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When is Malnutrition "Malnutrition"? A Comparison of WHO Growth Charts to Specialty Growth Charts in Medically Complex Children

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Disclosures

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Learning Objectives

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- Identify infant malnutrition and growth failure
- Explain the importance of nutrition and growth monitoring in children with complex medical conditions
- Describe how genetic conditions can affect growth patterns and nutritional needs, and understand where to find this information
- Discuss challenges and limitations of using genetic growth charts vs. WHO growth charts
- Discuss the use of energy and nutrient dense formula in managing infants with challenged growth and genetic conditions (Russell-Silver Syndrome)

What is Malnutrition?

- **"An imbalance between nutrient requirement and intake, resulting in cumulative deficits of energy, protein or micronutrients that may negatively affect growth, development and other relevant outcomes."**
- *Academy of Nutrition & Dietetics*
- *American Society of Parenteral & Enteral Nutrition*

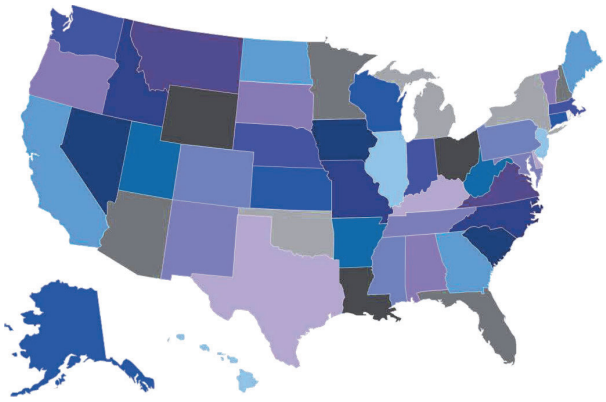
Mehta, et al. J Parenter Enteral Nutr. 2013;37(4):460-481

Malnutrition: Prevalence in US

45% Of children with chronic disease having nutrition risk

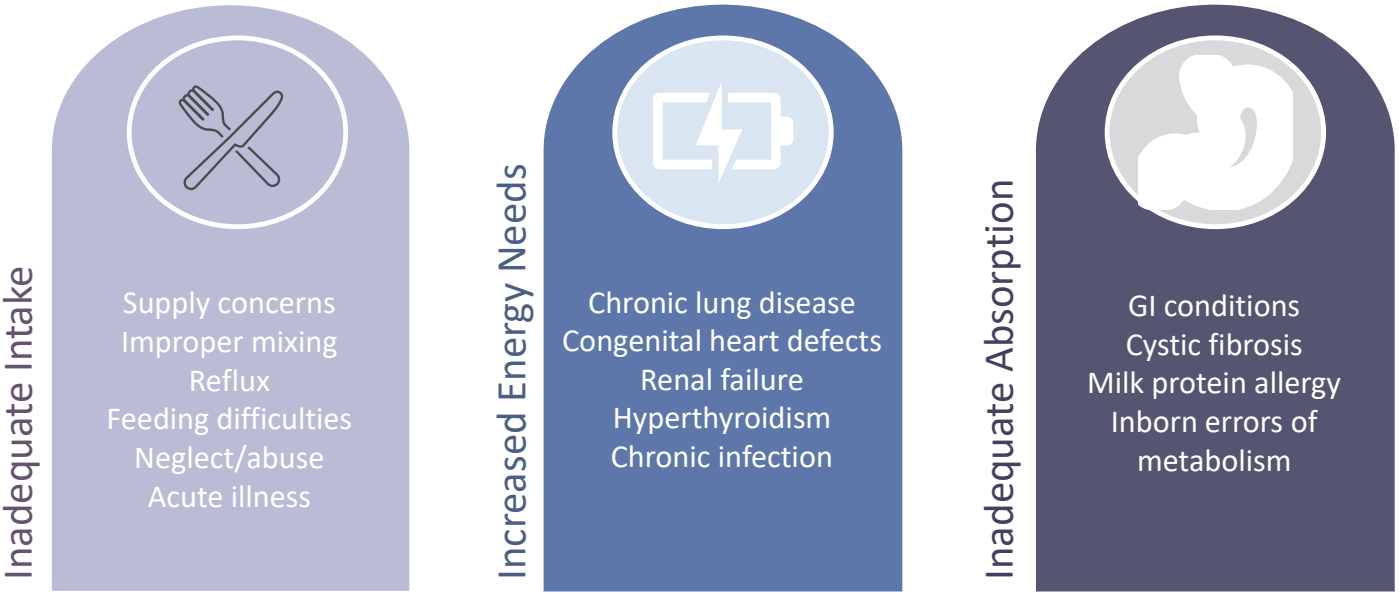
10% Of infants in primary care settings

4% Of hospitalized infants



Daymont, et al. Acad Pediatr. 2020;20:405-412. Carvalho-Salemi, et al. J Acad Nutr Diet. 2018;118:40-51

Malnutrition: Etiology



Carvalho-Salemi, et al. J Acad Nutr Diet. 2018;118(1):40-51

Malnutrition: Risk Factors

Medical

- Low birth weight
- Reflux
- Congenital anomalies
- Acute and chronic illness

Psychosocial

- Poor feeding techniques
- Post-partum depression (PPD)
- Poverty
- Abuse

Homan. American Family Physician. 2016;94(4):295-300

Malnutrition: Diagnostic Criteria

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Primary Indicators when a **Single Data Point** is Available

	Wt-for-lt z-score	BMI-for-age z-score	Lt/ht-for-age z-score	MUAC z-score
Mild Malnutrition	-1 to -1.9	-1 to -1.9	No data	≥ -1 to -1.9
Moderate Malnutrition	-2 to -2.9	-2 to -2.9	No data	≥ -2 to -2.9
Severe Malnutrition	-3 or greater	-3 or greater	-3	≥-3 or greater

Primary Indicators when **Two or More Data Points** are Available

	Wt gain velocity (<2y)	Wt loss (2-20y)	Deceleration in wt-for-lt/ht z-score	Inadequate nutrient intake
Mild Malnutrition	<75% expected	5% usual BW	Decline of 1	51-75% estimated
Moderate Malnutrition	<50% expected	7.5% usual BW	Decline of 2	26-50% estimated
Severe Malnutrition	<25% expected	10% usual BW	Decline of 3	≤25% estimated

Guo, et al. Reference data on gains in weight and length during the first two years of life. Pediatrics. 1991;119(3):355-362. World Health Organization data for patients <2 years old. http://www.who.int/childgrowth/standards/w_velocity/en/index.html

Implications for Growth Failure

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"The First 1000 Days"

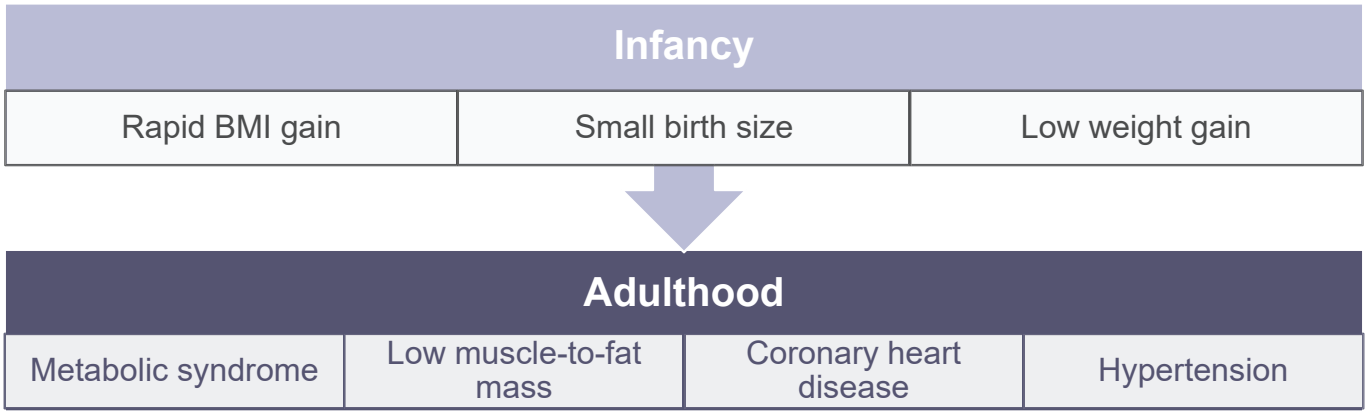
Critical period of brain growth & development

Inadequate nutrition support:
- Cognitive developmental delay
- Decreased growth potential
- Decreased immune function

Georgieff MK, et al. Acta Paediatr. 2018;107:1310-1312.

Implications for Growth Failure

Helsinki birth cohort:
factors in infancy linked with later negative health outcomes



1. van Abeelen, et al. Eur Heart J. 2012;33:538-545. 2. Barker. J Nutr. 2007;137:1058-1059. 3. Barker, et al. N Eng J Med. 2005;353:1802-1809.

Genetic Disorders and Growth

Growth is not solely mediated by nutrition, but also by genetics

If your parents are 5'5", and you are 6'5", we may have some concerns

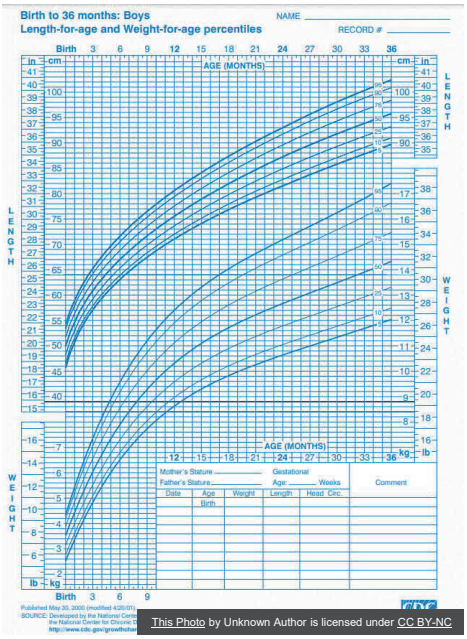
Typical linear growth expectations are assessed via mid parental height

Boys: average of paternal height and maternal height + 5 inches
Girls: average of paternal height minus 5 inches and maternal height.
SD of 3.35 inches (8.5 cm) creates a 6.7 inch range of acceptable heights

Being below or above expected range warrants evaluation, and one possible origin is genetic variation altering linear growth

Genetic Disorders and Growth

- Common disorders impacting linear growth:
  - Trisomy 21
  - Turner Syndrome
  - Noonan Syndrome
  - Prader-Willi Syndrome
- Some genetic abnormalities alter expected height, and these diseases have their own unique growth charts
- Some genetic disorders increase metabolic needs, meaning additional calories to support growth
- Some genetic disorders alter capacity to eat or absorb nutrition, requiring alternate feeding mechanisms or nutritional sources



When to Evaluate?

Abnormal medical history

- Prematurity, frequent hospitalization, known anatomic defects, known organ disease, immediate diarrhea at birth or with onset of feeding, dehydration, neuromuscular abnormalities, abnormal behavior

Abnormal facies or cosmetic features

Linear growth decoupled from nutrition

- Pt just gains weight not height

Weight gain and linear growth decoupled from intake

- May have genetic disorder with associated higher metabolic needs or absorptive challenges (Shwachman-Diamond Syndrome).

How to Evaluate?

F/u on newborn screen and ensure fully assessed

Consider karyotype/chromosomal microarray

Consider referral to genetics

Consider whole exome sequencing
- Would recommend having genetics on board if doing this

Zhou et al, Genetic evaluation in children with short stature, *Curr Opin Pediatr*, 2021

Resources

After you evaluate, you receive a letter noting mutations with a long series of letters and numbers. What to do next?

What to do with a suspected genetic source of growth faltering

- Step one:
  - Find out what size they should be
  - But… How to do that?

OMIM

- Online Mendelian Inheritance in Man
  - https://omim.org/
- Wonderful database linking all known clinical/basic data to specific mutations
  - Provides easy access to information and publications on the specific mutation
  - A bit …technical.

GeneReviews

- NCBI maintained narrative review format about specific genes and mutations
  - https://www.ncbi.nlm.nih.gov/books/NBK1116/
- Returns brief PubMed indexed articles
- Vastly less abstruse than OMIM
- Search on PubMed!

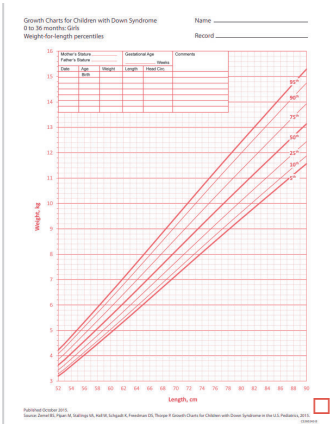
Example:
https://www.ncbi.nlm.nih.gov/books/NBK1394/

MedGen

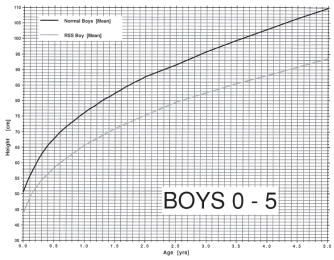
- Additional NCBI managed genetic data reference
  - https://www.ncbi.nlm.nih.gov/medgen/
- Less narrative than Gene Reviews
- More indexing of associated papers
- Fantastic for rarer or uncategorized mutations

Alternative Growth Charts

- Specific, more common conditions (Trisomy 21) often integrated into electronic medical record growth chart systems
  - CDC maintains Tri21 charts
- Some foundations seek to aggregate existing charts



- Magic Foundation https://www.magicfoundation.org/rss-sga-growth-charts

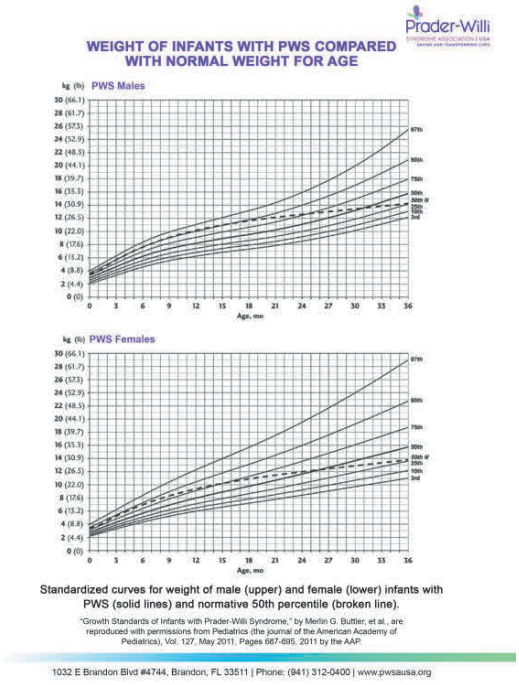


- Australia/New Zealand Pediatrics: https://anzsped.org/clinical-resources-links/growth-growth-charts/

Growth Charts for Children with Down Syndrome: Girls
RSSBoys0.5yr350.pdf - Google Drive

Alternative Growth Charts

- Disease specific organizations often host charts for manual plotting
  - Ex: Prader-Willi https://www.pwsausa.org/resources/medical-issues-a-z/



Growth-charts-untreated-infants.pdf

Disease Specific Growth Charts

- PubMed: In rarer conditions, often only 1-2 papers describing expected growth patterns
  - Search can identify a resource to provide some idea of benchmark height

ENDF in Genetic Disorders

Key to parse expected growth in order to determine goals

Many patients will have low expected growth, but underperform that due to other factors suppressing caloric intake

Primary factors:

- Associated developmental/neuromuscular/anatomic abnormality increasing difficulty of feeding, or limiting solids (DiGeorge, Prader-Willi in infancy, etc.)
- Associated increased metabolic burn (syndromes with renal, pulmonary, or cardiac issues, [Ex: Noonan Syndrome], or metabolic disease)

Solution:

- In older kids: 1.5 to 2.0 kcal/mL formula
- In infants, ENDF

Case Study

Case Study

7 mo M born to recent immigrant parents w/ known genetic abnormality c/w possible Russel-Silver Syndrome

- Referred for growth failure

History

- Initially breastfed → Formula at 5 months
- Taking 3.5 oz 5x daily of 27 kcal/oz formula and pureed baby foods BID
- Exam c/s RS syndrome, abnormal facies, small for age
- Inappropriately low fat deposition for age

Case: How do I know if a child with a genetic abnormality has growth faltering?

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A. Assess weight for length and weight trajectory

B. Determine if disease specific growth chart exists

C. Review OMIM entry

D. All of the above

Case Study : Russel Silver Growth Chart

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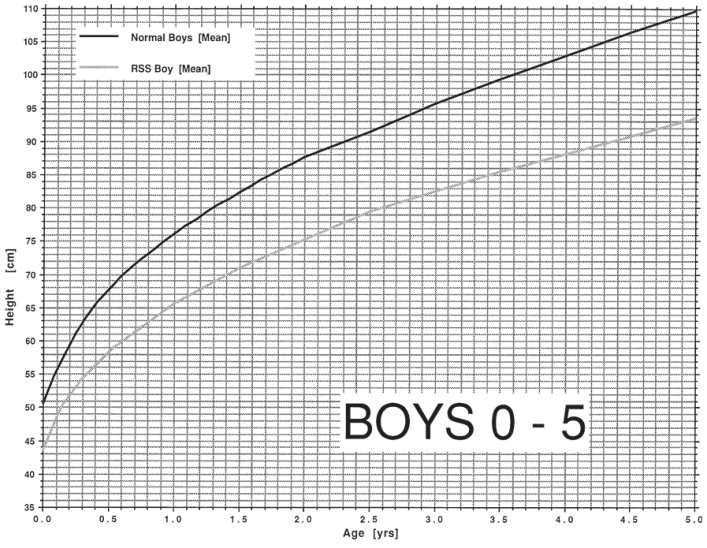
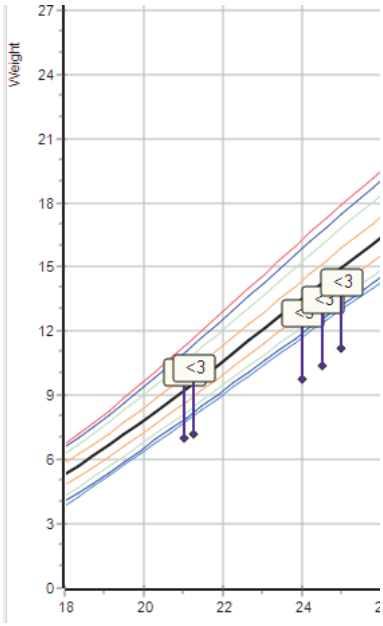
1 publication assessing height (not weight)

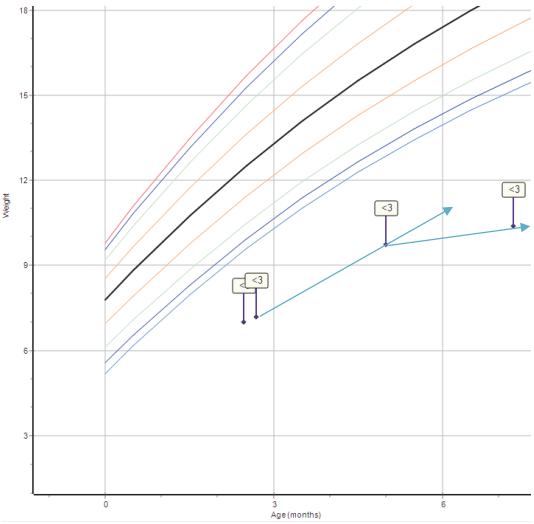


Wollmann et al, *European Journal of Pediatrics*, 1985

Case Study: Weight for Length/Trajectory

- Length consistent w/ published growth chart data
- Wt-for-Length low
- Weight trajectory slowed





Case Study: Russell-Silver

Russel-Silver: (AKA Silver-Russell depending if you are asking Russell or Silver)

- Clinically heterogenous condition characterized by IUGR (often severe), poor growth (sparing head growth mainly), abnormal craniofacial features, broad forehead, and body asymmetry.
- No association with malabsorption, and should not have significant increased energy needs

So… is this young man having growth faltering and caloric undersupply, or is he just genetically small?

Case Study: Can't it be Both?

Russel-Silver: (AKA Silver-Russell depending if you are asking Russell or Silver)

- Expected to have poor growth
- Standard weight charts are not available, disconnect between height trajectory and weight trajectory, as well as delta of weight trajectory, highly suggest a component of growth faltering.

It helps to note he was only gaining 5 g/day

Case Study: Management

Initial intake:

- Only 87 kcal/kg/day

Recommendations:

- Increase volume of feeding on 27 kcal/oz formula (15 to 22 oz) for total 128 kcal/kg/day to incorporate catch up (~50% increase in calories)

Case Study: Management

At follow up 4 weeks later:

- 107 kcal/kg/d
- Gaining 18 g/day

Recommendations:

- Increased total volume of feedings to 25 oz daily → 133 kcal/kg/d

Case Study: Management

At next f/u – 10 months old:

- Despite:
  - increased calories (124 kcal/kg/day formula alone)
  - increased solid PO intake
  - only gaining 6 g/day
- Strong concerns about mixing

Recommendations:

- Decision made to convert to 30 kcal/oz RTF ENDF at same volume (138 kcal/kg/day)

Case Study: How do you manage a kid with low appetite?

- Force feeding
- Gastrostomy tube
- Dronabinol
- Periactin®

Periactin®

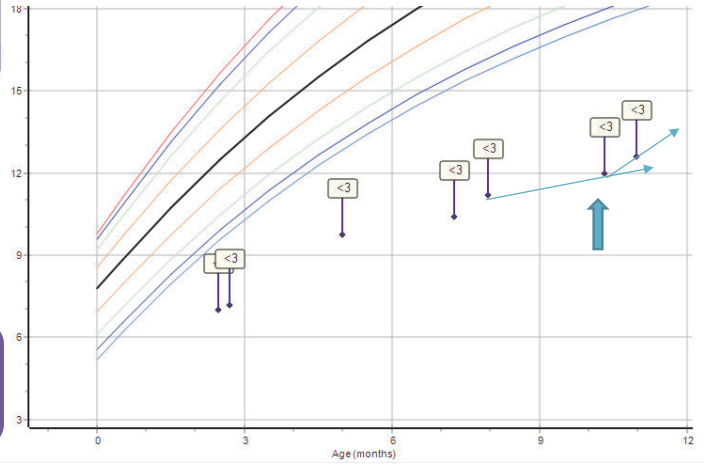
- AKA Cyproheptadine
- Histamine (H1) antagonist
  - H1 activation in the hypothalamus drives satiety, creates feeling of fullness
- 5-HT2A receptor blockade
  - 5-HT2A receptor (serotonin) additionally mediates hypothalamic driven satiety.
- Both signals primarily driven by gastric distension
- Medication makes you feel like you haven't eaten → eating more → weight gain.

Provensi et al, The Histaminergic system as a target for the prevention of obesity and metabolic syndrome, *Neuropharmacology*, 2015

Case Study: Outcome

At next visit:

- Weight gain improved, markedly → 16 g/d
- Remained inadequate for catch up
- Reflects likely component of mixing issues, as weight gain increased 3x with a 10% increase in nominal intake



Converted to toddler formula (30 kcal/oz

- Ultimately required conversion to 1.5 strength formula and Periactin initiated to support solid PO intake

Summary

- The growth chart is not one size fits all.
- “Healthy" growth is height/weight proportionate, even if genetic modifiers constrain height.
- Genetic conditions can induce a variety of challenges with nutrition and growth: OMIM, MedGen, and searching for disease specific growth charts are your best friend to determine if its nutrition, energy burn, or being born that way.

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THANK YOU!!