

12. Development of axial skeleton and extremities. Muscles and skin.

Timeline

- 19 days: somites emerge in the gastrula
- 4 weeks: sclerotome cells migrate along the neural tube
- 5 weeks: mesenchymal blastema of the axial skeleton
- 6 weeks: mesenchymal blastema of limbs
- 8 weeks: rotation of the limbs
- 8 weeks: individual muscles differentiate
- 10 weeks: primary ossification centres in diaphyses
- 3 months: bones of the skull develop
- 9 months: diaphyses ossified; secondary ossification centres emerge

In general, bone tissue originates from:

- the of the somitic paraxial mesoderm, namely from the ventromedial part, the sclerotome
- the head non-segmented mesoderm
- the somatopleuric lateral plate mesoderm → skeleton of limbs
- the neural crest, which differentiates into the head ectomesenchyme
- mesenchyme
  - its cells migrate and differentiate into fibroblasts, the source of the desmogenous (intramembranous) ossification
  - its cells imgrate and differentiate into chondroblasts, the source of the chondrogenous ossification of the hyaline cartilage models

Limbs

- week 4: limb buds
  - somatopleuric mesenchyme differentiates into bones and connective tissues
  - myogenic cells, angioblasts and nerves grow in
  - surface ectoderm thickens into the apical ectodermal ridge
- week 6: each limb is divided proximodistally into three components:
  - autopod (carpals, metacarpals, digits, or tarsals, metatarsals, toes)
  - zeugopod (radius and ulna, or tibia and fibula)
  - stylopod (humeus, or femur)
- in flattened handplates and footplates, the apical ectodermal ridge is separated by cell death into five parts and fingers and toes are formed
- the geometrical axis of the handplate is close to the 4th finger
- in week 6, hyaline cartilage models differentiate
- between the primordia of adjacent bones/cartilages, interzones are formed; the mesenchyme of the interzones differentiates into articular cartilage, synovial membranes, ligaments and joint capsules
- week 12: primary ossification centers appear in diaphyses (bone shafts) of all long bones
  - the subperichondral cartilage of the diaphysis undergoes desmogeneous ossification
  - blood vessels invade the primary ossification centers, carrying also osteoprogenitor cells, which turn into osteoblasts; the cartilage is destroyed by chondroclasts
  - the cartilage is replaced by bone tissue via the chondrogeneous ossification

  - the bone marrow cavity is formed
- at birth, diaphyses are usually ossified; the epiphyses are still cartilaginous
  - postnatally, secondary ossification centers appear in the epiphyses of long bones; in the distal epiphysis of femur, this center appears even before birth
  - the epiphyseal growth plate temporarily persists between epiphysis and diaphysis, producing new bone tissue towards the diaphysis
- small and short bones (e.g., phalanges) have only one epiphyseal plate at one of its extremities
- irregular bones (e.g., vertebrae) have usually more secondary centers
- bone age is based on the presence of various ossification centers; it can be assessed using radiological methods (RTG) to determine the proper maturation of skeleton

Limb defects

- meromelia – partial absence of a limb; amelia – complete absence of a limb
- phocomelia – rudimentary hands and feet are attached to the trunk by small, irregularly shaped bones; between 1957-1962, approx. 12,000 children were bonr with limb malformations, because their mothers had taken a drug named thalidomide (Contergan) as a sleeping pill and antinauseant; currently, the drug is being used to treat mycobacterial infections (leprosy, tuberculosis of skin)
- syndactyly- fusion of fingers or toes as a results of insufficient apoptosis
- polydactyly – extra fingers present (praepollex, postminimus)
- clubfoot (pes equinovarus) – abnormal plantar flexion of the talocrural joint
- amputations and ring constrictions of limbs or fingers/toes may be caused by amniotic bands, i.e., adhesions between the amnion and skin surface
- congenital hip dislocation and laxity of the hip joint capsule: an underdevelopment of the acetabulum and head of the femur; affects approx. 5% of infants in Central Europe; it is treated by abduction

Vertebrae and vertebral column

- 38-40 paired somites develop within the segmented paraxial mesoderm
  - a microscopic cavity within each somite is called somitocoel
  - each somite develops into three parts:
    - sclerotome (medial): produces the bone forming cells for the vertebrae and ribs
    - myotome: forms muscle cells precursors
    - dermatome (lateral): differentiates into the dermis of the skin
- the caudal ½ of each sclerotome fuses with the cranial ½ of the adjacent lower sclerotome, which is called a resegmentation; thus, a body of a vertebra is formed; from the body, following processes grow
  - neural processes → these surround the spinal cord and close the vertebral foramen, they fuse into spinous processses
  - transverse processes
  - costal processes
- (the cranial ½ of the C1 somite becomes part of the base of the skull)
- myotomes keep the original somitic segmentation → paravertebral muscles connect the adjacent vetrebral bodies
- the notochord degenerates within the vertebrae, but it persists within the intervertebral discs as the nucleus pulposus

Defects of vertebral column

- asymmetric fusion of halves of vertebrae, missing half of a vertebra (hemivertebra) → scoliosis
- variable number of vertebrae (24±1): the L5 may be sacralised or the S1 may be lumbalised
- spina bifida: incomplete fusion of neural processes → vertebral foramen not closed
  - s.b. occulta (hidden defect, sometimes without symptoms)
  - s.b. cystica associated with neural tube defects
  - folic acid is used in decreasing the risk of defect closure of neural tube

Ribs, sternum, and clavicle

- the ribs grow from the costal (costiform) processes of the thoracic vertebrae
- ventrally, costal cartilages persist
- the sternum develops independently in the parietal layer of lateral plate mesoderm in the ventral body wall
- paired sternal bars fuse in the midline to form cartilaginous manubrium, sternebrae, and xiphoid process
- the clavicle ossifies mostly via the desmogeneous ossification

Muscles

- skeletal muscle develops
  - from the somatopleuric mesoderm
  - from the paraxial mesoderm: somites and head mesoderm
- smooth muscle develops
  - from the splanchnopleuric mesoderm
  - from the neural crest (head and neck region)
  - from ectoderm (myoepithelium)
- cardiac muscle develops
  - from the cardiogenis mesoderm and splanchopleura surrounding the heart tube
- kosterní svalovina: z paraxiálního mesodermu, ze somitů a z hlavového nesegmentovaného mesodermu

Skeletal muscle

- **myotomes divide into**
  - epimeric muscles (epaxial)
    - dorsomedial
    - rami posteriores of the spinal nerves
    - deep muscles of the back
  - hypomeric muscles (hypaxial)
    - ventrolateral
    - rami anteriores of the spinal nerves
    - lateral and ventral body wall muscles
    - limb muscles: flexors & extensors
- myogenic cells → myoblasts → merging into myotubes → myofibrils produced → nuclei below the sarcolemma → skeletal muscle fibres

Origin of selected muscles

- deep muscles of the back: from the epimeres
- C hypomeres → mm. scaleni, m. geniohyoideus, prevertebral muscles
- Th hypomeres
  - → mm. intercostales externi, interni et intimi, m. transversus thoracis
  - → m. obliquus externus abdominis, m. obliquus internus abdominis, m. transversus abdominis
- L hypomeres → m. quandratus lumborum
- S, Co hypomeres → diaphragma pelvis, diaphragma urogenitale, m. sphincter ani externus
- ventral parts of hypomeres
  - C: infrahyoid muscles
  - T: m. rectus abdominis

Innervation of selected muscles according to the embryological origin

– m. rectus bulbi superior, m. rectus	– n. III (oculomotorius)
– m. obliquus superior	– n. IV (trochlearis)
– mm. masticatorii	– n. V (trigeminus)
– m. rectus lateralis	– n. VI (abducens)
– mm. faciei	– n. VII (facialis)
– m. stylopharyngeus	– n. IX (glossopharyngeus)
– mm. laryngis	– n. X. (vagus), n. XI (accessorius)
– mm. linguae	– n. XII (hypoglossus)

Limb muscles

- myogenic mesenchyme of the limb buds
- rami anteriores of the spinal nerves divide into dorsal and ventral branches → connecting again → nervous plexuses
- upper limb: segments C4-Th1
  - extensors and supinators
    - from the dorsal blastema
    - n. radialis from dorsal branches of segmental nerves
  - flexors and pronators
    - ventral
    - n. ulnaris, n. medianus from ventral branches
- lower limb: segments L1-S2
  - extensors
    - from the dorsal blastema
    - n. femoralis, n. peroneus communis from dorsal branches of the segmental nerves
  - adductors and flexors
    - from the ventral blastema
    - n. obturatorius, n. tibialis from ventral branches

Skin

- Ectodermal epidermis
  - from the embryonic periderm
  - since month 5 str. basale/spinosum/granulosum/corneum
  - melanocytes from the neural crest (melanosomes into the keratinocytes)
  - hair follicles and skin glands invaginated into the dermis
  - fingerprints are being formed since month 3 until birth
- Mesenchymal dermis + subcutaneous connective tissue
  - from the lateral somatopleuric mesoderm, dermatomes of the somites, from ectomesenchyme
  - dermal papillae
  - connective sheaths of the hair follicles, m. arrector pili
- vernix caseosa protects the epidermis from the amniotic fluid; it is produced by the sebaceous glands
- lanugo is lost/shed before the birth
- mammary ridge develops between the axilla andinguinal region
  - thoracic part persists only → approx. 20 epithelial primordia of lactiferous ducts
  - polythelia – accessory nipples
  - polymastia – accessory breast glands