Growth – Cram Sheet (2025 BRC)

GH-IGF Axis: GH acts on class 1 cytokine receptor, signaling through JAK/STAT pathway; IGF-1 circulates with ALS and IGFBP3 and binds IGF1R, a tyrosine kinase receptor.

FSS: BA=CA; height = MPH. **CDGP**: BA<CA, height < MPH; **pathologic short stature**: disproportionate growth, downward crossing of height centile after age 2, GV < -2 SDS x 1 year, height < -2 SDS.

Congenital GHD: AGA with decreased GV in 1st year; midface hypoplasia, high-pitched voice, truncal adiposity. **Acquired GHD**: growth failure (common in optic gliomas of NF1, craniopharyngiomas, radiotherapy, chemotherapy, trauma, Langerhan cell histiocytosis)

10-15% **SGA** infants have catch-up growth. ↑ premature adrenarche, metabolic syndrome

Laron Syndrome: GHR loss-of-function; post-natal growth failure, saddle nasal bridge, small face. ↓ IGF-1, IGFBP3, ALS; ↑ GH levels; ↓ GHBP. First try rhGH – if no benefit, consider rhIGF-1 therapy BID

IGF-1 or IGF-1R defects: prenatal and postnatal growth failure, neurocognitive deficits, hearing loss. Normal/↑ IGF-1, IGFBP3, and GH. First try rhGH, then rhIGF-1; neither very effective.

Chronic disease impact is multifactorial: undernutrition, inflammation, steroids, relative GH resistance, or altered extracellular fluid content. 50% Crohn Disease have poor growth before GI symptoms.

Childhood cancer survivors at ↑ risk of growth failure: CRT (GHD common!), spinal radiation, TBI, tyrosine kinase inhibitors, glucocorticoid therapy, ipilimumab → additive impact of various therapies.

Russell-Silver Syndrome: IGF2 hypomethylation; SGA, postnatal growth failure, relative macrocephaly, protruding forehead (triangular face), body asymmetry, feeding difficulties/low BMI. Dx is clinical; if mutation is found: 30-6% 11p15 LOM and 5-10% mUPD7.

Achondroplasia (rhizomelic dwarfism) and **hypochondroplasia** due to FGF3 gain-of-function. **Leri-Weil dyschondrosteosis** (mesomelic dwarfism, Madelung deformity) due to SHOX haploinsufficiency.

Turner Syndrome: always consider for girl with unexplained short stature! Intrinsic growth failure d/t *SHOX* haploinsufficiency. Mild IUGR, then rapid ↓ in centiles 0-2 years; suboptimal GV during childhood with absent/minimal pubertal growth spurt. Average AH is 20 cm below population mean. Scoliosis/kyphosis, cubitus valgus, Madelung, short 4th/5th metacarpals. Left-sided heart disease.

Noonan Syndrome: RAS/MAPK hyperactivation; hypertelorism, downslanted palpebral fissures, pectus, RIGHT-sided heart disease, uni/bilateral cryptorchidism. *PTPN11* most common. rhGH efficacy mixed.

LGA with postnatal overgrowth but normal AH: **Sotos** (*NSD-1* loss of function, large hands/feet with thickened subQ tissue), **Beckwith-Wiedemann** (IGF-2 excess, omphalocele, islet hyperplasia (hypoglycemia), embryonal tumors (Wilms, neuroblastoma)

Klinefelter Syndrome: 47,XXY, disproportionate tall stature (long legs), azoospermia, gynecomastia.

Postnatal overgrowth with tall AH**: Marfan** and **Homocystinuria** both: Marfanoid, ectopia lentis. Marfan ONLY: superior lens dislocation, joint laxity, aortic aneurysm. Homocystinuria ONLY: inferior lens dislocation, intellectual disability, thromboembolism.