Early risk factors

Interpretation of growth charts

When to suspect a specific etiology?

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Description of the course

The first part of this module focuses on some early risk factors of childhood obesity including:

- The discovery of the links between phenomena that take place during pregnancy and the outcome during the child's first two years of life, called "the 1000 days hypothesis".
- Evidence that the first two years are strong determinants of later health and obesity risks

The second part shows how to use anthropometry including:

- Which anthropometric criteria are useful to assess childhood obesity, taking into account height and weight for Public Health or for individual assessment.
- How a cautious clinical examination and reading of the growth charts allow detection of several distinct causes of early obesity and how it helps to choose optimal therapeutic strategies

Learning objectives

At the end of this module you should be able to:

1. **Detect early risk factors of obesity during pregnancy and the first 2 years of life**
2. **Know which growth charts apply to children and adolescents**
3. **Choose the appropriate anthropometric parameters to assess obesity for a clinical setting or for a Public Health survey**
4. **Assess growth charts in order to suspect various aetiologies of child and adolescent obesity and settle corresponding optimal therapeutic strategies**

EARLY RISK FACTORS

The 1000 days hypothesis

The biological background of early development

- Genetics :
  - Single gene polymorphisms are said to explain less than 5 % of obesity according to most populations studies

But: There are huge differences in weight gain in adults submitted to similar food excess intake in experimental conditions

- Twin and Adoption studies :
  - Adopted individuals resemble their biological parents and not their adoptive parents (Stunkard 1986)
  - Similar weight gain in monozygotic twins raised separately (Stunkard 1990)
  - Similar weight gain in overfed twins (Bouchard 1990)

The 1000 days hypothesis

The biological background of early development

EPIGENETICS

The gene environment interaction

- **Modulation of the expression of the genome by its environment within cells**
  - Methylation of the genes leading to silencing or over expression
  - Environment of the histones influencing gene expression
  - Transmission of epigenetic modification of the sperm to somatic cells of the child
  - Many unknown factors: endocrine disruptors, pesticides....
- **Transmission from generation to generation from mother and father**
  - Evidence started from world war 2 cohorts of pregnant women in the NL
  - Transmission from food deprived grandmothers to children and grand children

-> Increased risk of cardiovascular disease, type 2 diabetes, obesity

The 1000 days hypothesis

The biological background of early development

Gene mutations

- **Genes linked to**
  - Appetite regulation
  - Energy expenditure

- **Careful Clinical examination in search of a genetic syndrome**
  - Dysmorphic features ?
    - Microcephaly, almond shaped eyes, macroglossia, small hands and feet
  - Abnormal neonatal features ?
    - LGA, SGA, hypotonia, hypoglycemia, failure to thrive
  - Impaired psychomotor development ?
  - Tall or short stature ?

Growth curves are often suggestive

Early risk factors

1. During pregnancy

- Obesity in the mother
- Excessive weight gain during pregnancy
- Pregestationnal and gestational diabetes
- Intrauterine growth retardation

2. Birth and first 2 years of life

- ***Low birth weight with excessive/continuous catch up growth***

  > Is the highest catch up weight gain the best ?

- ***High birth weight***

  Early feeding, weaning period and diversification critical for growth pattern regulation

3. Beyond 2 yrs of age

- Increasing influence of family lifestyle on the expression of the personal biological background

ANTHROPOMETRIC MEASUREMENTS

AND

GROWTH CHARTS

Which anthropometric measurements better assess obesity in children and adolescents?

The ideal anthropometric method to assess body composition to diagnose childhood obesity should :

1. accurately estimate fat mass
2. be independent of other covariates of body mass such as height
3. have low cost, be acceptable and reproducible
4. have appropriate reference norms

- ✓ Anthropometric references play a central role in identifying children that are overweight or obese, or at risk of becoming so.
- ✓ The assessment of growth based on the appropriate use and interpretation of anthropometric indices is the most widely accepted technique to identify growth problems in individual children and assess the nutritional status of groups of children .

The correct interpretation of accurate and reliable anthropometric measurements to assess risk, classify children according to variable degrees of overweight and obesity, or evaluate child growth trajectories, is heavily dependent on the use of appropriate growth curves to compare and interpret anthropometric values.

Mercedes de Onis, ECOG ebook

WHY GROWTH CHARTS ?

- Growth characterises childhood and adolescence until the end of puberty
- Obesity is considered as a growth disorder
- Body shape, i.e. the relationship between bodyweight and height varies until the end of puberty
- Body Mass Index (Body Weight (kg)/Height (m^2)) (BMI) can serve as an easily obtainable clinical estimate of adiposity

➢ BMI cut offs vary according to age. Adult limits do not apply for children and adolescents younger than 18 years for age. They should be compared to the age and sex appropriate limits

➢ ***Childhood obesity cannot be defined by a single threshold value as in adults***

GROWTH CHARTS
IN CHILD AND ADOLESCENT OBESITY

Growth charts allow to

1. understand the dynamic of obesity development
2. assess its degree according to age and sex
3. compare weight and height velocity
4. suggest a specific cause
5. define therapeutic goals
6. perform public health surveys

Which growth charts are useful to interpret and assess obesity in children and adolescents?

Weight and height

- Simple growth indicators
- Sex difference
- Weight for height ratio allow to detect stunting
- *Allow to detect if weight increase or height levelling off or both are responsible for body mass index increase*

Body mass index

- Combines weight and height: weight (kg)/height $(m)^2$
- ***Well correlated to subcutaneous fat mass***
- ***Reflects the change in body shape of the children during growth***
- Validity across age ranges
- Differences according to ethnicity
- Should never be interpreted alone in clinical setting

Which growth charts are useful to interpret and assess obesity in children and adolescents?

Skinfolds thickness

- Subcutaneous fat varies according to, sex, age and ethnicity
- No tight relationship to the risk of metabolic complications, as visceral fat does.
- Measurements techniques and reference values difficult to standardize.

Trunk circumferences

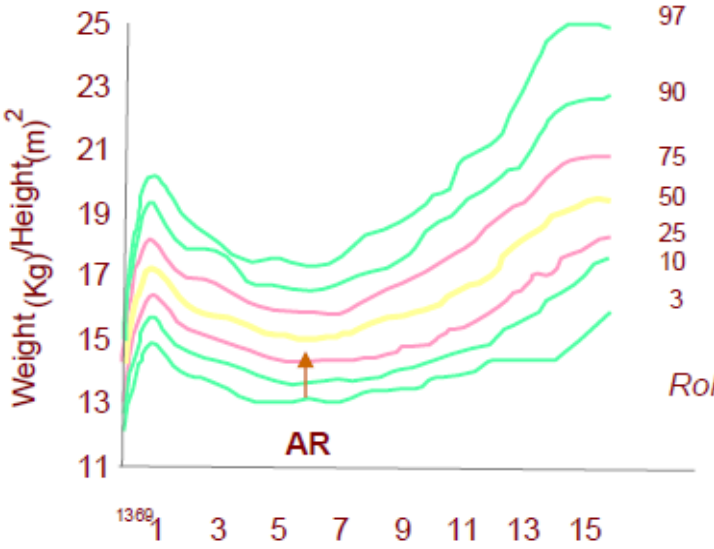
- Abdominal fat correlated with metabolic abnormalities in children and adolescents as in adults
- Waist and hip circumferences, waist/hip ratio

Adiposity development (BMI and Skinfolds)

BMI pattern is similar with the pattern of skinfold thickness

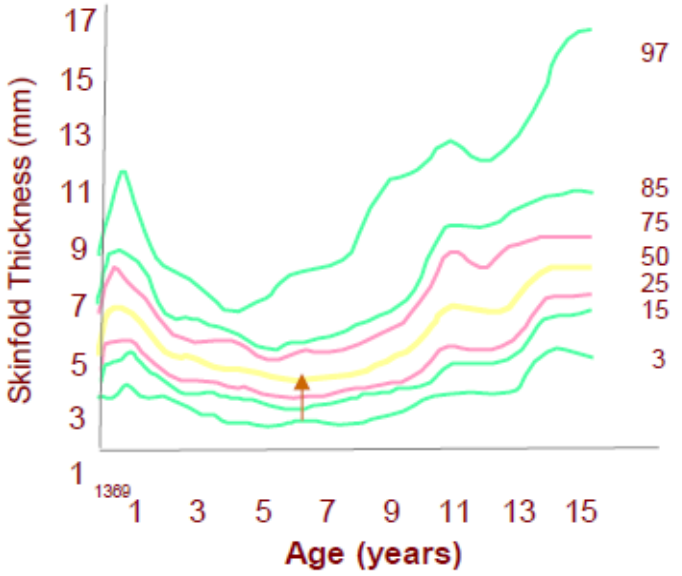
The nadir of the curve is named the « Adiposity rebound » (AR)

$BMI_{(kg/m^2)}$ = Weight/Height²



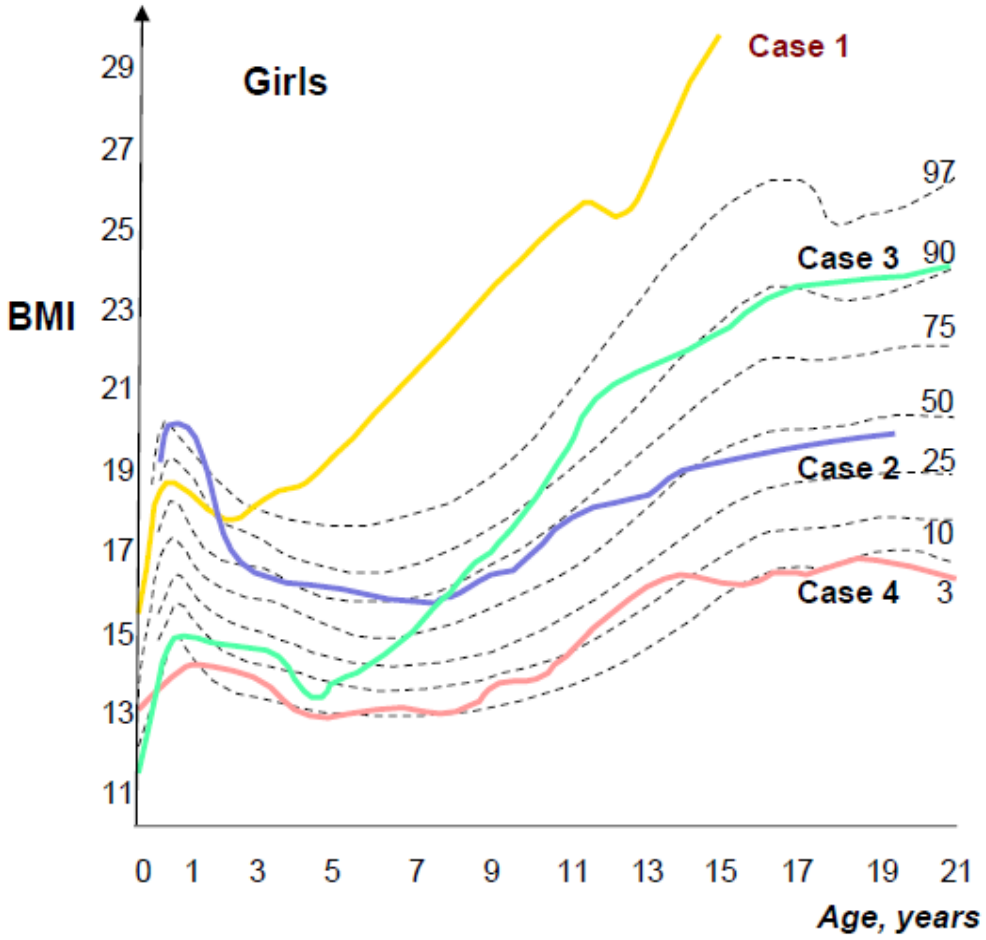
Rolland-Cachera et al.,AJCN 1982

Subscapular skinfold (mm)



(Sempé et al., 1979)

Four examples of individual BMI development and age at Adiposity Rebound (AR)



A fat child can stay fat after an early AR (n° 1), but join average after a late rebound (n°2)
A thin child stay thin after a late AR (n°4) or become fatter after an early rebound (n° 3)
(after Rolland-Cachera et al., ***Ann Hum Biol*** 1987)

Which growth charts ?

1. **International Obesity Task Force (IOTF) BMI only**
   - *For epidemiological purpose only*
   - Mathematical construction based on data of 6 populations around the world
   - Brings continuity between obesity threshold in children and adolescents and adults.
   -
2. **World Health Organization (WHO) W, H, BMI**
   - Established until the age of 5 yrs on the longitudinal follow up of healthy breast fed children from all continents
   - Repeated cross-sectional measurements beyond 5 yrs of age up to 18 yrs old

3. **Centre for Disease Control of the USA and other National Growth Charts W, H, BMI**
   - CDC: widely used
   - All of them reflects a local population's growth pattern and may be modified over time

***Table 1:* WHO Classification of nutrition conditions in children and adolescents based on anthropometry**

Classification	Condition	Age: Birth to 60 months[1,3] Indicator and cut-off	Age: 61 months to 19 years[2,3] Indicator and cut-off
Based on body mass index (BMI)	Possible risk of overweight	BMI-for-age (or weight-for-height) > 1SD	
	Overweight	BMI-for-age (or weight-for-height) > 2SD	BMI-for-age >1SD(equivalent to BMI 25 kg/m^2 at 19 y)
	Obese	BMI-for-age (or weight-for-height) > 3SD	BMI-for-age >2SD (equivalent to BMI 30 kg/m^2 at 19 y)
	Thin		BMI-for-age < –2 to –3 SD
	Severely thin		BMI-for-age <–3 SD
Based on weight and height	Stunted	Height-for-age <–2SD to –3SD	Height-for-age <–2SD to –3SD
	Severely stunted	Height-for-age <–3SD	Height-for-age <–3SD
	Underweight	Weight-for-age <–2SD to –3SD	Weight-for-age (up to 10y) <–2SD to –3SD
	Severely underweight	Weight-for-age <–3SD	Weight-for-age (up to 10 y) <–3SD
	Wasted	Weight-for-height <–2SD to –3SD	
	Severely wasted	Weight-for-height <–3SD	

Note that stunting may be associated to obesity in short for age children

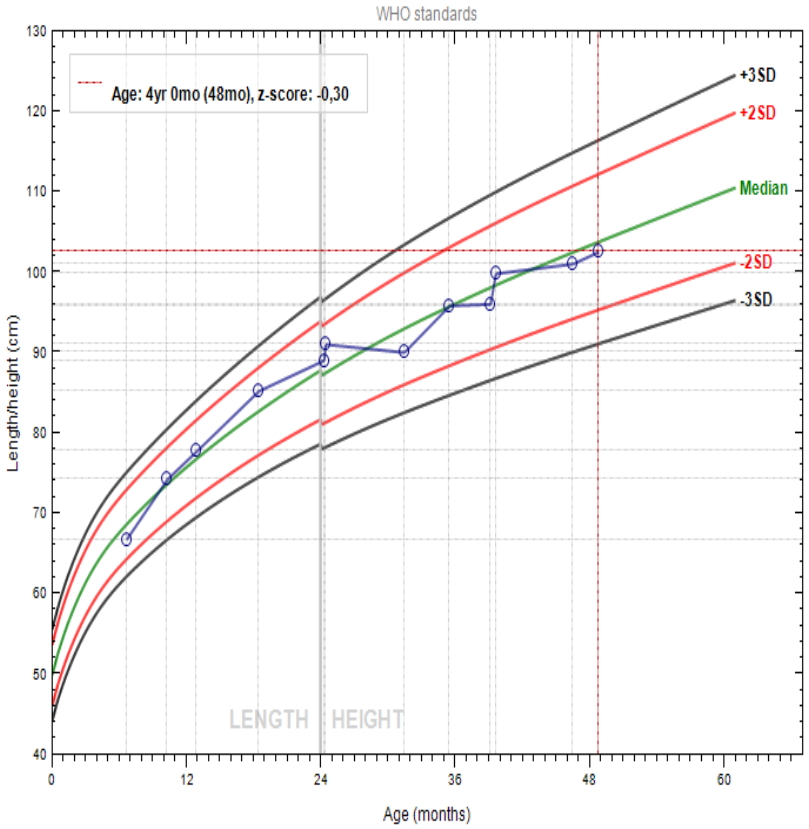
Examples of growth charts

Orientation to some specific aetiologies of obesity

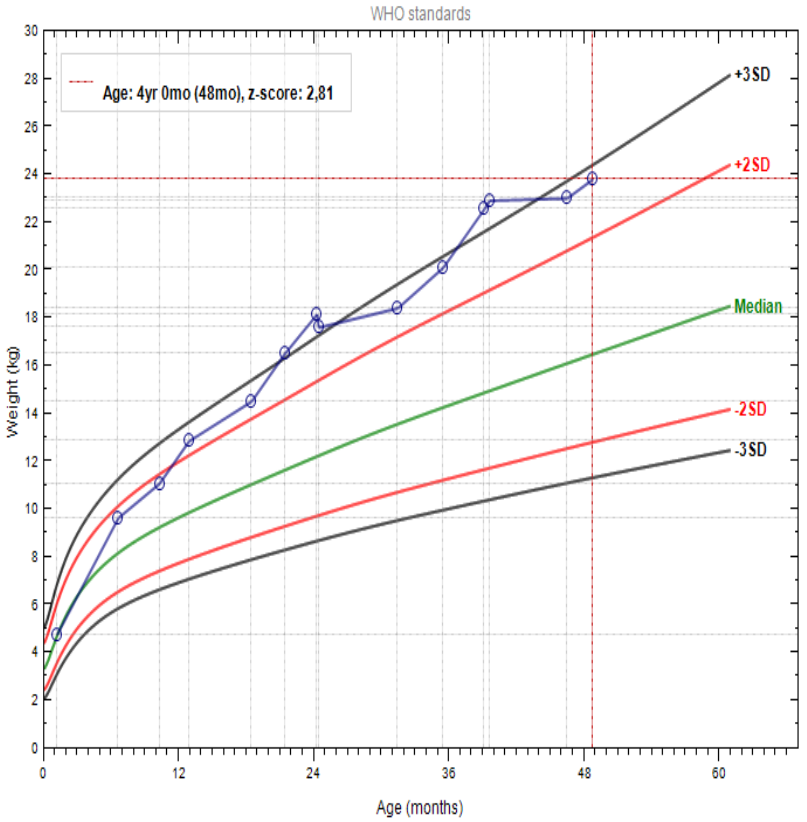
1. **Common obesity of likely polygenic origin**
2. **Obesity of psychological cause**
3. **Hypothyroidism**
4. **Growth hormone deficiency**
5. **Prader Willi syndrome**
6. **Mutation on the leptin pathway**

Common obesity of likely polygenic origin

HEIGHT FOR AGE

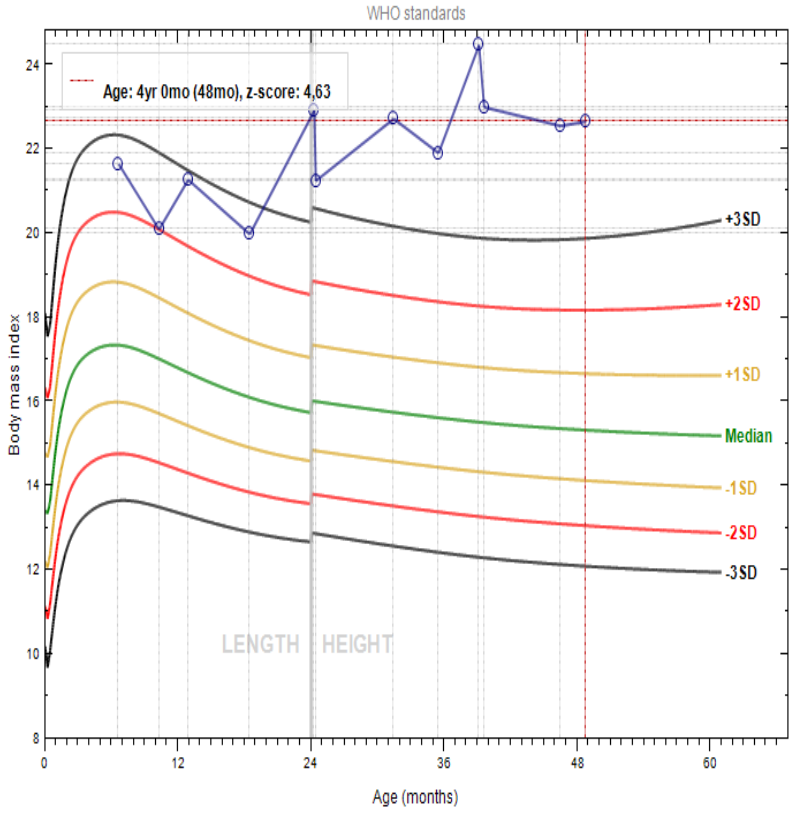


WEIGHT FOR AGE



Common obesity of likely polygenic origin

BMI FOR AGE



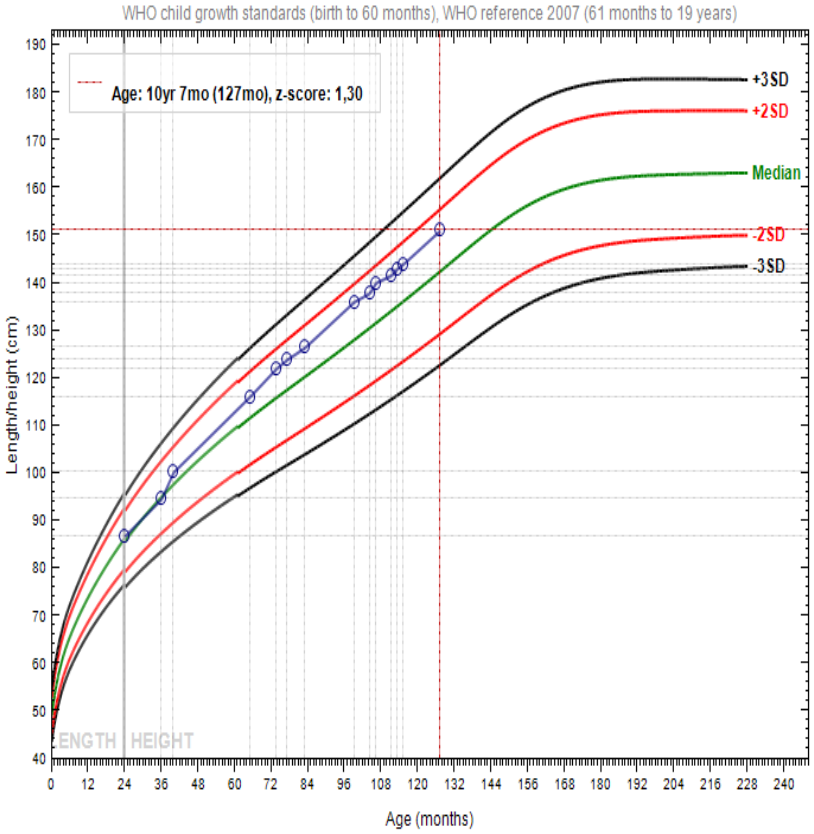
- Progressive increase of BMI

despite periods of improvement due to diet restriction/lifestyle changes

- Obesity since early childhood
- Increased appetite since early childhood
- Height velocity normal
- Positive family history of obesity : 1 or 2 parents
- Normal fT3,fT4, TSH
- Increased insulin levels
- Normal or slightly advanced bone age

Obesity due to psychological reason

HEIGHT FOR AGE



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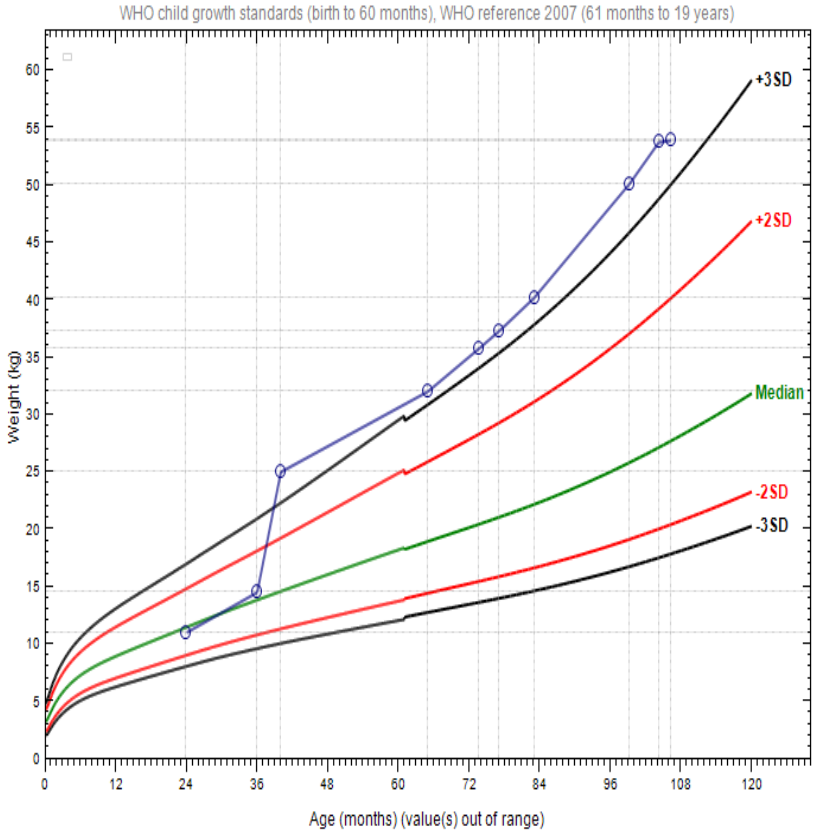
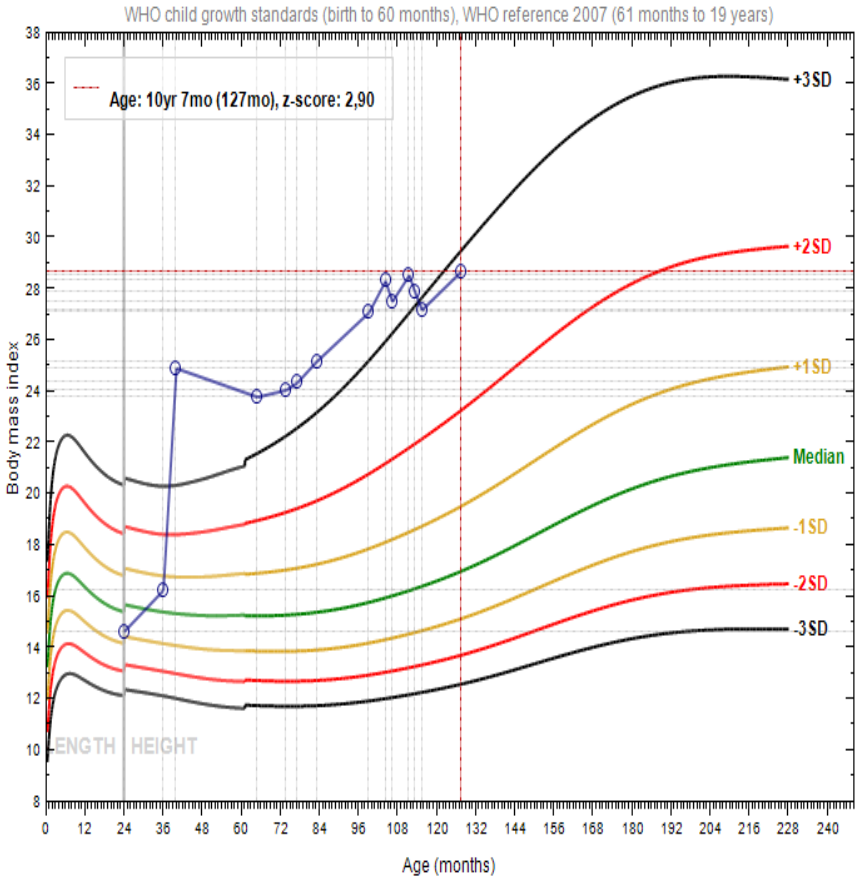


Obesity due to psychological reason

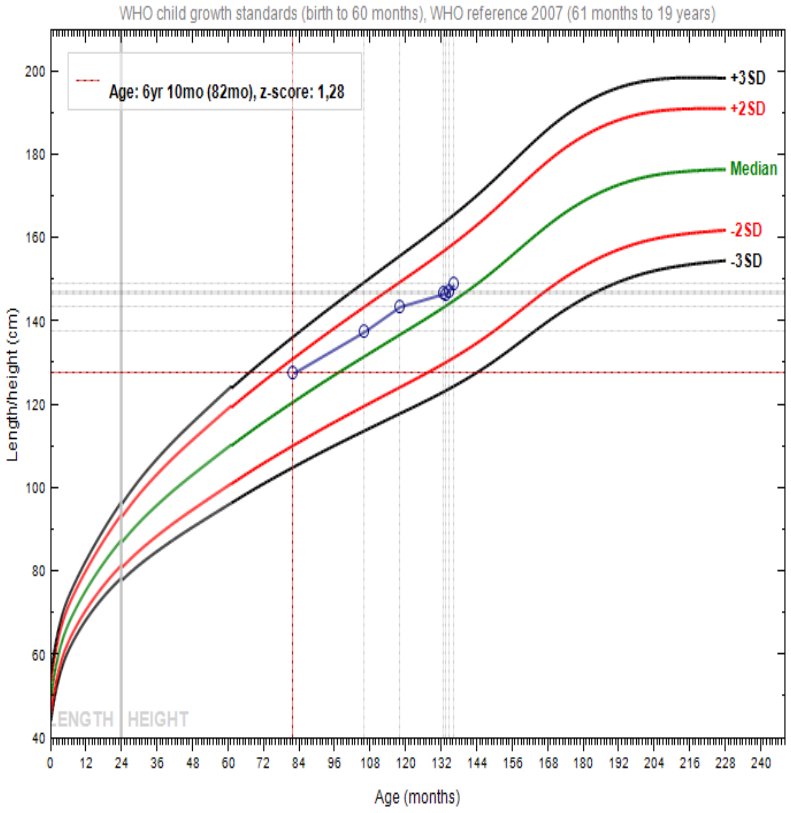
BMI FOR AGE



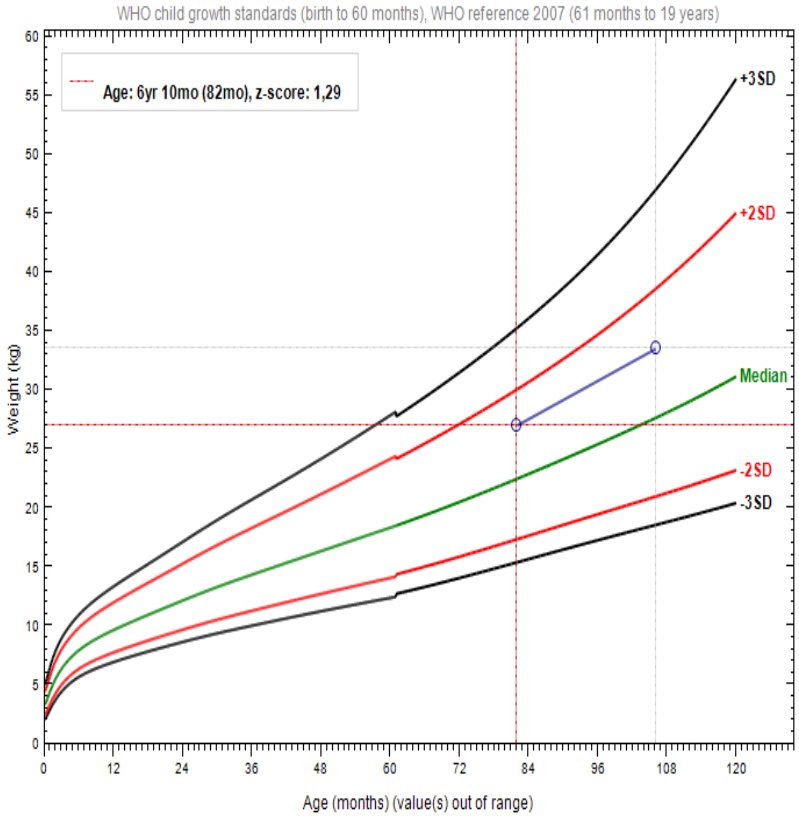
- **Sudden weight gain**
- **Increased or normal height velocity linked to sudden huge weight gain**
- Increased food intakes
- Mood changes
- Clinical examination
  - Little or no striae
  - No sign of intracranial hypertension
  - Normal blood pressure
  - No polyuria polydipsia
- Biology and MRI rule out secondary obesity of tumoral origin
- Psychological examination confirms underlying psychological cause

Hypothyroidism

HEIGHT FOR AGE

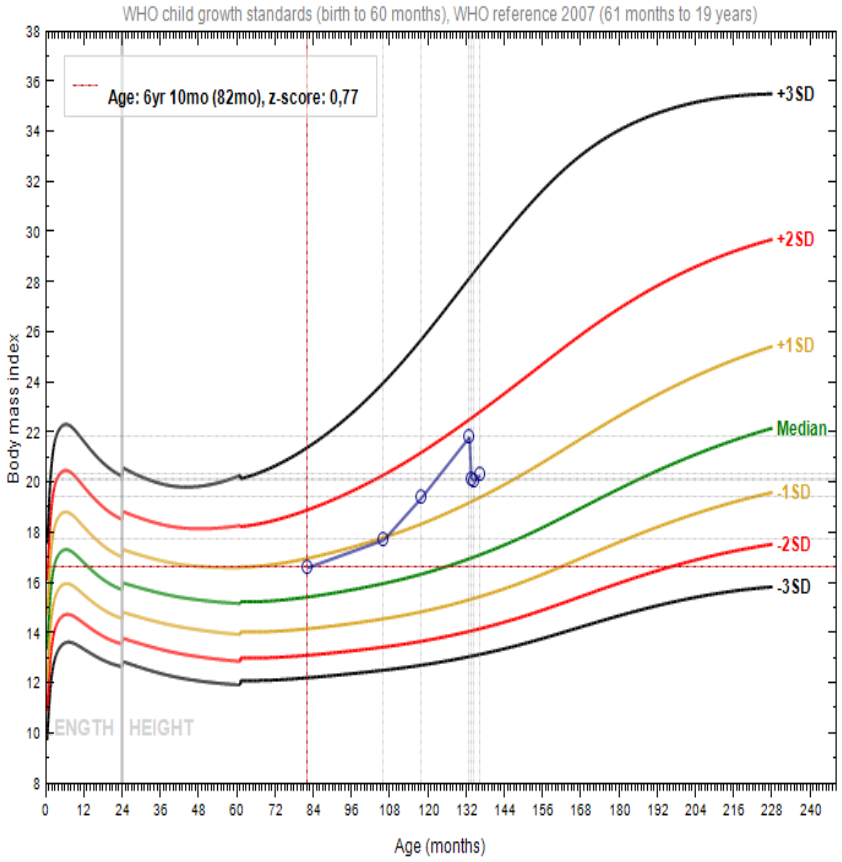


WEIGHT FOR AGE



Hypothyroidism

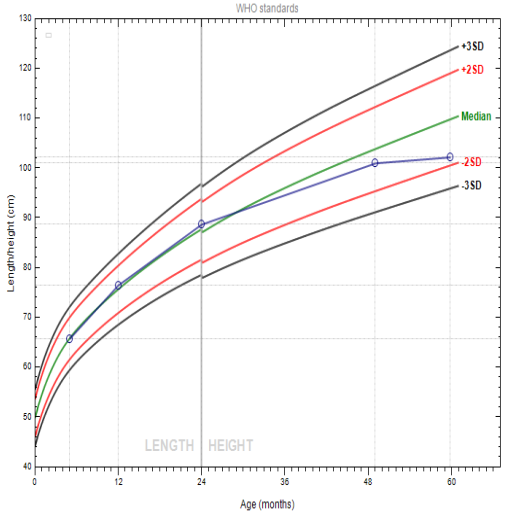
BMI FOR AGE



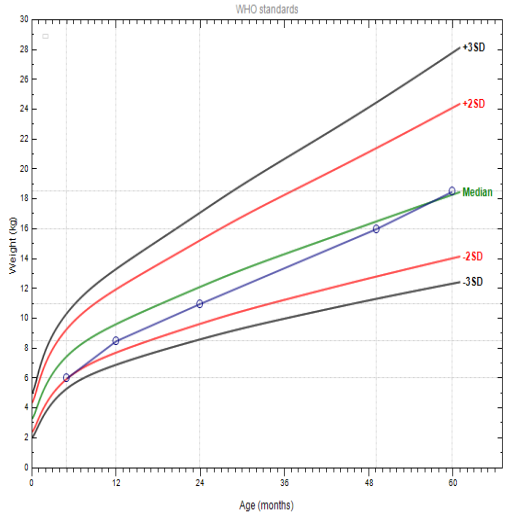
- Progressive weight gain
- Progressive decrease in height velocity
- No change in appetite nor life style
- On questioning reports easy fatigue
- Palpable enlarged thyroid gland
- Decreased fT3,fT4
- Increased TSH
- Delayed bone age
- Treatment: thyroid hormones

Growth Hormone (GH) deficiency

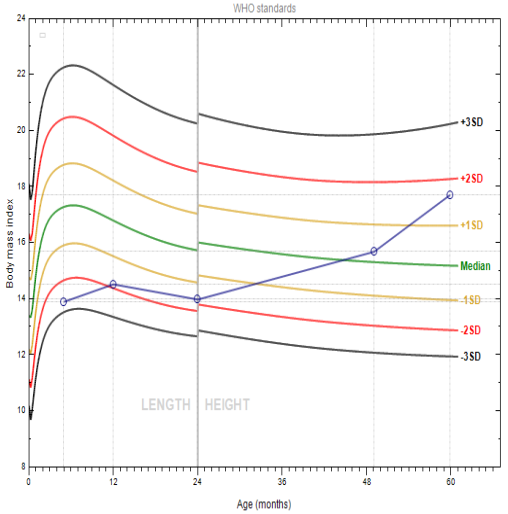
HEIGHT FOR AGE



WEIGHT FOR AGE



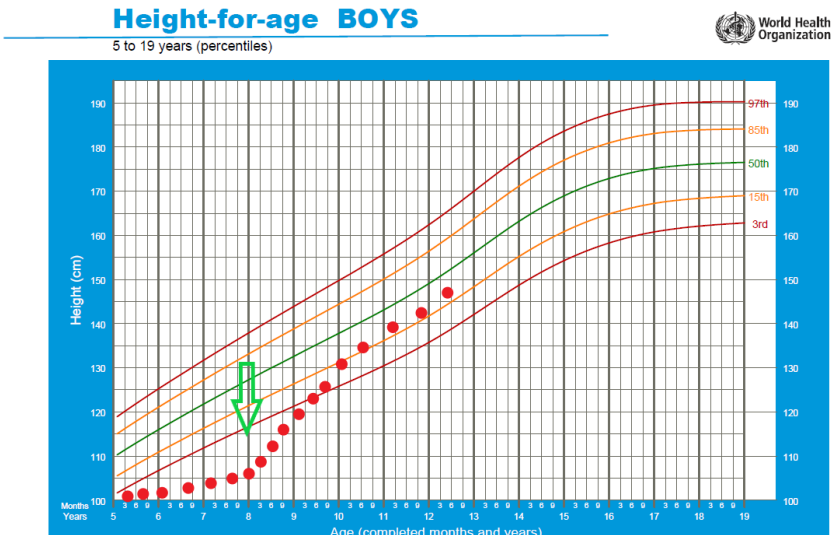
BMI FOR AGE

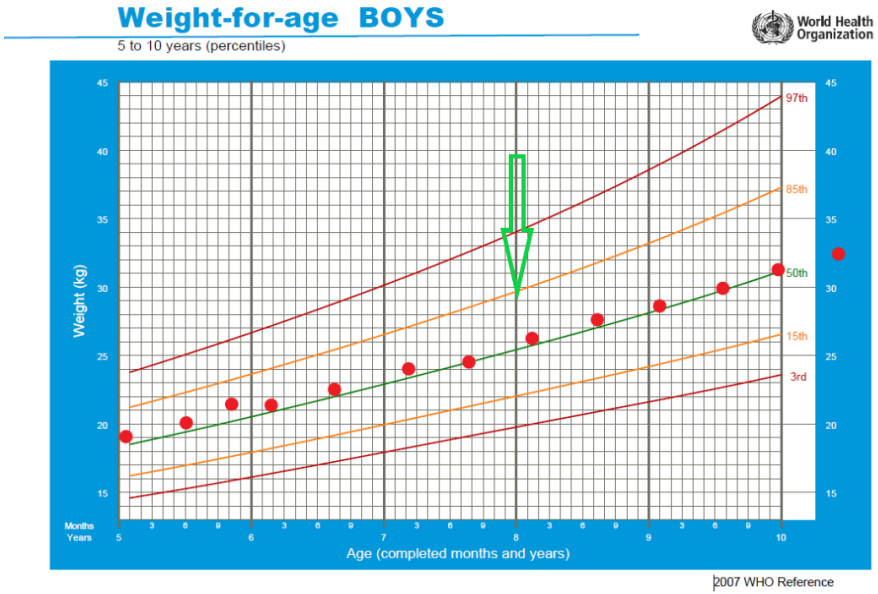


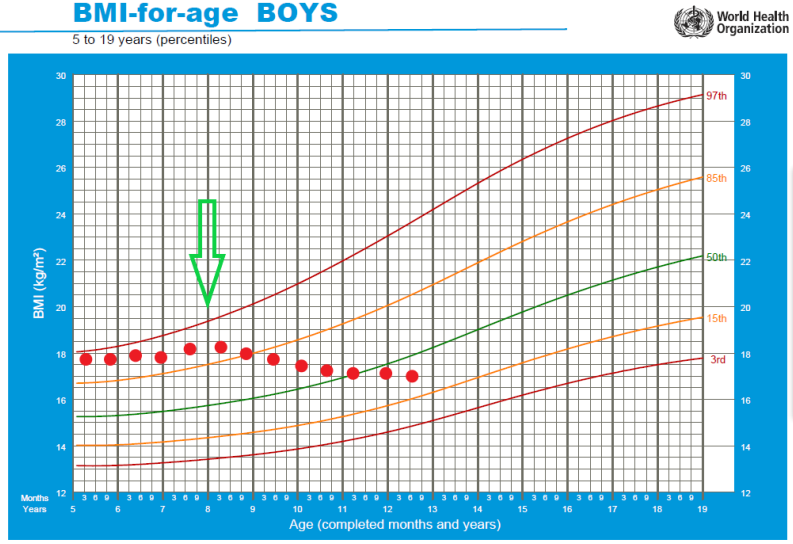
- Progressive weight gain
- Progressive decrease in height velocity
- No change in appetite nor life style
- No other abnormal clinical feature
- Normal fT3,fT4, TSH , cortisol, steroids
- Decreased IGF-I
- Delayed bone age

Growth hormone deficiency

Follow up and effect of GH injection



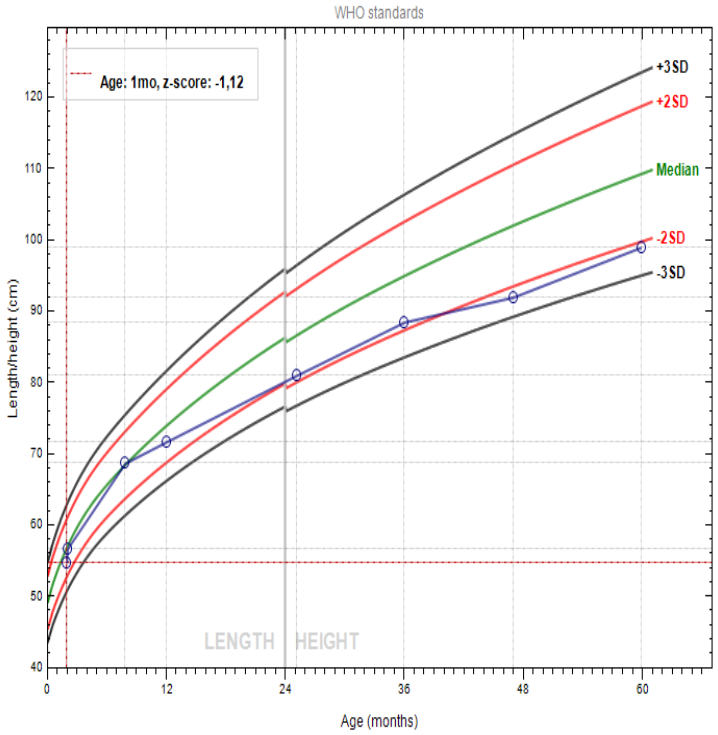




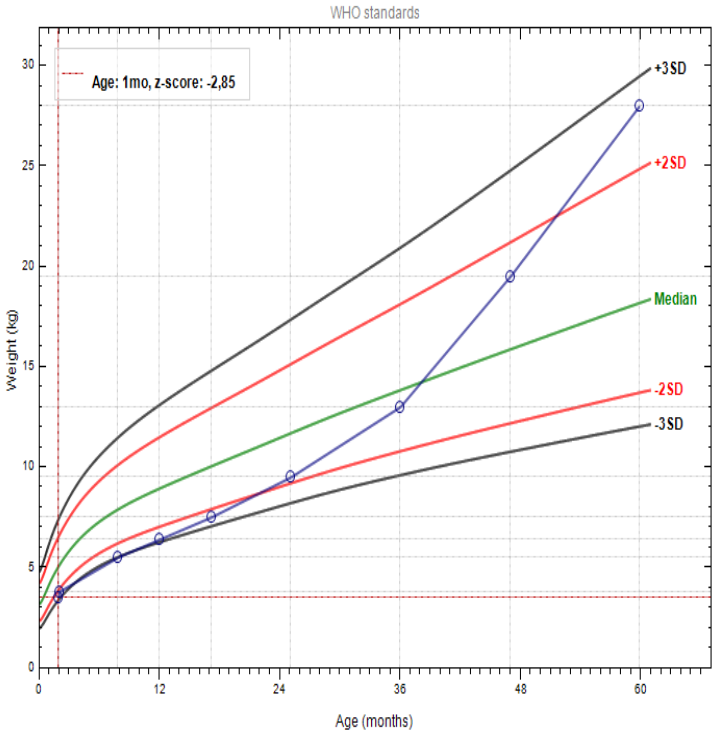
The treatment of the GH deficiency induces a height increase and a reduction of BMI.
Weight gain remains regular on the 50th centile for age and sex..

Prader-Willi Syndrome

HEIGHT FOR AGE

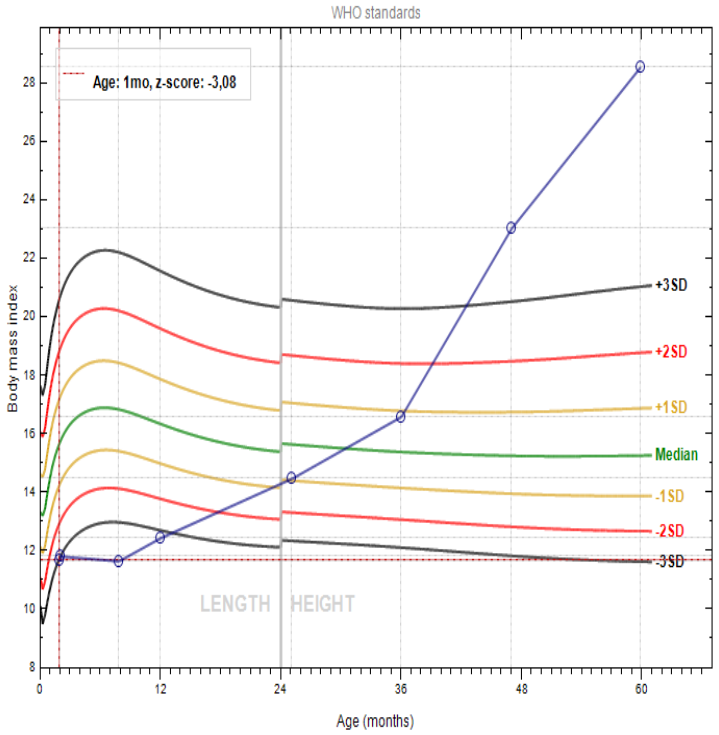


WEIGHT FOR AGE



Prader Willi Syndrome

BMI FOR AGE

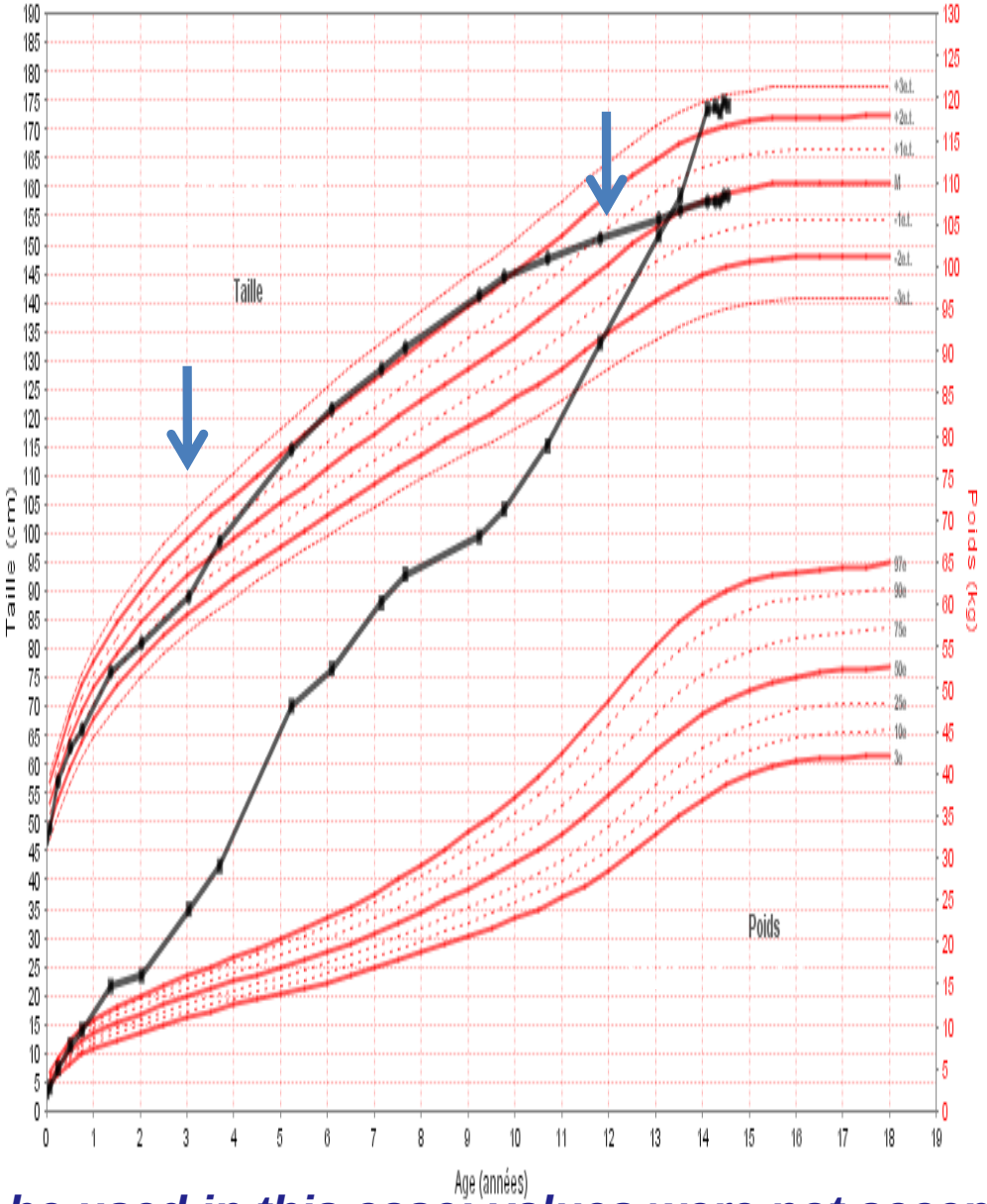


- Normal birth weight but marked hypotonia and early feeding difficulties
- Delayed motor skills and mental development
- Mild dysmorphia
- ***Sudden major increase in appetite around 18 months***
- Height gain decrease despite major weight gain
- Common association to secondary GH deficiency
- Genetic test confirms the deletion of the 15q11.2 region
- Note that current therapeutic strategies may avoid the onset of obesity

DOUBLE MUTATION OF THE LEPTIN RECEPTOR

Birth 3100 g 49 cm
Full term, healthy baby
Lean parents
No dysmorphic feature
Normal mental development
Delayed puberty until 14 yrs

- ✓ Severe early obesity
- ✓ Temporary increased height velocity
- ✓ Height spurt of puberty buffered



The WHO software could not be used in this case: values were not accepted !

Key points 1

- Follow up of pregnancy and the first two years of life (1000 days) are unique opportunities to reduce the early risk factors of obesity

- Childhood obesity is a growth disorder at the expense of fat mass with multiple underlying aetiologies some of which require specific treatment

- Primary obesity of multigenic origin triggered by modern lifestyle changes is by far the most common situation

- Information about
  - pregnancy and neonatal events
  - clinical examination
  - growth pattern
  - ➢ Together lead to detect putative causes of obesity
  - ➢ Are mandatory before setting a therapeutic plan

- First steps toward assessing a specific aetiology is based on simple blood tests and comparison of bone age to actual chronological one

Key points 2

- **Growth charts**
  - WHO growth charts apply to all children around the world until adulthood
  - Do not accurately reflect ethnic variations in body fat and lean mass
  - Allow to follow-up individual children and perform epidemiological study
  - Are mandatory in order to interpret all growth disorders including obesity and malnutrition
  - WHO charts are the best free of access tool at present

- **Growth charts and the diagnosis of obesity**
  - The diagnosis of obesity in childhood is based on weight, height and BMI measurements
  - Anthropometry should always be interpreted in the light of clinical data
  - BMI reflects skin folds thickness, i.e. subcutaneous fat mass and total fat mass in an age and sex specific manner
  - There is a need for adaptation to ethnicity
  - There is no single BMI cut-off for the diagnosis of obesity across childhood and adolescence

questions

1. What does the 1000 day hypothesis mean

- ❑ That the first 1000 days after birth are essential for child health
- ❑ That the 1000 days that include pregnancy duration and the first 2 years of life are essential for child health
- ❑ Neither of those: it is just an hypothesis

2. **Which cut off of BMI is used to define childhood obesity**

- ❑ 18 kg/m²
- ❑ 24 kg/m²
- ❑ None of them: threshold varies with growth

3. **Which charts should be drawn in priority when facing a child with obesity?**

- ❑ Weight
- ❑ Height
- ❑ Body mass index
- ❑ Subscapular skin fold
- ❑ Waist circumference

questions

1. Is body mass index well correlated in children to ?

- ❑ Limb fat mass
- ❑ Total fat mass
- ❑ Lean body mass

2. **Which among these hormone deficiency may be associated to severe early obesity ?**

- ❑ Thyroid hormones
- ❑ Growth hormone
- ❑ Leptine or leptine receptor

3. **Which is the most common cause of obesity in children?**

- ❑ Common obesity of polygenic origin
- ❑ Type 2 diabetes
- ❑ Low birthweight
- ❑ Prematurity

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