



Review of Bone Age

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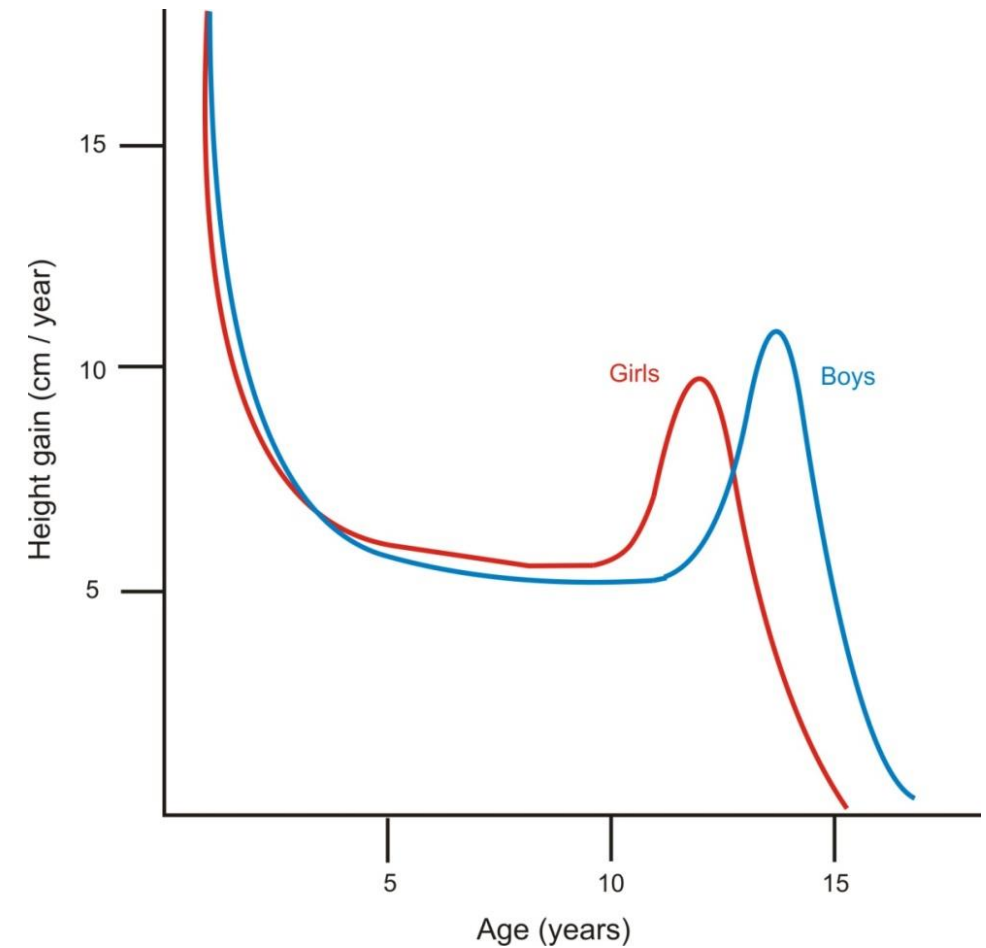
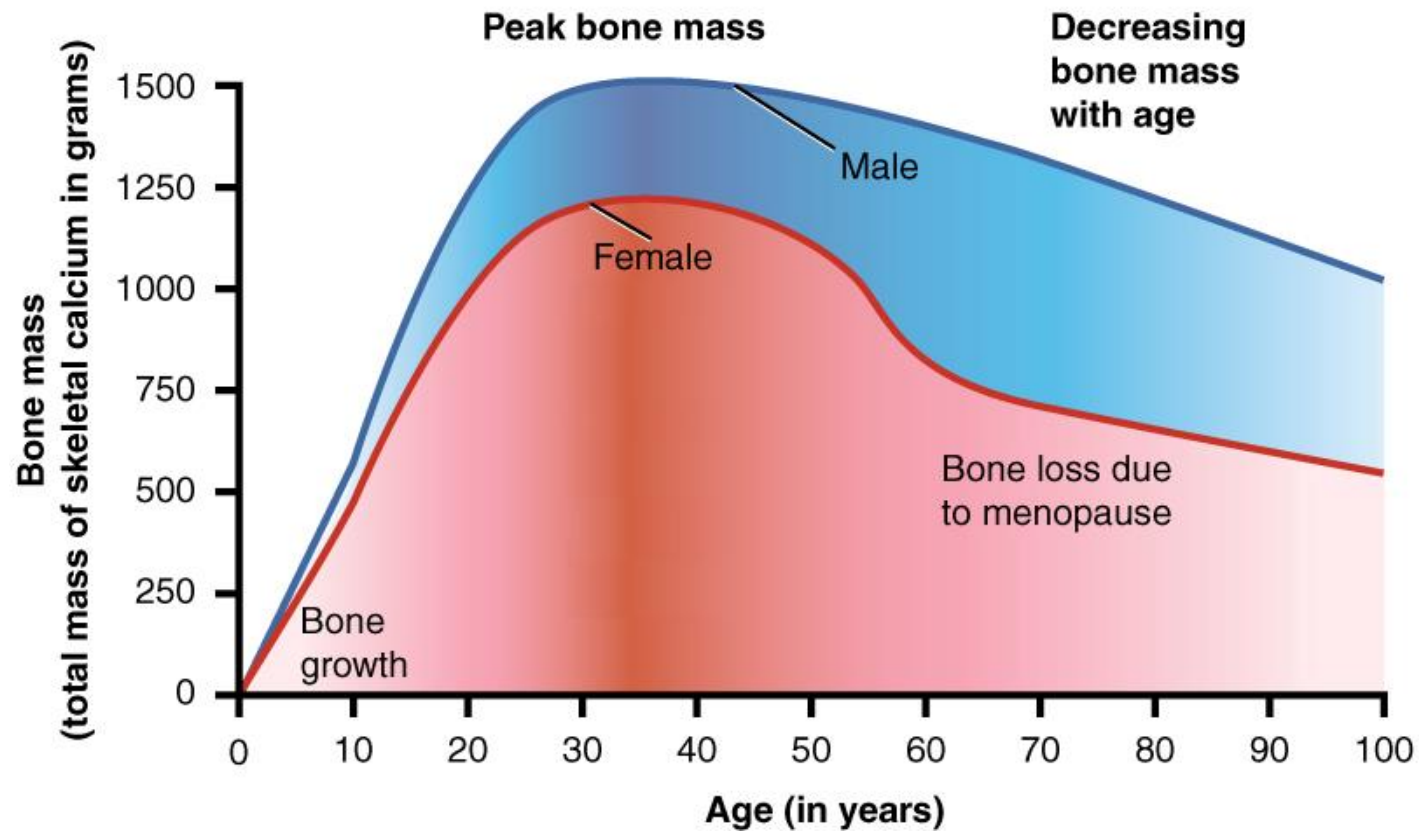
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Overview

- Pubertal Delay
- Skeletal Development
- Definition of Bone Age
- Methods for assessing Bone Age
- Causes of delayed and accelerated Bone Age

Development of the musculoskeletal system with age



Pubertal Timing Predicts Previous Fractures and BMD in Young Adult Men: The GOOD Study

Jenny M Kindblom,^{1,2} Mattias Lorentzon,^{1,2} Ensio Norjavaara,³ Asa Hellqvist,⁴ Staffan Nilsson,⁴ Dan Mellström,⁵ and Claes Ohlsson¹

- 642 Swedish men aged 18-20 years
- Older age at peak height velocity (indicative of pubertal timing) predicted:
 - Lower cortical vBMD (pQCT) (explained 14% of variance)
 - Lower trabecular vBMD (pQCT)
 - Lower aBMD at all sites (DXA) (i.e. lower peak bone mass)
 - Greater odds of upper limb fracture (OR 1.35 [1.04, 1.75])

Genetically Determined Later Puberty Impacts Lowered Bone Mineral Density in Childhood and Adulthood

2017

Diana L Cousminer,^{1,2} Jonathan A Mitchell,^{3,4} Alessandra Chesi,¹ Sani M Roy,⁵ Heidi J Kalkwarf,⁶ Joan M Lappe,⁷ Vicente Gilsanz,⁸ Sharon E Oberfield,⁹ John A Shepherd,¹⁰ Andrea Kelly,^{4,11} Shana E McCormack,^{4,11} Benjamin F Voight,^{2,12,13} Babette S Zemel,^{3,4} and Struan FA Grant^{1,4,11}

- Sex-specific polygenic risk scores for pubertal timing in Mendelian Randomisation Analyses
- Later puberty (menarche and voice breaking) associated with lower aBMD at LS and FN in males & females

Skeletal Development

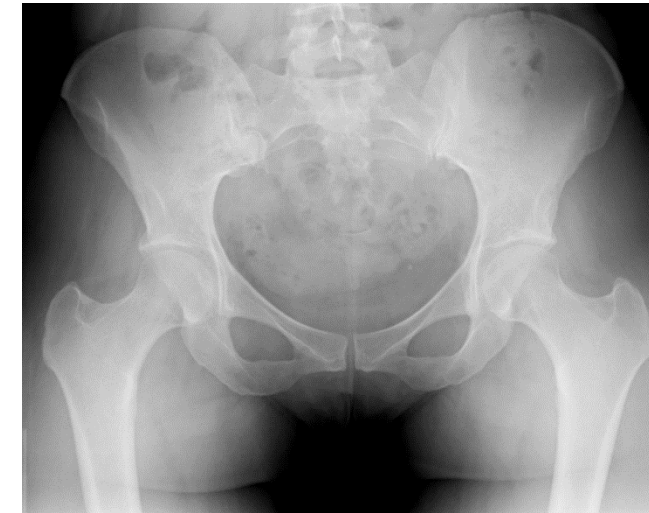


**X-ray of a newborn.
Gaps between bones
indicate cartilage**

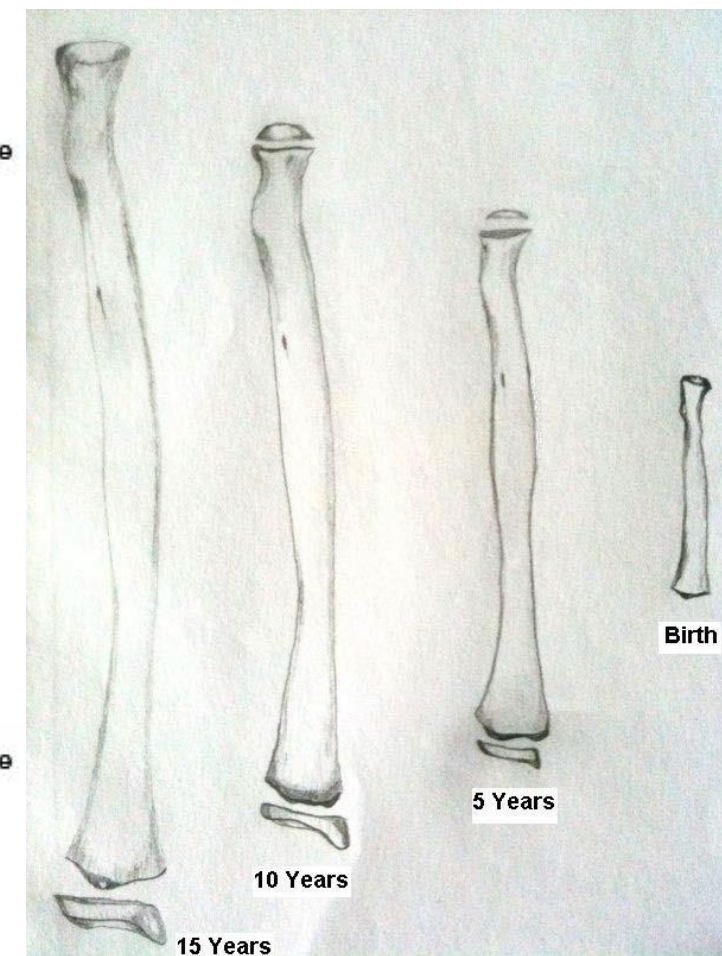
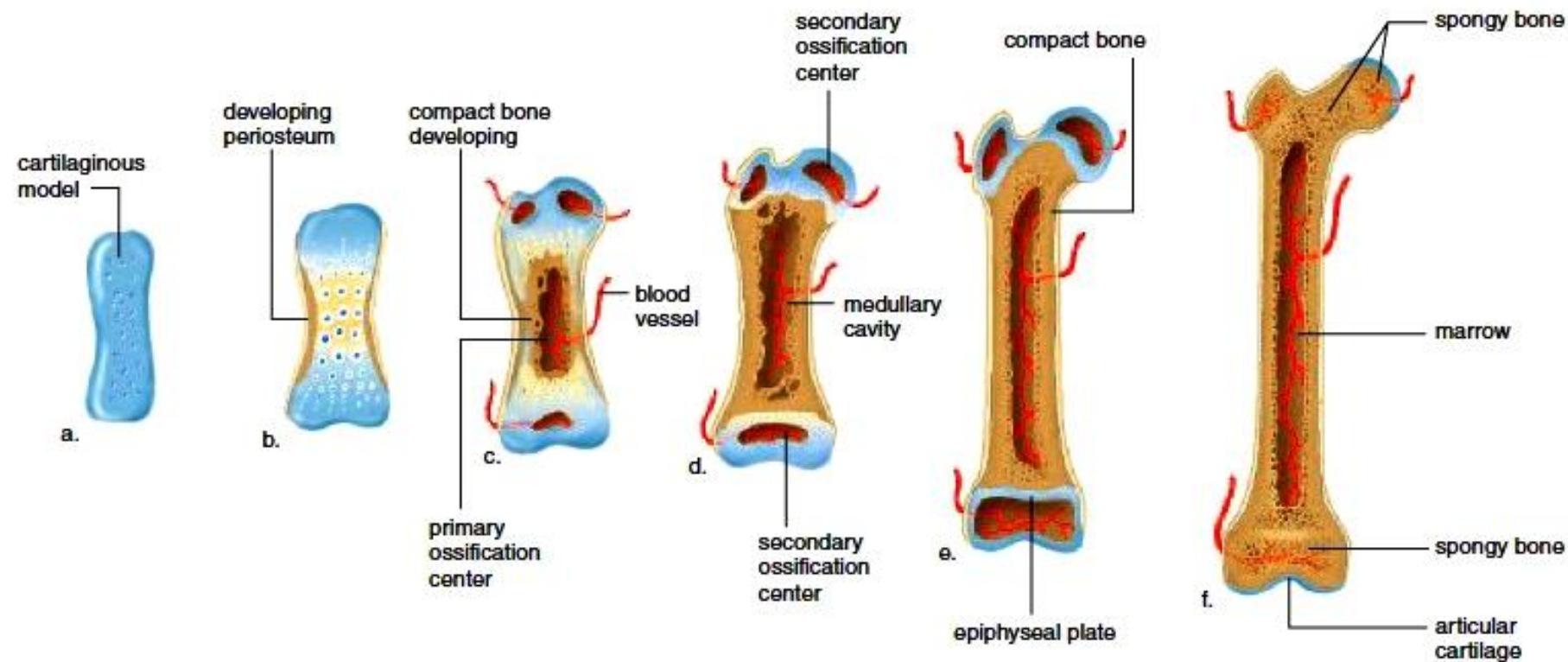
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Adult



Skeletal Development

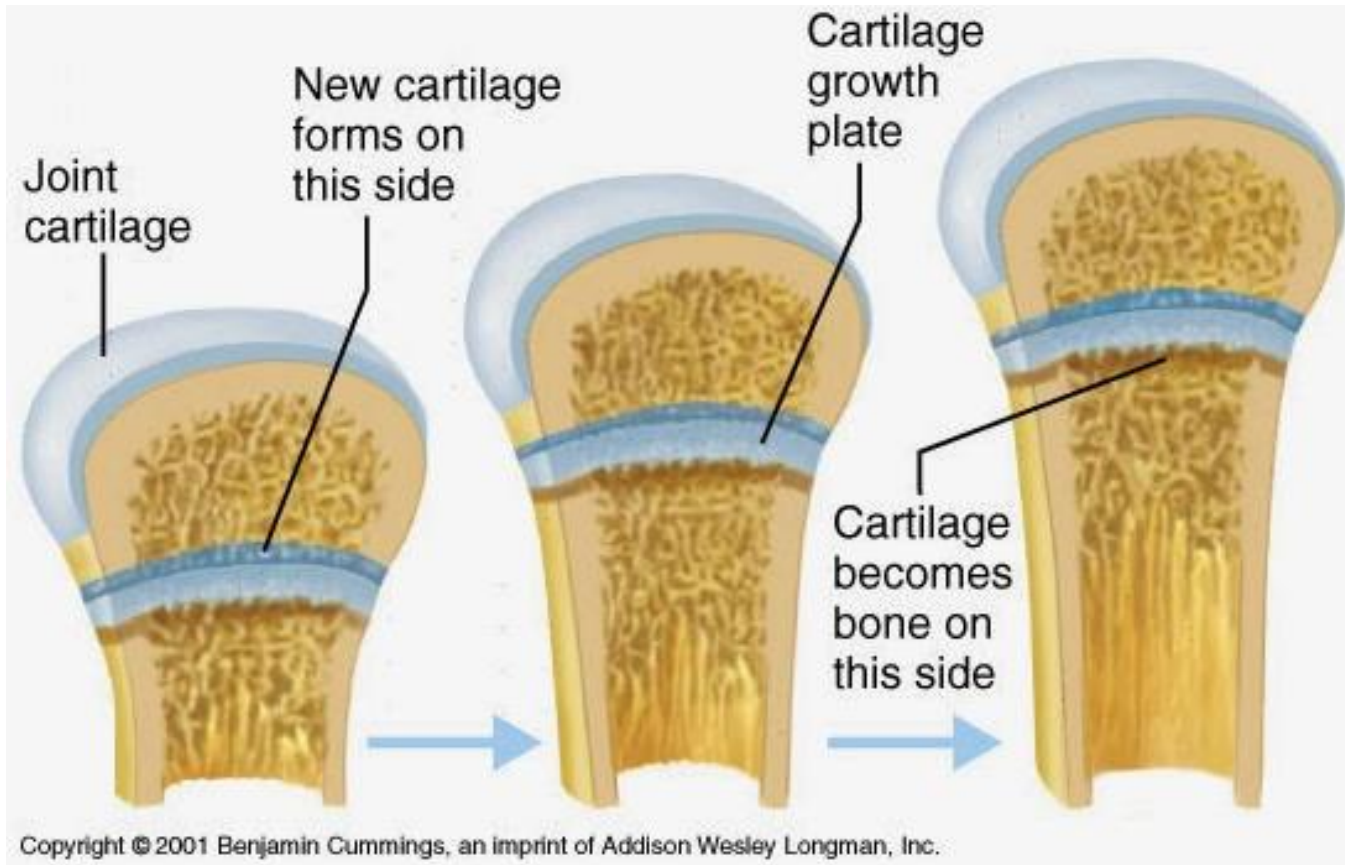


Skeletal mineralization begins in 3rd trimester
Calcium: 25g at birth – 1000g as adult

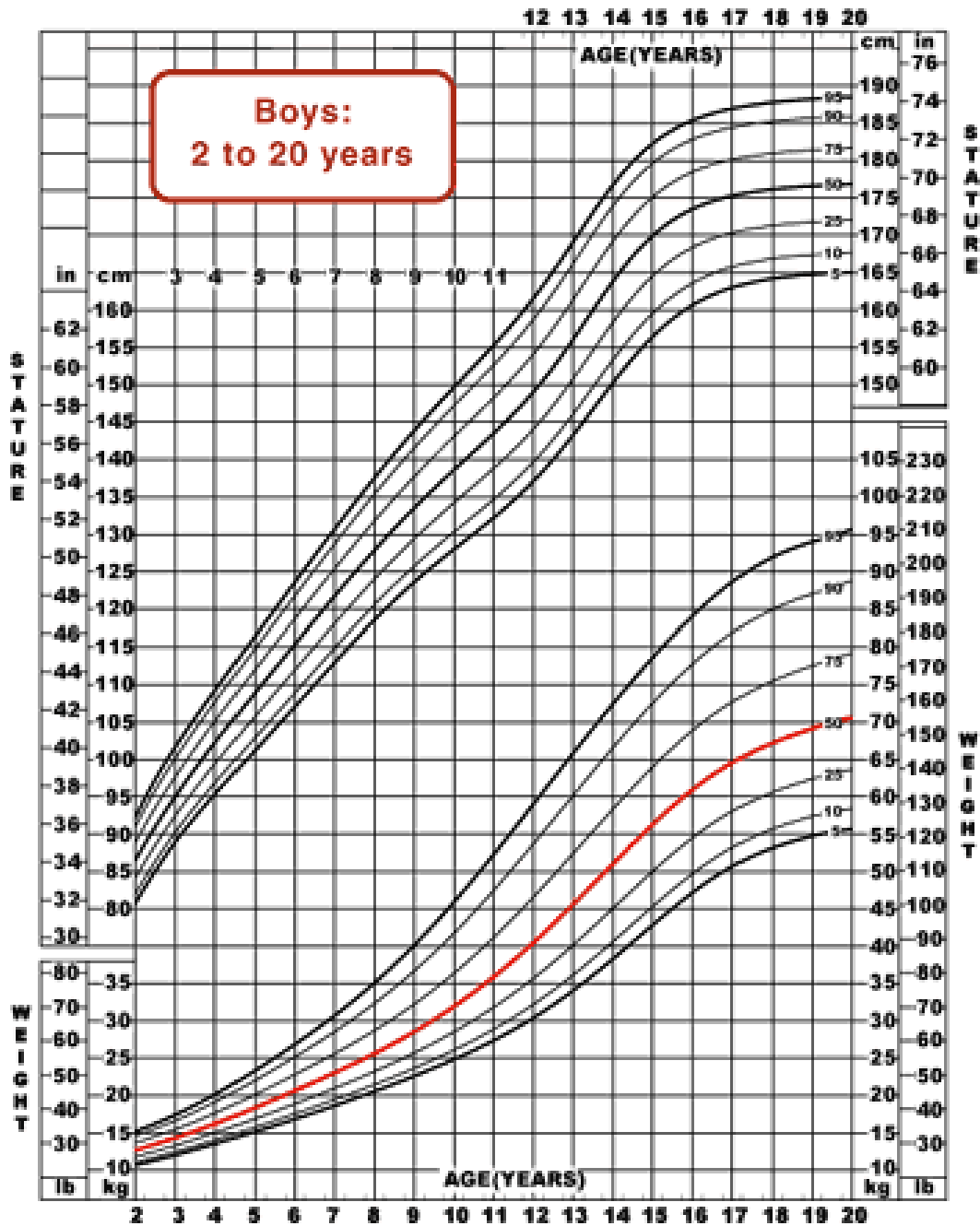
Developmental stages of a human radius from birth to 15 years (Bass, 1995)

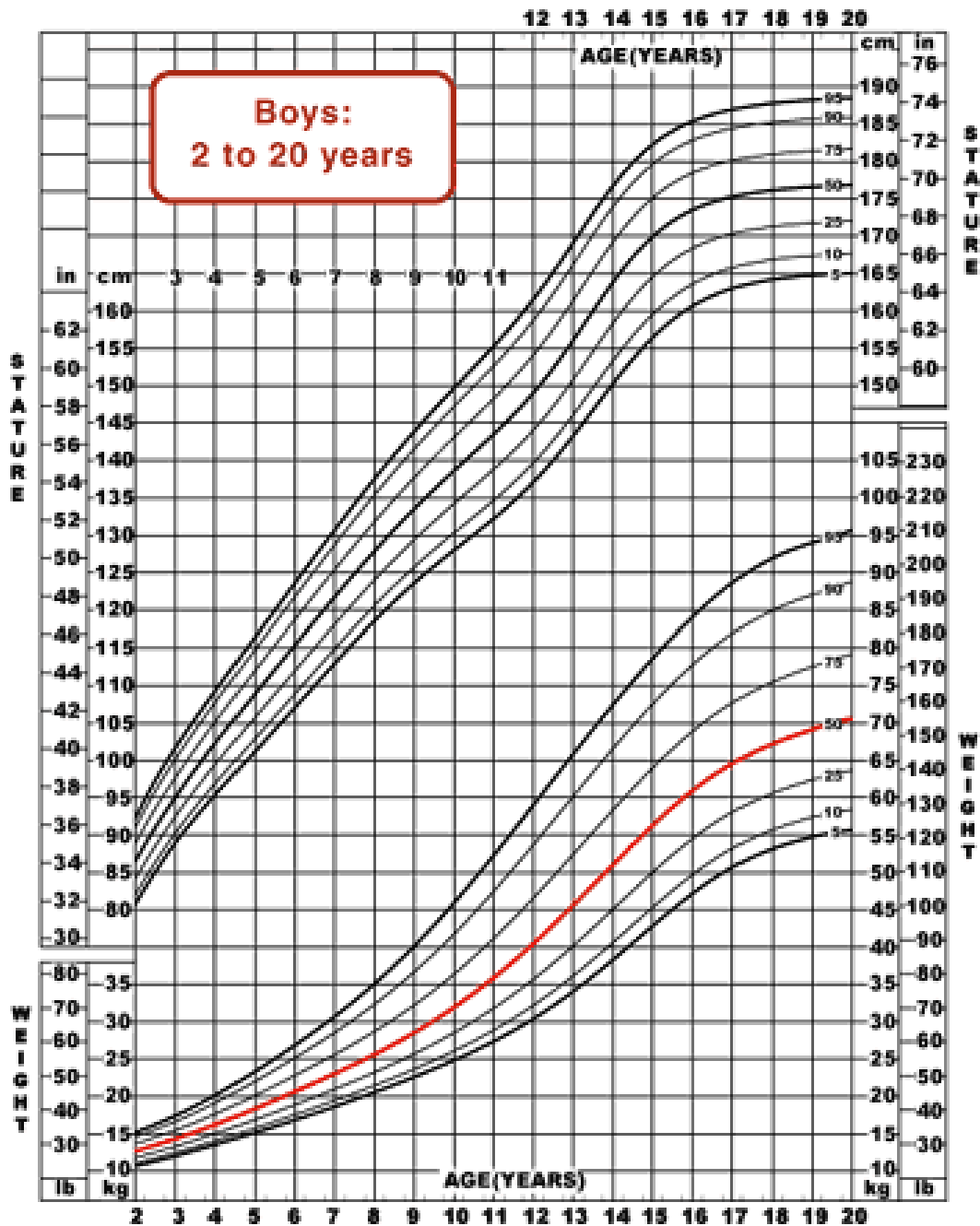
When growth plates (Epiphyseal plates) fuse, longitudinal growth ceases

Long bones grow in length by Endochondral Ossification at the growth plate

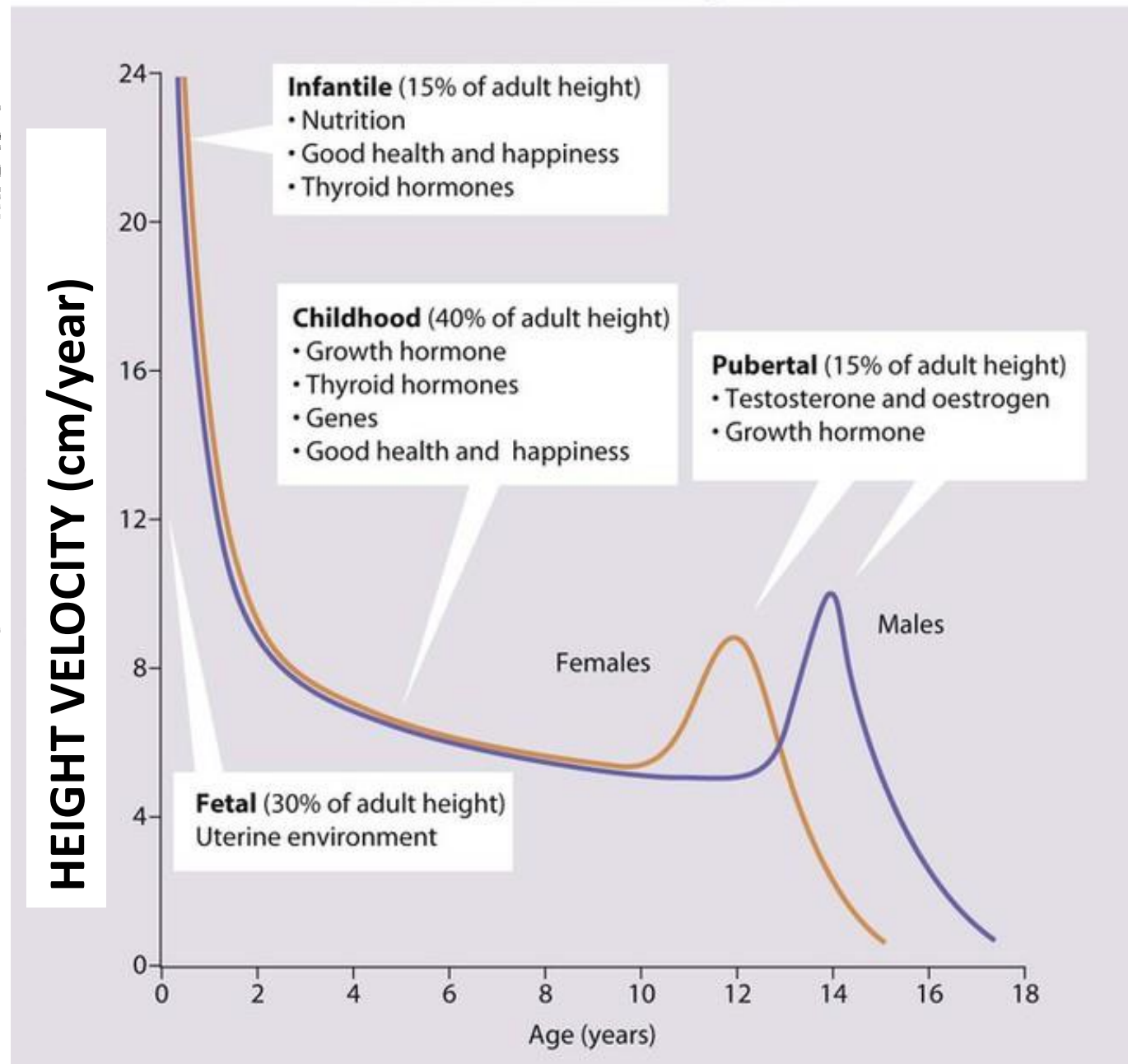


Growth curves

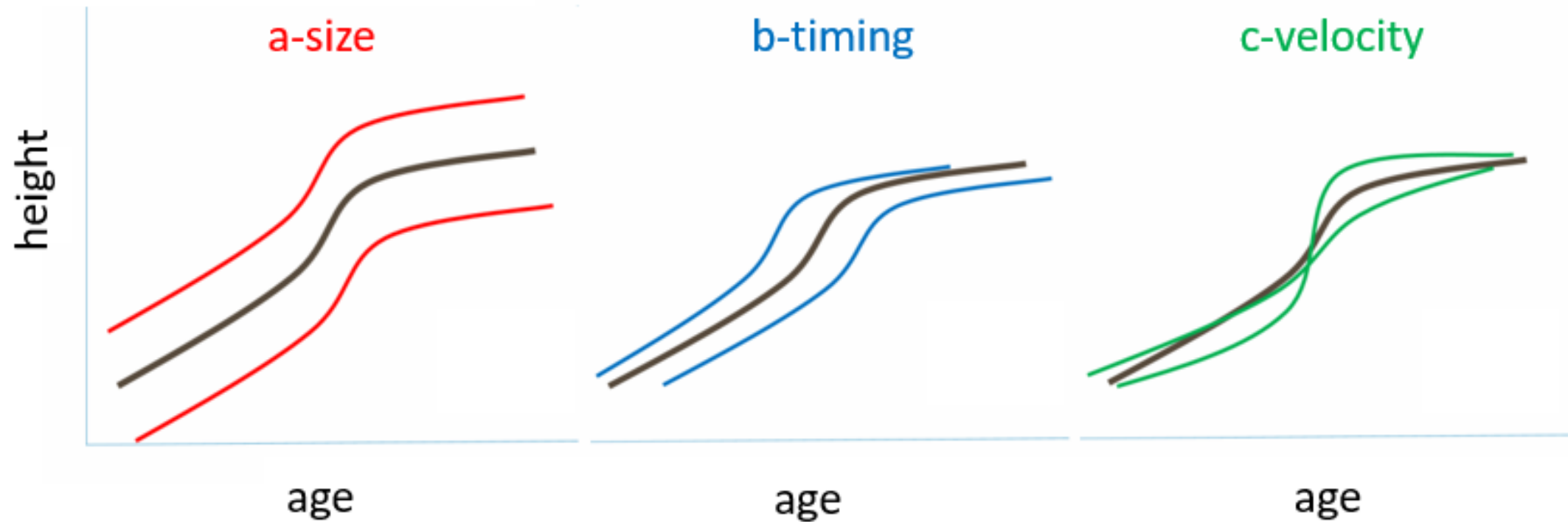




Determinants of childhood growth

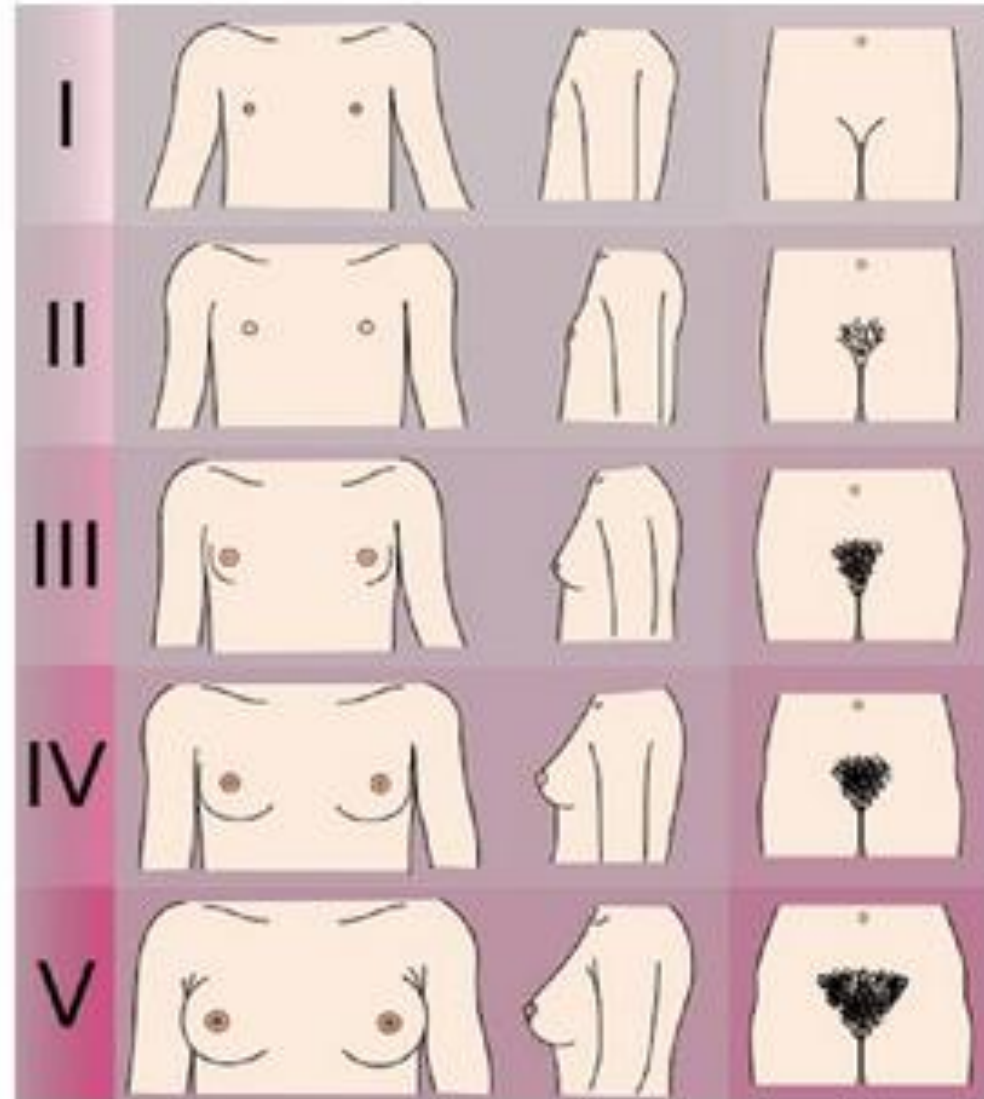
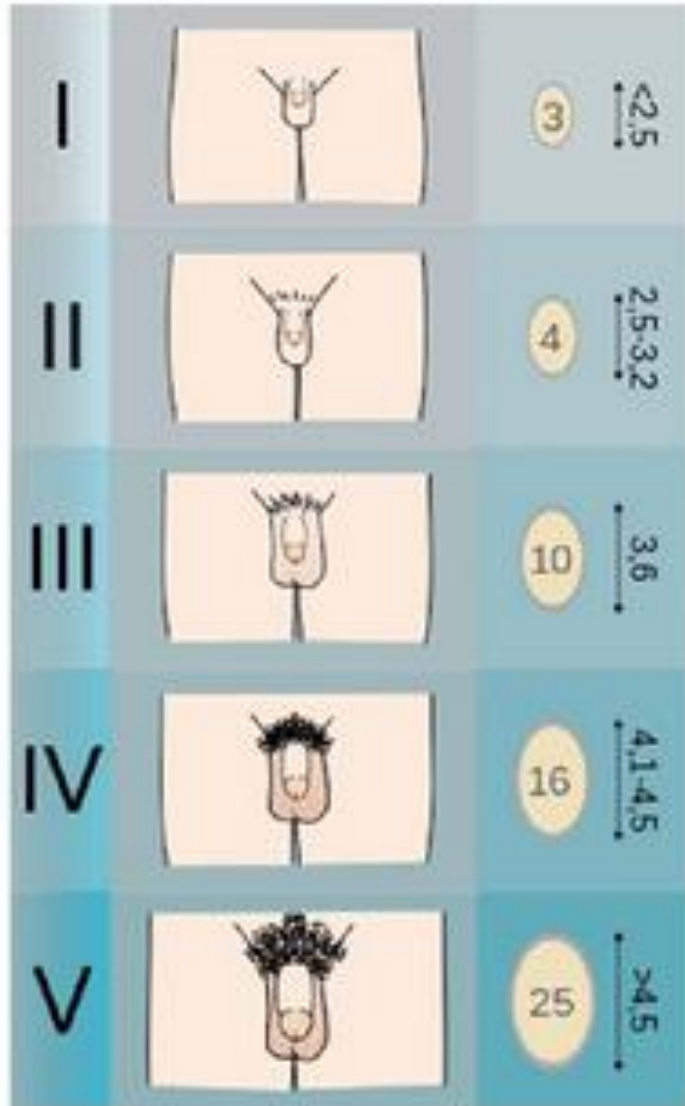


Growth modeling with SITAR methods



SuperImposition by Translation And Rotation (SITAR) Cole, *et al.* (2010) *IJE*.

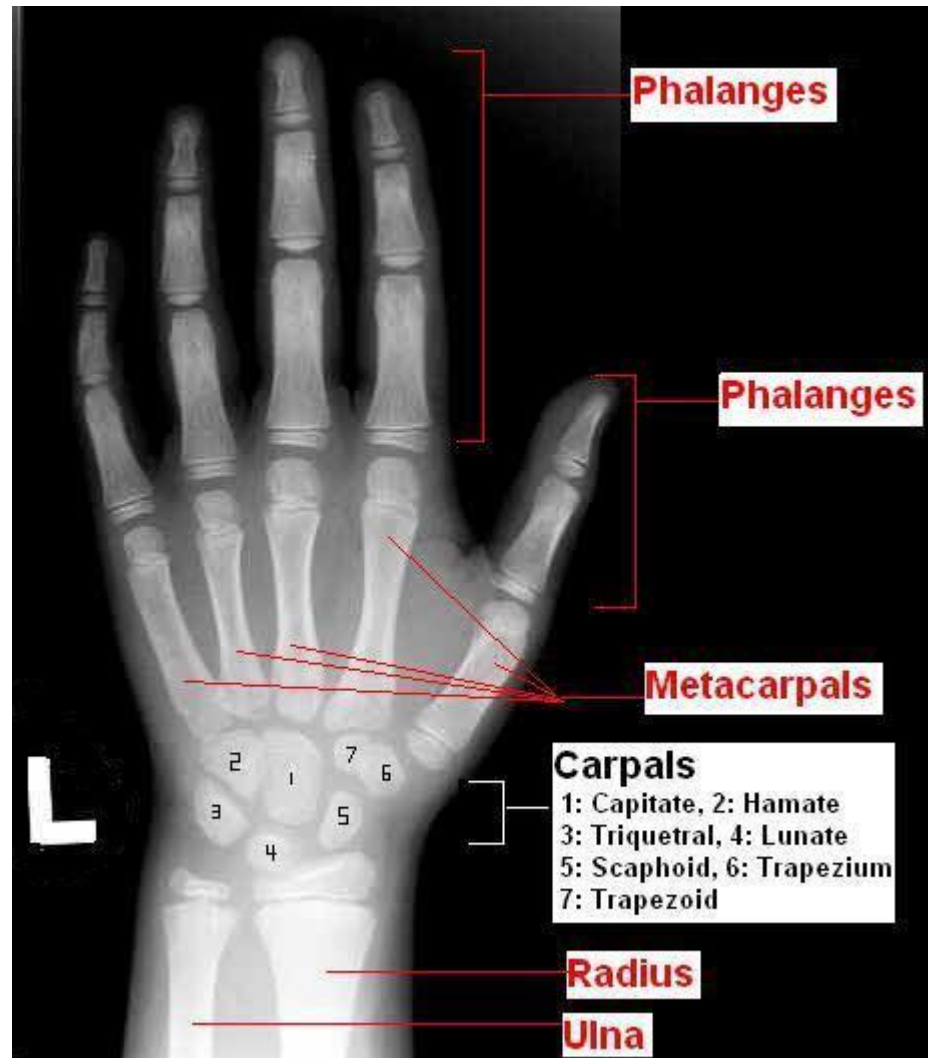
Tanner Staging



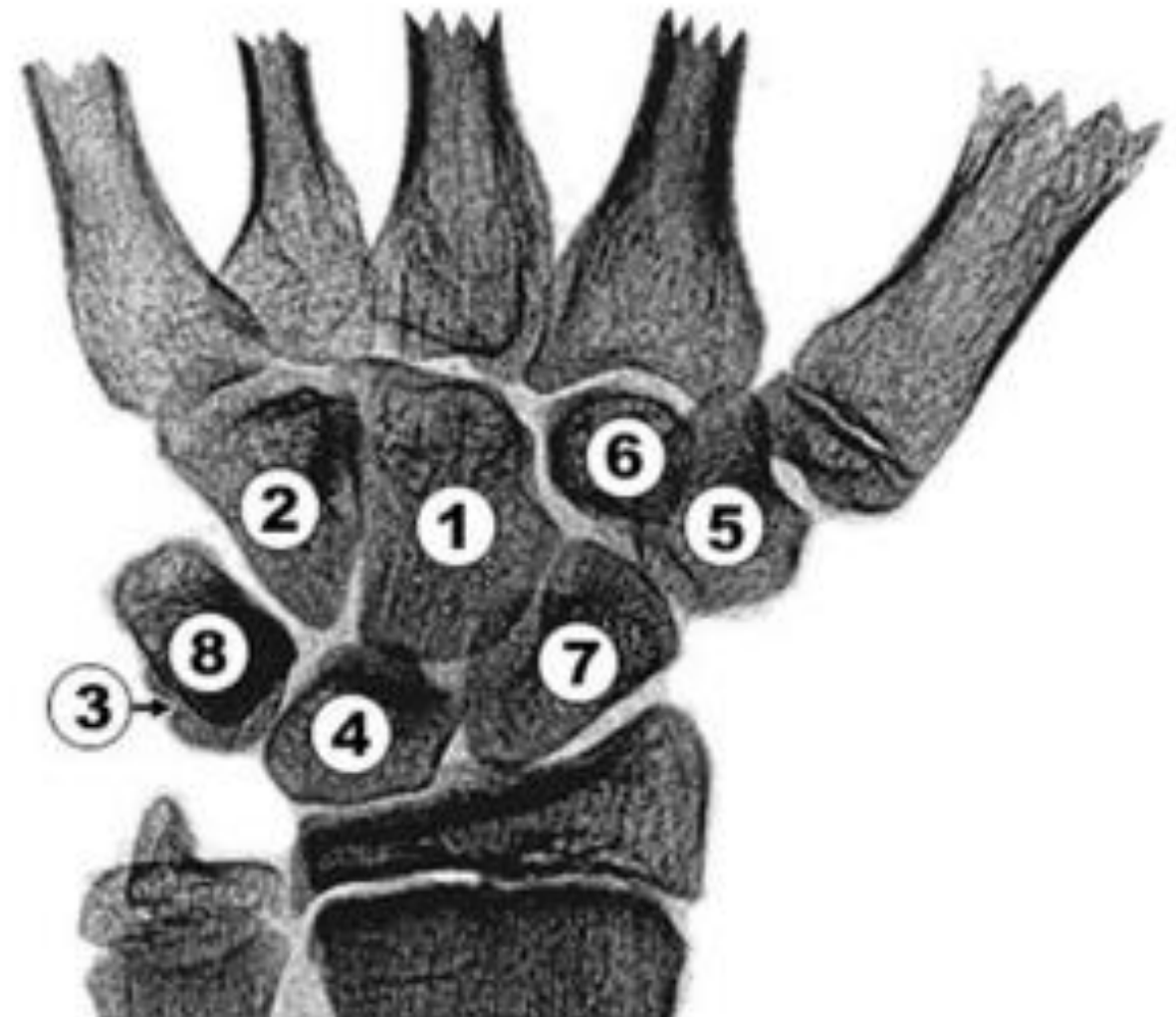
Definition of Bone Age

- The degree of skeletal maturity during childhood
- Different from chronological age (calculated from date of birth)
- If bone age \neq chronological age by more than 10%, can indicate endocrine/genetic disease
- Most frequently defined from plain hand & wrist radiographs (PA)
(radiation: 0.0001-0.1 mSV)

Left hand radiograph



The order in which carpal bones ossify



Methods for assessing Bone Age on Hand/Wrist Radiographs

Atlas-based methods

1. Greulich and Pyle (GP) (1959) ——— Compares vs. atlas of hand radiographs of American Caucasian males and females (quick)
2. Fels (1988) ————— Computer-assisted, 98 statistically weighted age & sex-specific maturity markers of hand & wrist. American Caucasian ref popn. (time consuming)
3. Tanner Whitehouse (TW) ————— Scoring approach, generates an age range, British ref popn (not as quick as GP)
4. Gilsanz and Ratibin (GR) (2005)

Automated Skeletal Bone Age assessment

5. Bone Xpert (uses TW and GP)
 - Bones used in all include distal radius and ulna, the carpals, metacarpals and phalanges



Bone age

Infancy

Toddlers

Pre-Puberty



Females: Birth to 10 months
Males: Birth to 14 months

Females: 10 months to 2 years
Males: 14 months to 3 years

Females: 2 to 7 years
Males: 3 to 9 years

Bone age

Early & Mid-Puberty



Females: 7 to 13 years
Males: 9 to 14 years

Late Puberty



Females: 13 to 15 years
Males: 14 to 16 years

Post-Puberty



Females: 15 to 17 years
Males: 17 to 19 years

Bone age

Early & Mid-Puberty

Late Puberty

Post-Puberty



Females: 7 to 13 years
Males: 9 to 14 years

Females: 13 to 15 years
Males: 14 to 16 years

Females: 15 to 17 years
Males: 17 to 19 years

Assessing bone age using other skeletal sites

Iliac Bone, Femoral Head, Cranial Sutures, Cervical Vertebrae



Infant



Child



Adult

Causes of accelerated skeletal maturation *i.e.* bone age > chronological age

Early puberty

Obesity

Endocrine disorders of precocious Puberty

e.g. Thyrotoxicosis

Cushing's Syndrome

Congenital disorders of precocious puberty

e.g. McCune-Albright syndrome

Pseudohypoparathyroidism

Causes of delayed skeletal maturation *i.e.* chronological age > bone age

Delayed puberty

Chronic illness

e.g. Perinatal HIV

Malnutrition

Rickets

Endocrine disorders

e.g. Hypothyroidism

Congenital disorders

e.g. Down Syndrome

Skeletal Dysplasia's

BoneXpert Software

The screenshot displays the BoneXpert software interface. The main window shows an X-ray of a hand with yellow dashed lines outlining the bones. Numerical values are placed near the bones, representing measurements. The software title bar indicates 'BoneXpert - Version 2.5.0.2 (c) Visiana 2013'. The menu bar includes 'File', 'View', 'Report', 'Settings', 'Batch/Import', and 'Help'. Below the menu bar are buttons for 'Intray', 'Search BoneXpert', 'Analyze', 'Print', and 'Delete'. The data panel on the right contains the following information:

BoneXpert	
Last name	
First name	
ID	
Birth date	10/12/2017
X-ray date	10/12/2017
Image file	00010001
Hand	Left
Referring physician	
Gender	Female
Ethnicity	Caucasian
Age	0.00 years
Bone age (GP)	17.37 years
Bone age SDS	
BA (TWJapan)	15.92 years
Bone Health Index	5.10
BHI SDS	
Height (cm)	
Father's height (cm)	
Mother's height (cm)	
Pred.adult height (cm)	Please enter height

At the bottom of the window, the taskbar shows the system tray with the date '17:12 11/03/2017' and the SAMSON logo. The SAMSON logo includes the text 'SAMSON Sub-Saharan African Musculoskeletal Network'.



Bone age and DXA

- DXA Z-scores are usually calculated based on chronological age using reference population data
- Reference data should be sex and ethnicity specific
- In children with delayed maturation, the applicability of chronological age to derive Z-scores is debated
- Adjusting DXA Z-scores for bone age helps to take account of skeletal maturation
- Bone age reference data are needed for Zimbabwe



Summary

- Bone age is seldom exactly the same as chronological age
- Bone age reflects (accurately) the degree of pubertal maturation
- Bone age is measured on a plain PA radiograph of the left hand
- Bone age can be automated using Bone Xpert (at a cost) provided population reference data are available
- In musculoskeletal research studies involving children and adolescents, measurement of bone age is recommended

Thank you



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