Growth, Puberty and Bone in Boys with DMD

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Take-Home Message

Whatever the question is for pediatric endocrinology, the answer is ?
Take-Home Message

Growth Curve!
Short Stature

3% = -1.88 SDS
2.3% = -2.0 SDS
1.2% = -2.25 SDS
Normal Growth

• Normal growth follows established patterns based on studies of several different populations and follows the trajectories of standard growth charts.

• Normal growth falls between the 3rd and 97th percentiles of all children; that is, the shortest and tallest 3% fall outside the bounds of “normal” stature. Thus, it is a **statistical** definition.
Normal Distribution/Standard Deviation Scores/Percentiles

68% of the population
95% of the population
99% of the population

-3 -2.5 -2 -1.5 -1 -0.5 0 0.5 1 1.5 2 2.5 3

0.1% 0.5% 1.7% 4.4% 9.2% 15.0% 19.1% 19.1% 15.0% 9.2% 4.4% 1.7% 0.5% 0.1%

-2.25 -1.88 -1.2% 3% 2.3%
Child Stadiometer

- Shoeless, feet together, back straight, in contact with posterior vertical surface
- Head looks straight ahead
- Headpiece of stadiometer placed at the top of the head
- Frankfort plane (arrow)
Infant Stadiometer

- Infant lying down
- Top of the head (chin up) and extended feet held against both ends of the stadiometer
Normal Growth Rates During Childhood

<table>
<thead>
<tr>
<th>Age</th>
<th>Growth (cm/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth to 1 year</td>
<td>17–26</td>
</tr>
<tr>
<td>1 to 2 years</td>
<td>10–13</td>
</tr>
<tr>
<td>2 years to puberty</td>
<td>5–7</td>
</tr>
<tr>
<td>Puberty</td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>7–12</td>
</tr>
<tr>
<td>Boys</td>
<td>8–13</td>
</tr>
</tbody>
</table>
Height Velocity (Boys)
Definitions

- Short stature—more than 2 SDs below the mean height for children of that gender and chronological age (and ideally of the same racial-ethnic group)
- Tall stature—more than 2 SDs above the mean height...

Strictly statistical convention

SD = standard deviation.
Variations of Normal Growth

- A normal pattern is evidence that the general health of a child or adolescent is good.
- On the other hand, children with just about any subacute or chronic illness may (transiently) grow slowly.
Normal Variants of Growth

- Genetic disorders
- Endocrine disorders
- Psychosocial deprivation
- Systemic disorders
- SGA/IUGR

GI = gastrointestinal; SGA = small for gestational age; IUGR = intrauterine growth restriction.

- Constitutional growth delay
- Genetic short stature
- Early or late puberty
- Rapid puberty
Bone Age

• *Aka* biological age
  - Skeletal maturation is marked by an orderly and reproducible sequence of recognizable changes in the appearance of the skeleton during childhood.
    • timing and sequence of appearance of ossification centers
    • alterations in the contours of the bones
    • timing and sequence of the ultimate closure of the growth plates
Bone Age
Why Do Percentiles Cross?

- Upward percentile (or SDS) peaks shortly *after* age at PHV for early maturing adolescents.
- Downward percentile (or SDS) peaks shortly *before* age at PHV for late-maturing adolescents.
- Age at PHV can be used as an estimate for maturational *tempo*—biological anchor.

PHV = peak height velocity.
Growth Disturbances

Relationships among

- Chronological age
- Height age
- Bone age
- Growth velocity
Illness and Growth

• Short-term interruptions to general trajectory
• Interspersed lags with catch-up
• Examples
  – cystic fibrosis
  – starvation
  – congenital adrenal hyperplasia
Puberty timing

- “Normal” timing and progression
The Normal Course of Puberty According to Tanner

Girls

Boys

Bone Mass

Peak bone mass

Childhood

Adulthood

Age
Bone Mass

- Improve Bone Acquisition
- Build Bone
- Reduce bone loss & prevent falls

Bone Mass:
- Childhood
- Adulthood
- Elderly
Fracture risk in children and use of ICS

Effect of BDP or Salmeterol on growth

Change in Height from Baseline (sd scores)

Verberne et al. AJRCCM 1997;156:688-695.
Change in height during one-year treatment with IN-BDP

Cumulative ICS exposure and bone density in adults

Effect of Long-term Treatment with Inhaled Budesonide on Adult Height

Agertoft and Pedersen. NEJM 2000;343:1064-9
Corticosteroids for Asthma: Benefits and Risks

Benefits
- Treat inflammation
- Most effective treatments
- May help decrease morbidity/mortality

Risks
- Dose, drug, & route dependent
- Known and can be monitored
Reversal of GC-associated growth suppression with exogenous GH therapy

Response to GH therapy in a pubertal GC-dependent female with SLE
Relationship of GC dose to growth rate after 1 yr of treatment

Effects of GH in GC-dependent children with JRA

Comparisons using Student's t-test: # comparisons to pre-treatment values, ## comparisons to values after one year of rhGH treatment

Touati et al. JCEM 83:403-409;1998
Growth Suppression by Glucocorticoids: advice and interventions

• GC inhibit growth at multiple sites
• ICS most common therapeutic GC
• Safety of ICS > oral GC
• ICS ≠ systemic CS
• ↓ dose and systemic exposure
• Monitor growth
• GH treatment can reverse some GC-induced growth failure
“As children get older they get bigger”.

Robert B. Reed
Professor of Biostatistics
Maternal and Child Health
Harvard University
“Take your time. Do you see the person who got the ball in the low post, spun around and — without regard to human life — dunked over your head?”
THANK YOU
A maze illustrating the chemical reactions that interconvert small molecules and cells.
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“If it were not for the great variability among individuals, medicine might be a science, not an art”.

Sir William Osler
The Principles and Practice of Medicine
1892
Things look simple when you don’t know much!