🦴 The Axial Skeleton

Embryological Development

1. Origin of Axial Skeleton

- Structures included → skull, vertebral column, ribs, sternum

- Germ layer sources:

  - Paraxial mesoderm → somites (from occipital region downwards)
  - Paraxial mesoderm in head → somitomeres
  - Lateral plate mesoderm (parietal layer) → bones of girdles, limbs, sternum
  - Neural crest cells → mesenchyme of face and skull (especially anterior skull & face)

2. Somite Differentiation

- Somites → segmental blocks on either side of neural tube

- Differentiate into:

  - Sclerotome (ventromedial) → axial skeleton
  - Dermomyotome (dorsolateral) → dermis and skeletal muscles

- End of 4th week → sclerotome cells become mesenchyme (migratory embryonic connective tissue)

  - Mesenchyme can differentiate into → fibroblasts, chondroblasts, osteoblasts

3. Types of Ossification

Type	Process	Examples
Intramembranous	Mesenchyme → bone directly	Flat bones of skull
Endochondral	Mesenchyme → cartilage → bone	Base of skull, limbs

Skull

A. Subdivisions

- Neurocranium → protects brain
- Viscerocranium → forms face

B. Neurocranium

i. Membranous Neurocranium

- Formed from neural crest + paraxial mesoderm
- Ossification type → intramembranous
- Forms flat bones of vault
- Develop via bone spicules radiating from primary ossification centers
- Growth mechanism → apposition (outer surface) + osteoclastic resorption (inner surface)

ii. Newborn Skull

- Flat bones separated by sutures (from neural crest & paraxial mesoderm)
- Wider junctions → fontanelles
  - Anterior fontanelle most prominent
- Function → allow molding (overlapping of bones) during birth
- Closure times:
  - Anterior fontanelle → by 18 months
  - Posterior → by 1–2 months
- Sutures remain open in early childhood to allow brain growth

iii. Cartilaginous Neurocranium (Chondrocranium)

- Initially separate cartilaginous pieces

- Prechordal chondrocranium (anterior to pituitary) → from neural crest
- Chordal chondrocranium (posterior to that) → from occipital sclerotomes
- Form base of skull by endochondral ossification

C. Viscerocranium

- Derived mainly from 1st and 2nd pharyngeal arches

Arch	Derivatives	Ossification
1st arch (maxillary process)	Maxilla, zygomatic bone, part of temporal bone	Intramembranous
1st arch (mandibular process)	Mandible → formed around Meckel's cartilage	Intramembranous
1st + 2nd arch (dorsal tips)	Ear ossicles (malleus, incus, stapes) – *first bones to fully ossify (4th month)*	Endochondral

- Other facial bones (nasal, lacrimal etc.) also from neural crest cells

Growth of Face

- Initially small compared to neurocranium due to:

1. Lack of paranasal sinuses
2. Small jaws

- With eruption of teeth and development of sinuses, the face becomes proportionately larger

Craniofacial Defects & Skeletal Dysplasias

🔹 Neural Crest Cells

- Form facial skeleton + part of the skull.

- Highly susceptible to teratogens during migration → therefore craniofacial abnormalities are among the most common congenital defects.

🔹 Major Craniofacial Defects

Condition	Cause/Pathology	Key Features
Cranioschisis	Failure of cranial neuropore closure	Cranial vault absent → brain exposed to amniotic fluid → degenerates → anencephaly (lethal)
Cranial meningocele	Small defect in skull	Meninges herniate
Meningoencephalocele	Skull defect	Meninges + brain tissue herniate
Craniosynostosis	Premature closure of one or more sutures	Skull shape depends on which suture closes

Types of Craniosynostosis

Closed Suture	Resulting Skull Shape
Sagittal suture (most common – 57%)	Long & narrow skull → Scaphocephaly
Bilateral coronal sutures	Short, broad skull → Brachycephaly

Unilateral coronal suture	Asymmetric skull → Plagiocephaly

🧠 Molecular Regulation

- TGF-β, FGFs and FGFRs regulate cellular proliferation and differentiation.
- FGFR1 & FGFR2 → craniofacial pre-bone regions
- FGFR3 → cartilage growth plates of long bones & occipital region
- Mutation effects:
  - FGFR1/2/3 → craniosynostosis
  - FGFR3 → skeletal dysplasia (e.g. achondroplasia)
- MSX2 mutation → Boston-type craniosynostosis (parietal bones)
- TWIST1 mutation → Saethre-Chotzen syndrome → craniosynostosis + syndactyly

🔹 Skeletal Dysplasias

Condition	Inheritance / Cause	Key Features
Achondroplasia (ACH)	Autosomal dominant (≈90% new mutations); mutation in FGFR3 gene	Disproportionate short stature, short long bones, macrocephaly, midface hypoplasia, short fingers (trident hand), spinal curvature
Thanatophoric Dysplasia	Autosomal dominant; FGFR3 mutation	Neonatal lethal skeletal dysplasia Type I: short, curved femur (telephone-receiver shape) ± cloverleaf skull Type II: straight long femur + severe cloverleaf skull (Kleeblattschädel)
Hypochondroplasia	Autosomal dominant; FGFR3 mutation	Milder form of achondroplasia, mainly affects long bone growth; short stature but less severe skeletal abnormalities
Cleidocranial Dysostosis	Autosomal dominant; mutation in RUNX2 gene affecting intramembranous ossification	Delayed fontanelle closure, decreased suture mineralization, frontal/parietal/occipital bossing, hypoplastic or absent clavicles, dental abnormalities (supernumerary teeth)
Acromegaly	Excess growth hormone (GH) after epiphyseal closure, usually due to pituitary adenoma	Enlargement of face, hands, feet, prognathism, thickened soft tissues; if GH excess occurs before epiphyseal closure → gigantism

Microcephaly	Failure of normal brain growth (genetic or environmental causes)	Abnormally small skull, severe intellectual disability, developmental delay

Development of the Vertebral Column, Ribs & Sternum

I. Vertebral Column

Origin

- Source → Sclerotome of somites (from paraxial mesoderm)
- A typical vertebra consists of → body, vertebral arch, vertebral foramen, transverse processes, and spinous process

Migration (4th week)

- Sclerotome cells migrate around the spinal cord and notochord
- Cells from adjacent somites merge across the midline

Resegmentation

- Caudal half of one sclerotome fuses with cranial half of the next → forms one vertebra
- Regulated by HOX genes
- Clinical relevance → explains why spinal nerves exit between vertebrae

Intervertebral Disc Formation

- Mesenchyme between sclerotomes → annulus fibrosus
- Notochord persists in disc → forms nucleus pulposus

Functional Consequence of Resegmentation

- Myotomes bridge two vertebrae → allow movement
- Spinal nerves now lie next to intervertebral foramina
- Intersegmental arteries now cross over the vertebral bodies

Spinal Curvatures

Curvature	Type	Time of Appearance
Thoracic & Sacral	Primary	During embryonic development
Cervical	Secondary	When infant starts holding head
Lumbar	Secondary	When child begins to walk

Clinical Correlates – Vertebral Defects

Defect	Description / Cause

Scoliosis	Asymmetric fusion or absence of part of vertebrae → lateral curvature
Klippel-Feil sequence	Fusion of cervical vertebrae → short neck, limited mobility
Spina bifida occulta	Failure of vertebral arches to fuse; spinal cord intact, covered by skin (no neuro deficits)
Spina bifida cystica	Failure of neural tube closure + vertebral arch formation → neural tissue exposed; often neurological deficits
Prevention	Folic acid supplementation before conception

2. Ribs

Structure	Embryologic Origin
Bony part of rib	Sclerotome cells growing from costal processes of thoracic vertebrae
Costal cartilage	Sclerotome cells that migrate into lateral plate mesoderm (lateral somitic frontier)

3. Sternum

- Develops independently in the parietal (somatic) layer of the lateral plate mesoderm

- Two sternal bands form on either side of the ventral body wall → fuse in midline → form cartilaginous model of:

  - Manubrium
  - Sternebrae
  - Xiphoid process

Clinical Correlates – Ribs & Sternum

Defect	Description / Consequence
Cervical ribs (1%)	Extra rib from C7 → may compress brachial plexus or subclavian artery
Cleft sternum	Failure of sternal bands to fuse → thoracic organs covered only by skin
Hypoplastic ossification centers	Premature fusion or defective ossification → common in congenital heart defects

Multiple manubrial ossification centers	Seen in 6–20%, especially Down syndrome
Pectus excavatum	Posteriorly depressed sternum ("funnel chest")
Pectus carinatum	Anteriorly projecting sternum ("pigeon chest")

-> The End <-