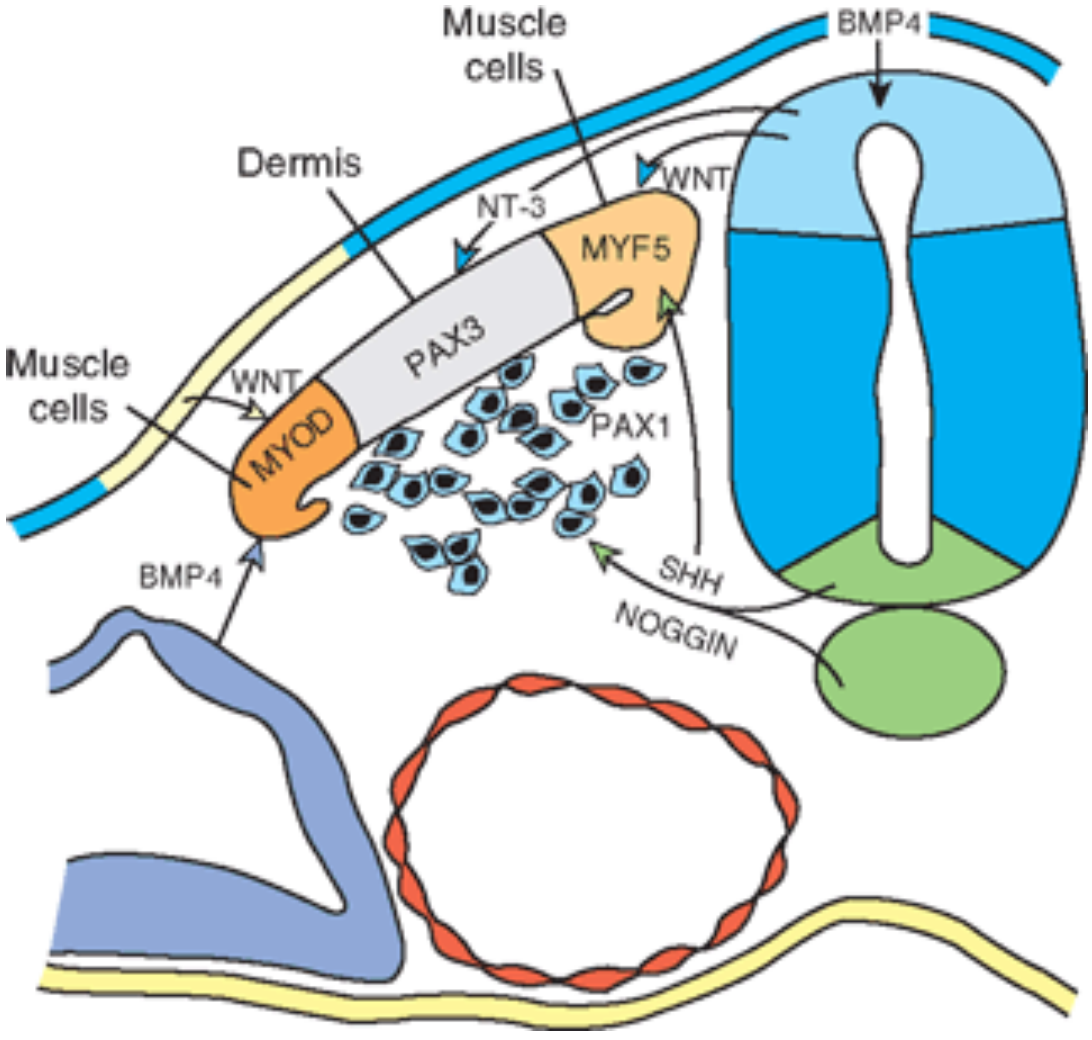
Bone Morphogenetic Proteins (BMPs)
Pattern the **dorsal** neural tube

*(***R** = *roof plate cells)*



E. Kandel *et al.* (2000) , Principles of Neural Science (4e), McGraw-Hill

Regulation of embryogenesis – somite differentiation



Sonic hedgehog, noggin

↓

Sclerotome

↓

PAX1

↓

Vertebrae formation

BMP4, WNT, NT-3

↓

PAX3

↓

Dermis

BMP, WNT

↓

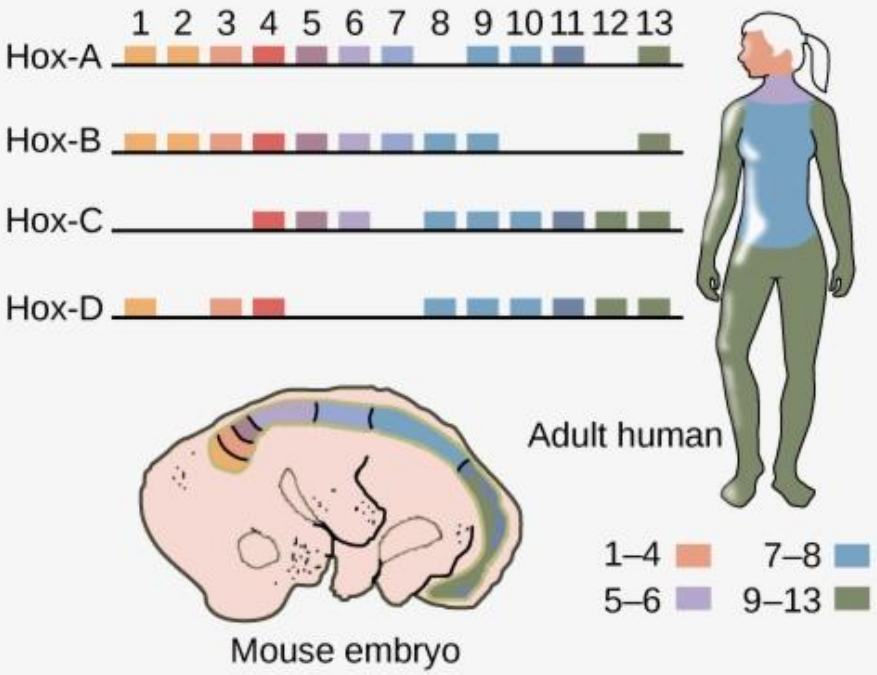
MYF5, MyoD

↓

Muscle

Regulation of embryogenesis – body segmentation

HOX genes control body segmentation



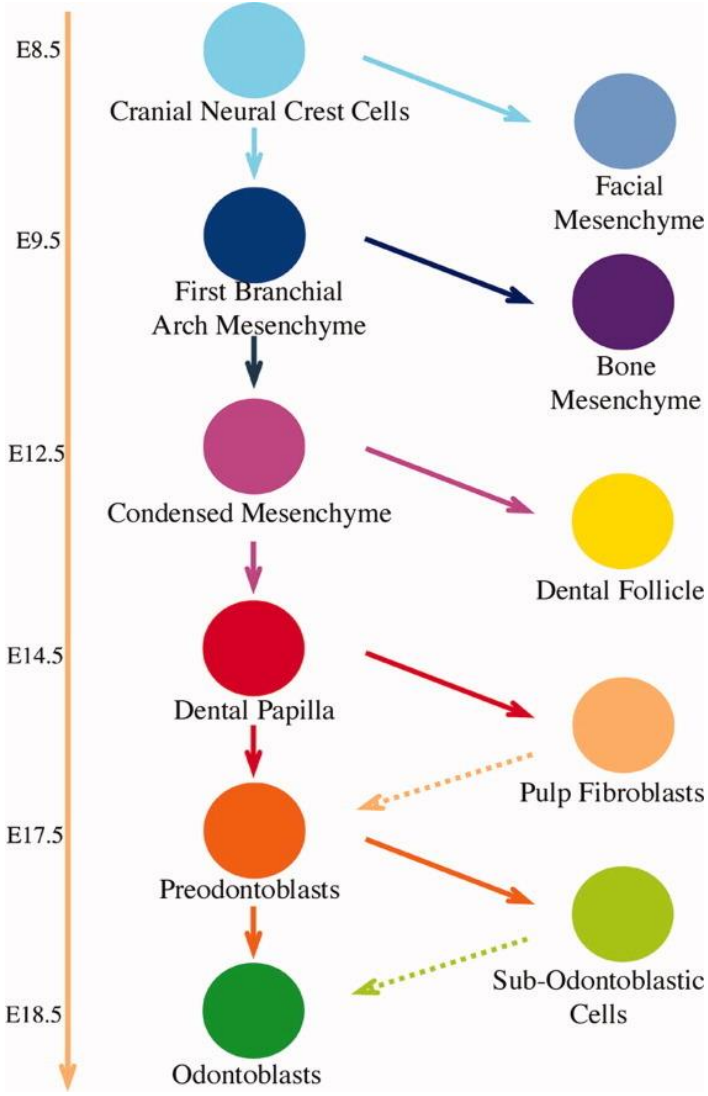
Involved in establishing the anterior-posterior axis and the identity of each body segment.

Tightly regulated temporal and spatial gene expression.

Oral embryology >>> Year 1 semester 2 + Year 2

Year 1 semester 2
(Craniofacial Anatomy)

Year 2
(Oral Biology, Microbiology and Immunology)



Learning Objectives:

- Describe the stages of development of the embryo from fertilisation to implantation.
- Describe the formation of a three layered embryo and derivatives of ectoderm, mesoderm and endoderm.
- Describe the beginnings of nervous system formation.
- Describe the folding of embryo and the main consequences of this folding.
- Describe the migration of neural crest cells and explain their importance.
- Explain briefly the importance of signalling molecules in embryonic development.

Resources:

Antonio Nanci
Oral Histology: Development, Structure, and Function