NOTES
SKELETAL DYSPLASIA

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Disorders affecting bone development

CAUSES

- Inherited/sporadic (*de novo*) genetic mutation

COMPLICATIONS

- Caused by bone malformations, depend upon affected bones

SIGNS & SYMPTOMS

- Commonly involve growth impairment, bone malformation

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray/CT scan/MRI

- Bone malformation, impaired ossification visualization
- Bone-age estimation

Ultrasound

- Prenatal diagnosis

TREATMENT

SURGERY

- Bone malformation correction if warranted/ desired

ACHONDROPLASIA

osms.it/achondroplasia

PATHOLOGY & CAUSES

- Genetic disorder, causes dwarfism with disproportionate short stature
- Relatively normal-sized torso, short limbs, normal–large head (macrocephaly) with prominent forehead (hence "disproportionate dwarfism")
- Average height
  - *Biologically-male:* 131cm/4'4''
  - *Biologically-female:* 123 cm/4'

CAUSES

- Heterozygous "gain-of-function" mutation in *fibroblast growth factor receptor 3* (*FGFR3*) gene on chromosome 4; individuals with homozygous mutation usually do not survive
  - Mutated receptor displays "constitutive activity" (activated in ligand binding absence) → inhibits chondrocyte proliferation
  - Endochondral ossification affected → inhibits long bone elongation (e.g. humerus, femur)

- Intramembranous ossification less affected → relatively normal flat bone growth (e.g. skull, ribs)
- Autosomal dominant inheritance pattern (20%); sporadic mutation in most cases (80%)

COMPLICATIONS

- Eustachian tube narrowing → recurrent middle ear infection
- Narrowing of
  - Lumbar spinal canal → spinal stenosis
  - Foramen magnum → cervical medullary compression
- Venous obstruction at sigmoid sinus → hydrocephalus
- Midface retrusion → obstructive sleep apnea
- Obesity

SIGNS & SYMPTOMS

- Long bone malformations
  - Rhizomelic (proximal) limb shortening
  - Varus/valgus leg malformations
  - Short metacarpals
  - Short phalanges (brachydactyly)
  - Trident hand (fingertips cannot touch)
- Flat bone malformations (less common)
  - Enlarged head
  - Frontal bossing (prominent forehead)
  - Flattened nasal bridge (saddle nose malformation)
  - Narrow foramen magnum
  - Spinal kyphosis/lordosis

DIAGNOSIS

DIAGNOSTIC IMAGING

Prenatal ultrasound

- Skull width to femur length ratio higher than normal

X-ray/MRI/CT scan

- Large skull with small skull base
- Narrow foramen magnum, spinal canal
- Short, flattened vertebral bodies
- Small flat squared iliac wings ("mickey mouse ear")
- Fibular overgrowth
- Metaphyseal flaring: diaphysis narrowing, metaphysis widening

LAB RESULTS

- DNA test
  - *FGFR3* mutation-positive

TREATMENT

SURGERY

- Bone malformation correction warranted/desired

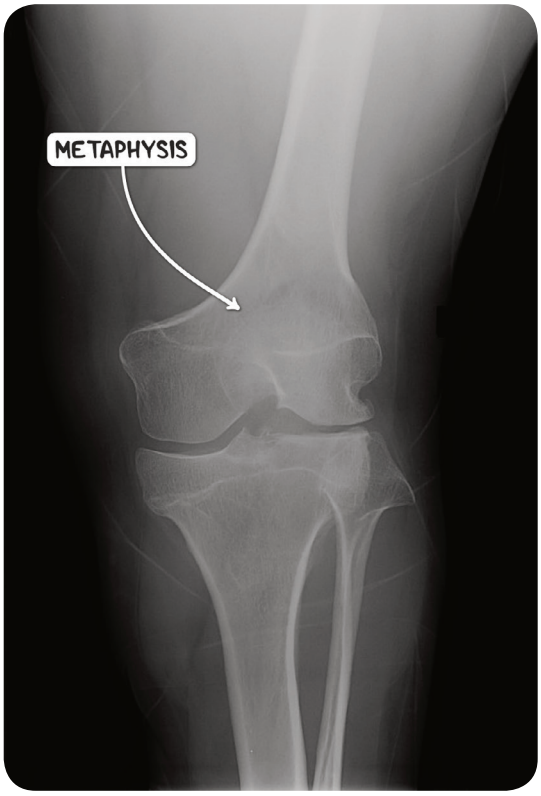

Figure 118.1 An X-ray image of the knee of an individual with achondroplasia. There is flaring of the distal femoral metaphysis typical of the disease.

CLEIDOCRANIAL DYSPLASIA

osms.it/cleidocranial-dysplasia

PATHOLOGY & CAUSES

- AKA cleidocranial dysostosis
- Skeletal dysplasia
  - Predominantly affects intramembranous ossification-derived bone development
  - Clavicles (cleido-), skull bones (-cranial)
- Abnormal teeth development, delayed cranial fontanelle closure, clavicle underdevelopment/absence, distinctive craniofacial features

CAUSES

- Heterozygous runt-related transcription factor 2 (*RUNX2*) gene mutation (transcription factor involved in osteoblast, chondrocytes differentiation → delayed ossification; 30% of cases are idiopathic)
- Autosomal dominant inheritance pattern, can be sporadic

COMPLICATIONS

- Osteoporosis (adults)

SIGNS & SYMPTOMS

- Dental abnormalities
  - Supernumerary teeth (up to 13), delayed/failed permanent teeth eruption, abnormal deciduous dentition
- Delayed cranial fontanelle closure → soft skull areas
- Short stature
- Hypoplastic/aplastic clavicles → shoulder hypermobility
- Maxilla, mandibular prognathism hypoplasia
- Midface hypoplasia, flattened nasal bridge
- Frontal/parietal bossing
- Abnormal ear ossicles → hearing loss

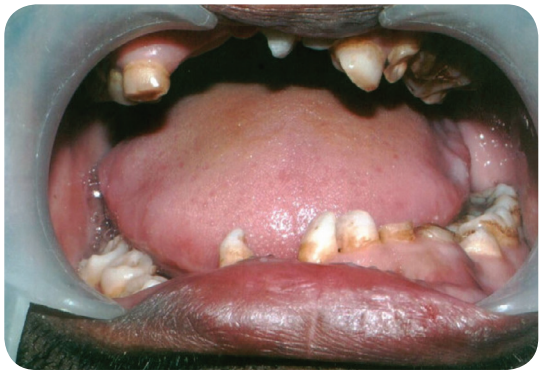

Figure 118.2 Retained deciduous teeth in the mouth of an individual with cleidocranial dysplasia.

DIAGNOSIS

DIAGNOSTIC IMAGING

X-ray

- Hypoplastic/aplastic clavicles
- Widened fontanelles
- Wormian bones (multiple small bones between sutures)
- Frontal/parietal bossing
- Supernumerary teeth
- Supernumerary ribs
- Iliac bone hypoplasia
- Symphysis pubis widening (diastasis)
- Small, highly positioned scapulas

LAB RESULTS

- Genetic testing (confirmation)

TREATMENT

SURGERY

- Bone malformation correction if warranted/desired

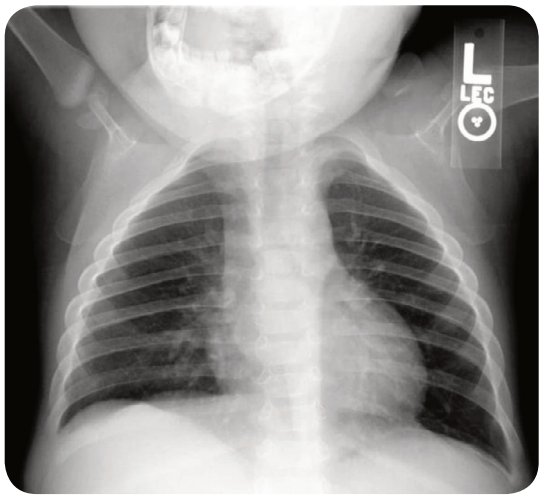

Figure 118.3 A chest radiograph of a neonate with absent clavicles, consistent with a diagnosis of cleidocranial dysplasia.

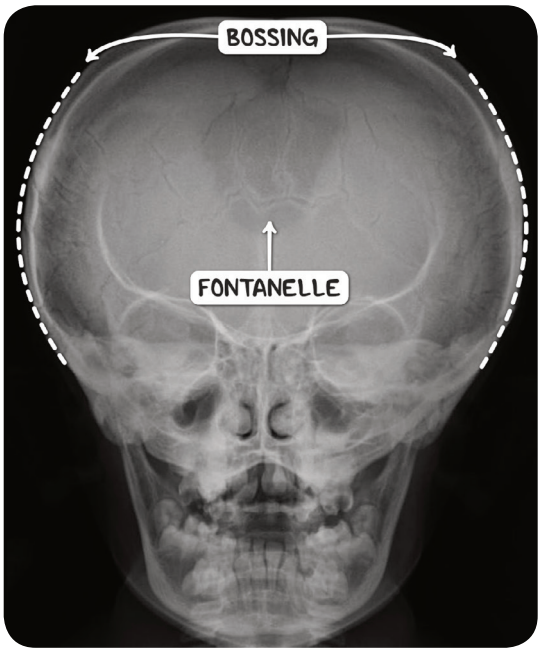

Figure 118.4 An X-ray image of the skull of a child with cleidocranial dysplasia. There is bitemporal bossing and a widened frontal fontanelle. The posterior lambdoid suture (not visible) contains multiple wormian bones.