MMed and DCH Lectures

Endocrine problems in children

May 17th , 2021

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7-year-old girl, unwell 3 weeks, weight loss, lethargy, respiratory distress

Blood gas

pH	6.9	
pCO_2	11.1	
pO_2	101	
HCO_3	2	
BE	-22	

Electrolytes

Na^+	128	(135-145)
K^+	5.6	(3.5-5)
Cl^-	92	(95-110
Urea	10.6	(2.5 to 7)
Creat	120	(70-100)

Metabolic acidosis

Poorly compensated

Anion gap?

(Na + K) - (Cl + HCO3) = 39.6

Normal anion gap 3-10 mmol/L

What are the unmeasured anions?

Lactate 3.3 mmol/L

Ketonuria ++++

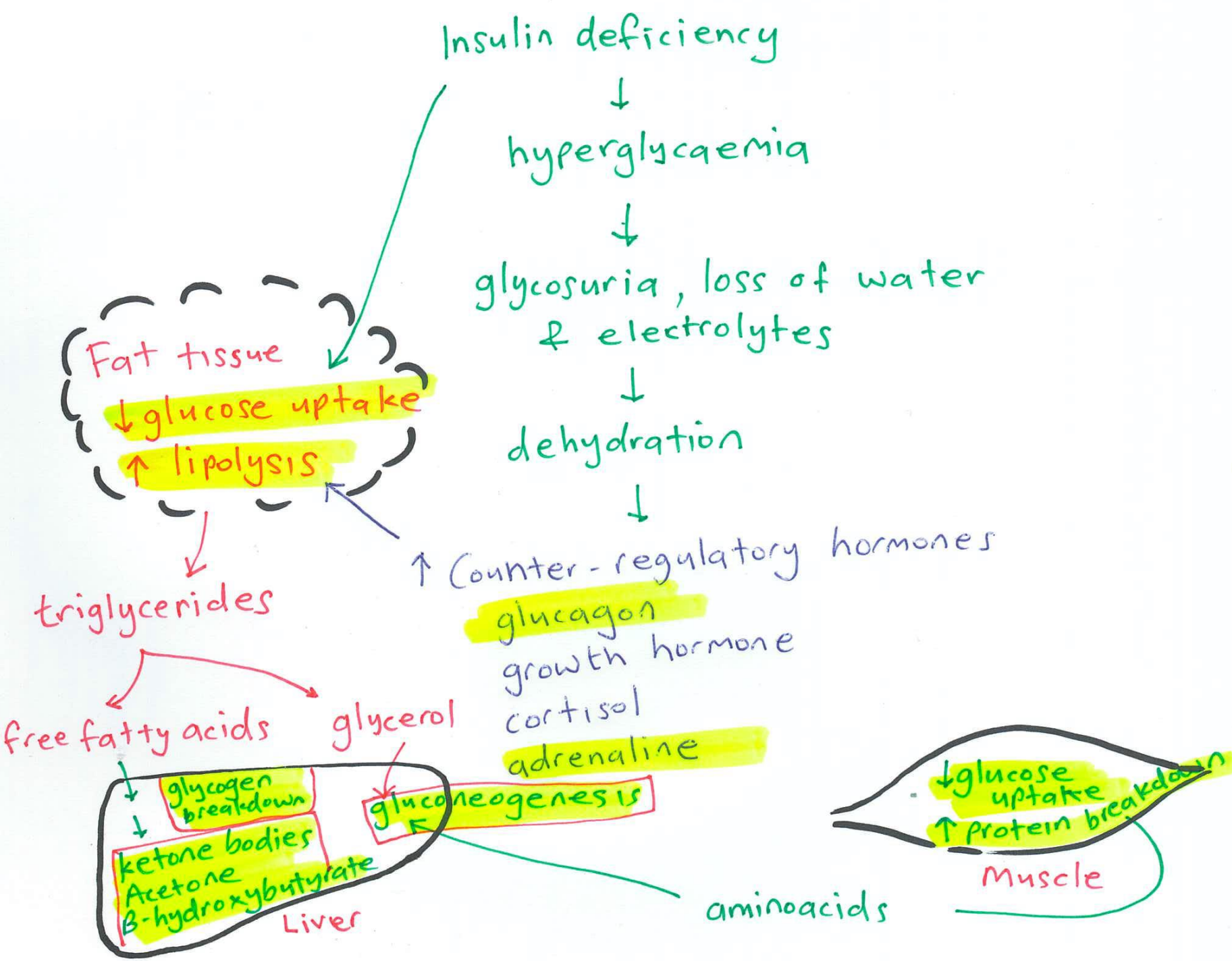
Glucose ++++ (35 mmol/L in lab)

Diabetes

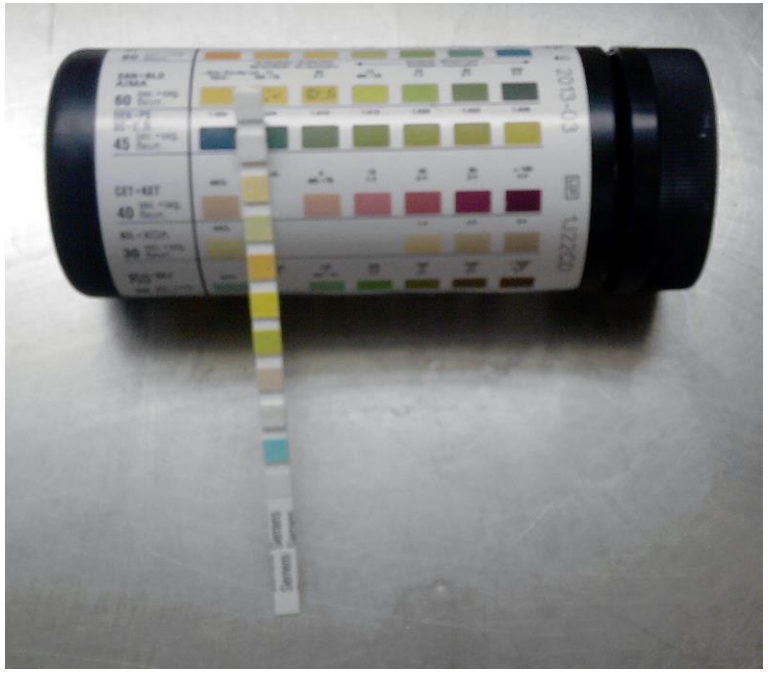
- Type I diabetes increasing around the world
- Cases reported in PNG since 2000.
- Type II diabetes increasing in children and adolescents (NZ / Polynesia)
- Clinical features
  - Weight loss
  - Thirst
  - Polyuria
  - Vomiting (ketosis)
  - Confusion, coma

Insulin functions

- Hormone for energy storage and anabolism (growth)
- Under the influence of insulin, glucose
  - Enters cells
  - Stored as glycogen in the liver
  - Stored as triglyceride in fats
- Under insulin deficiency, and influence of counter-regulatory hormones
  - Failure of glucose to enter cells
  - Glycogen breakdown
  - Triglyceride breakdown
  - Hepatic gluconeogenesis (from amino acids + glycerol)


Insulin deficiency
↓
hyperglycaemia
↓
glycosuria, loss of water & electrolytes
↓
dehydration
↓
↑ Counter-regulatory hormones
glucagon
growth hormone
cortisol
adrenaline
Fat tissue
↓ glucose uptake
↑ lipolysis
triglycerides
free fatty acids
glycerol
glycogen breakdown
ketone bodies
Acetone
β-hydroxybutyrate
Liver
gluconeogenesis
aminoacids
↓ glucose uptake
↑ protein breakdown
Muscle

Urine analysis



Leukocyte esterase			Tr		+		++		+++			
Nitrite			Pos		Pos							
pH		5.5		6.0		6.5		7.0		7.5		8.0
Protein		Tr		+		++		+++		++		
Blood		Tr		Tr		Tr		+		++		+++
Specific gravity		1.005		1.010		1.015		1.020		1.025		1.030
Ketones			Tr		+		++		+++		++	
Glucose			Tr		+		++		+++		++	
Bilirubin			+		++		+++					

Pathogenesis of type I diabetes

- Autoimmune destruction β-cells in Islets of Langerhans, which produce insulin
- T-lymphocytes infiltration of islet cells *months or years before*
- Genetic susceptibility, triggered by many different environmental agents
  - Genetic markers – multiple loci
  - Autoimmune markers – islet cell autoantibodies (85%), anti-insulin antibodies
- Role of virus infections - similarity to antibodies to coxackie B virus (IgM +ve in 39% of new diagnosis IDDM) and enterovirus

Pathophysiology of diabetic ketoacidosis

- Insulin deficiency → hyperglcaemia
- Fat and protein catabolism → ketone bodies (energy) → acidosis
- Dehydration (vomiting, osmotic diuresis from glucose and ketones) → acidosis
- Acidosis (ketosis, dehydration)
- Potassium (commencing insulin drives potassium into cells, so K+ will be low,

DKA treatment

- Replace fluid deficit
  - Correct shock if present (10-20ml/kg)
  - Correct dehydration over 48 hours
  - Use isotonic fluid
  - Pitfalls in estimation of dehydration – tachypnea, acidosis
- Replace potassium deficit (40-60mmol/L in rehydration fluid)
- Commence insulin infusion
  - 0.05-0.1 IU per kg per hour continuous IV
  - **OR 4th hourly 0.8–1 IU per kg per day divided by 6 subcutaneously**

7 y/o ♀ c DKA, 20 kg, dehydrated

insulin dose

1 IU x 20 = 20 IU/day

= 20/6 every 4 hours

≈ 3 IU 4th hourly

Type of fluid

Isotonic - Hartman's solution

+ 40 mmol KCl per Litre.

(10ml ampoule of KCl 1g = 13·4mmol

≒ 3 ampoule of KCl = 3g = 40 mmol)

fluid

~10% dehydrated

Maintenance

10 x 100 = 1000ml

10 x 50 = 500ml

= 1500ml

defecit 10% x 20L

≈ 2000ml

replace deficit over 48h

⇒ 2000/48 = 42ml/HR

+ maintenance

1500/24 = 63ml/HR

⇒ 105ml/HR for 48h

Monitoring in acute diabetic ketoacidosis

- Clinical signs of rehydration
- 4-6 h blood sugar
  - Fall in blood glucose – if <12mmol/L, add glucose to hydration fluid
- Resolution of ketosis
- [Na+] should increase

Treat complications

- Why did the child present *now*?

  Infection?

  - Staphylococcal infection
  - Urinary tract infection
  - Fungal infection

Types of insulin

Type of insulin	Onset	Peak	Duration	Example	Purpose
Rapid	15 mins	30-60	3-5 hours	NovoRapid	Reduce blood glucose levels at meal times
Regular	30-60 mins	2-4 hours	5-8 hours	Actrapid	
Intermediate	1-3 hours	8 hours	12-16 hours	Humulin / Protaphane	Manage the body's general insulin needs
Long	4 hours	No peak	24 hours	Lantus	

Mixed:

Humulin 30/70 (30% short, 70% intermediate acting Humulin)

Mixtard 30/70 (30% short, 70% intermediate Protaphane)

Establishing children with type I diabetes on treatment

- 1 IU per kg per day
- 2 subcutaneous injections
- 2/3 of total daily dose in morning, 1/3 at night
- 1/3 of each dose as short-acting insulin, 2/3 of each dose as intermediate-acting insulin

7 y/o ♀ 20 kg Type 1 diabetes

1 unit /kg /day = 20 IU

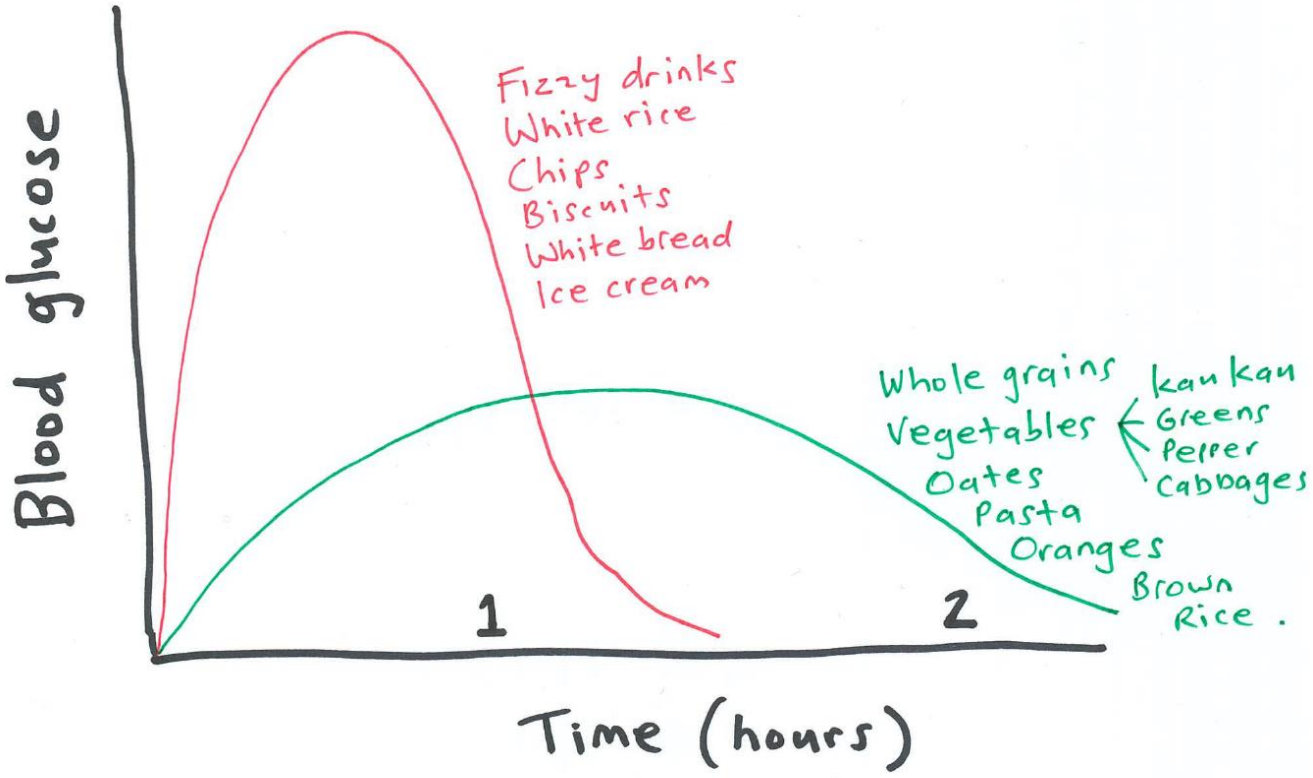
2/3 mane = 13 IU
- 9 IU intermed
- 4 IU actrapid

1/3 nocte = 7 IU
- 5 IU intermed
- 2 IU actrapid

mix intermediate acting & actrapid
give s.c. thigh, abdomen (lateral)
wipe skin c alcohol swab.

Ongoing management

- Diet
  - Complex carbohydrates
  - Avoid processed sugar
  - “Glycemic index”
- Exercise
- Supply of insulin
- Refrigeration at home
- Glucometer - regular BSL testing
- Urine checking for ketones, glucose
- Log-book
- HbA1C – measure of glycaemic control over the lifespan of red blood cells (120 days): normal 4-6%

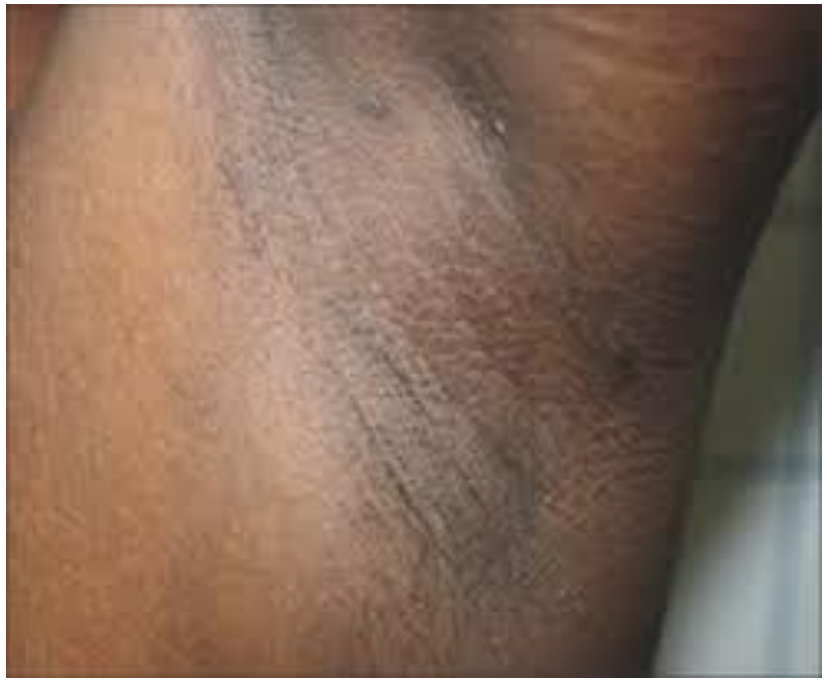


Risks

- Hypoglycaemia
  - Relative insulin overdose, especially if lack of adequate food supply, and especially overnight
- Palpitations, tachycardia, dizziness, pallor, weakness, seizures
- All children should carry source of glucose (glucose containting sweets)
- Reduce nocte insulin and assess diet if overnight hypoglycaemia

Longer term issues – from adolescents onwards

- Nephropathy – proteinuria
- Retinopathy – new vessel formation
- Neuropathy
- Cardiovascular disease
- Peripheral vascular disease
- Development issues (hypoglycaemia, recurrent DKA)
- Mental health issues



Skin

Acanthosis nigricans (type II)

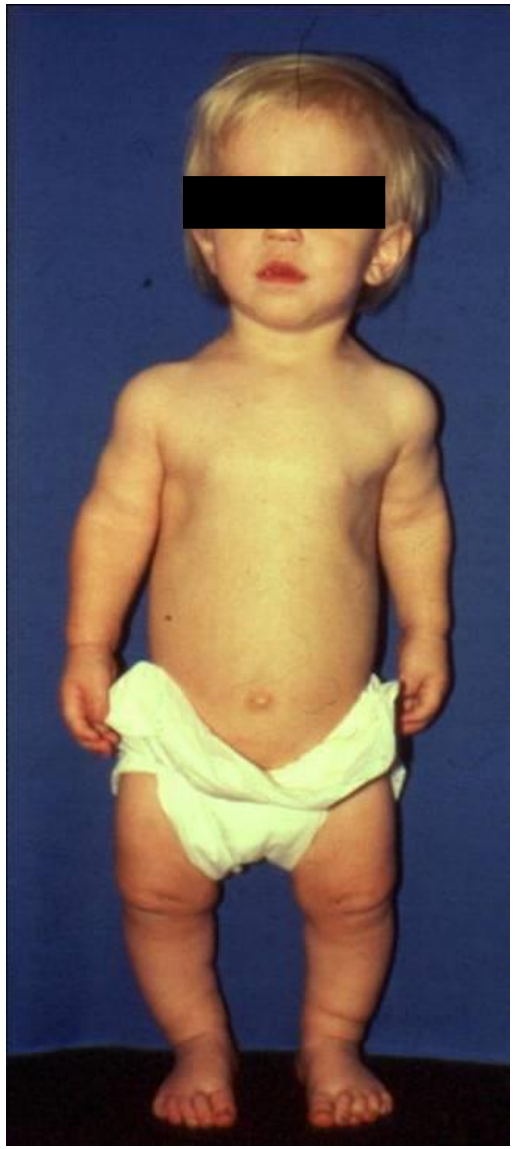
Fungal infection

Staph sepsis

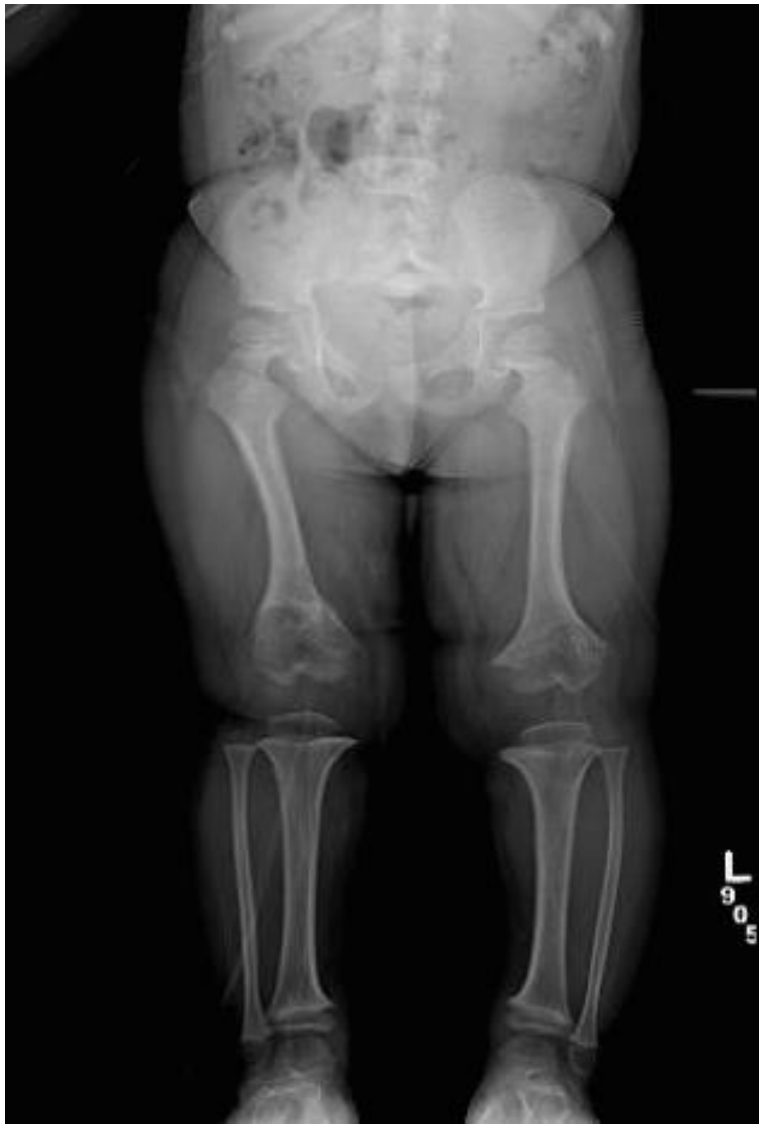
Lipoatrophy

Growth

- Genetic
  - Short parents have short children
  - Genetic syndrome – achondroplasia, Turner syndrome
- Nutritional
  - Stunting – chronic under-nutrition
  - Intrauterine under-nutrition – SGA
  - Chronic disease
- Hormonal (endocrine) factors
  - Growth hormone
  - Hypothyroidism
  - Steroid exposure

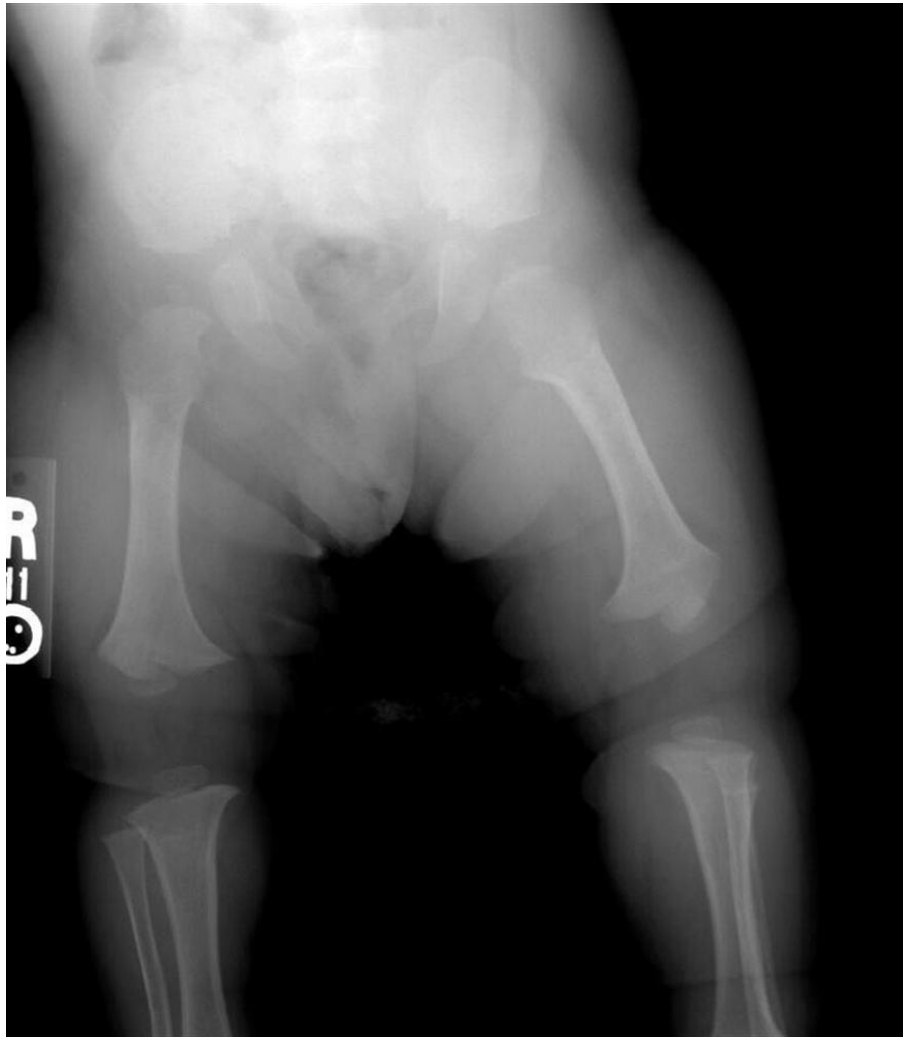


Large head, frontal bossing, small midface, flattened nasal bridge
Thoracic-lumbar kyphoscoliosis
Lumbar stenosis – cord compression
Foramen magnum stenosis



Achondroplasia

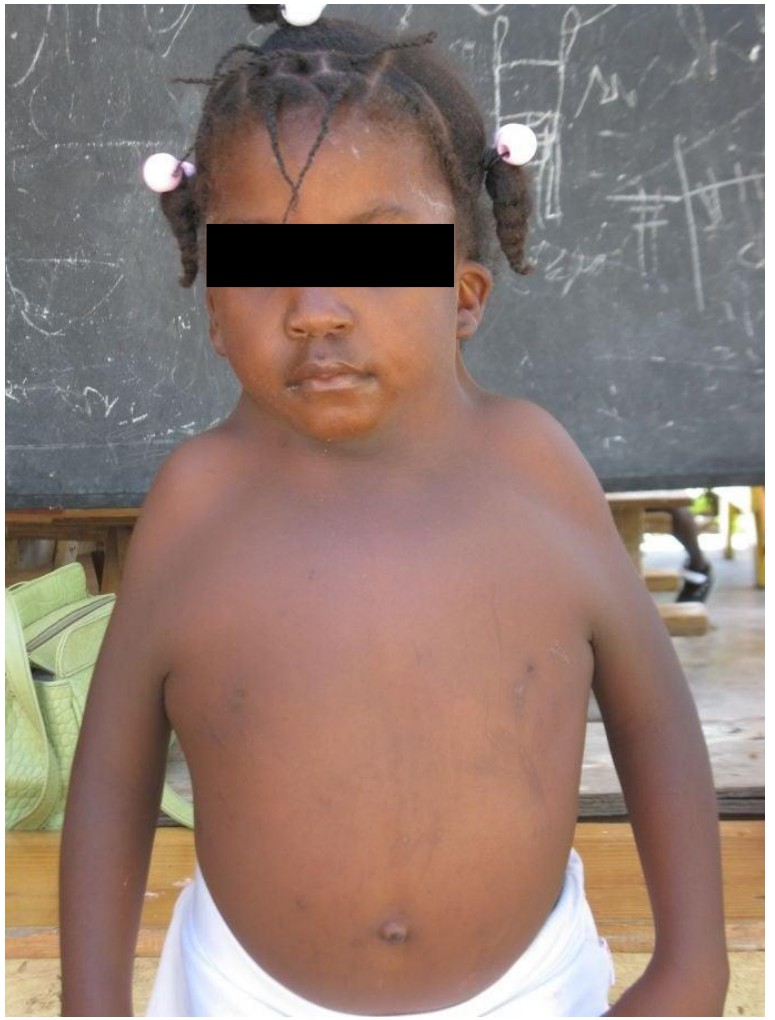
- Cartilage defect
- Mutation which inhibits chondrocyte proliferation in area of bone growth
- Normal intelligence
- Most children with achondroplasia will be healthy
- Recurrent otitis media
- Spinal cord compression
- Hydrocephalus
- Sleep apnoea



Clinical management of achondroplasia Arch Dis Child 2012;97:129–134

Turner syndrome (XO)

- Most common chromosomal cause of short stature.
- Some mosaic – mild and variable phenotype
- Webbed neck
- Broad chest
- Kyphoscoliosis
- Sensorineural hearing loss
- Coarctation of aorta, bicuspid aortic valve
- Horseshoe kidneys
- Amenorrhea
- Boys with similar phenotype Noonans syndrome (short stature and right heart obstruction)



Congenital hypothyroidism

- Lethargy
- Hoarse cry
- Feeding problems, often needing to be awakened to feed
- Constipation
- Puffy (myxoedema) and/or coarse facies
- Macroglossia
- Umbilical hernia
- Large fontanels
- Hypotonia
- Dry skin
- Hypothermia
- Prolonged jaundice, primarily unconjugated hyperbilirubinemia

If central hypothyroidism, also

- Hypoglycaemia (growth hormone and adrenocorticotropic hormone)
- Micro-penis (growth hormone and/or gonadotropins)
- Undescended testes (gonadotropins)
- Diabetes insipidus (vasopressin).

Causes of congenital hypothyroidism

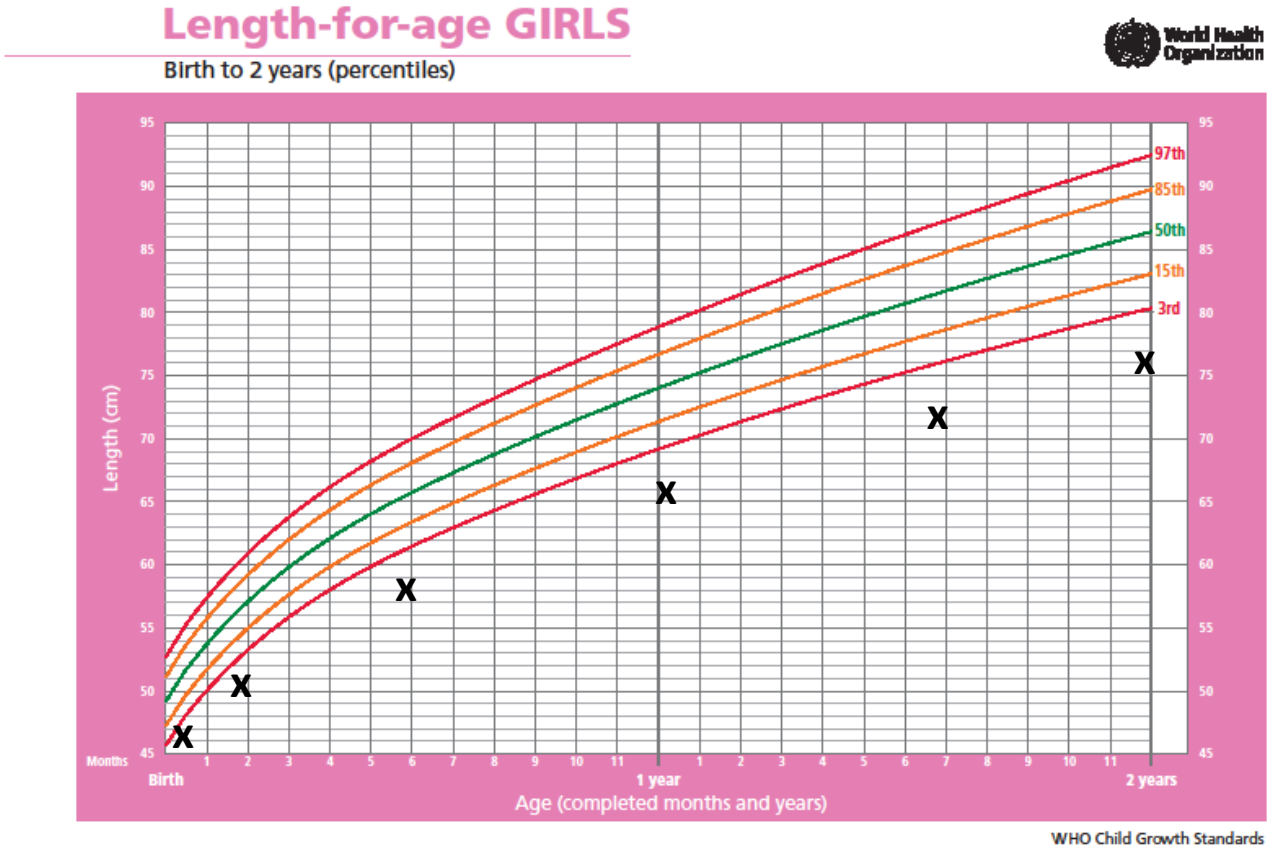
- 85% sporadic genetic mutations causing thyroid dysgenesis or agenesis: (ectopia, thyroglossal cyst, lingual thyroid, hypoplasia, hemi-agenesis, small thyroid)
- 15% hereditary inborn errors of thyroid hormone synthesis (autosomal recessive)
- **Iodine deficiency (endemic cretinism)** common in mountainous areas (sea salt contains iodine, fish and vegetables grown near the sea), e.g. Simbu
- Maternal hypothyroidism due to severe iodine deficiency: thyroid hormone is needed for normal maturation of the central nervous system, particularly myelination.
- **For the first 12 weeks of gestation, the foetus is completely dependent upon maternal T4**. During the 10th to 12th week of gestation, foetal TSH appears, and the foetal thyroid can concentrate iodine and synthesise iodothyronines. But the foetal thyroid makes little T4 until 20 weeks gestation.

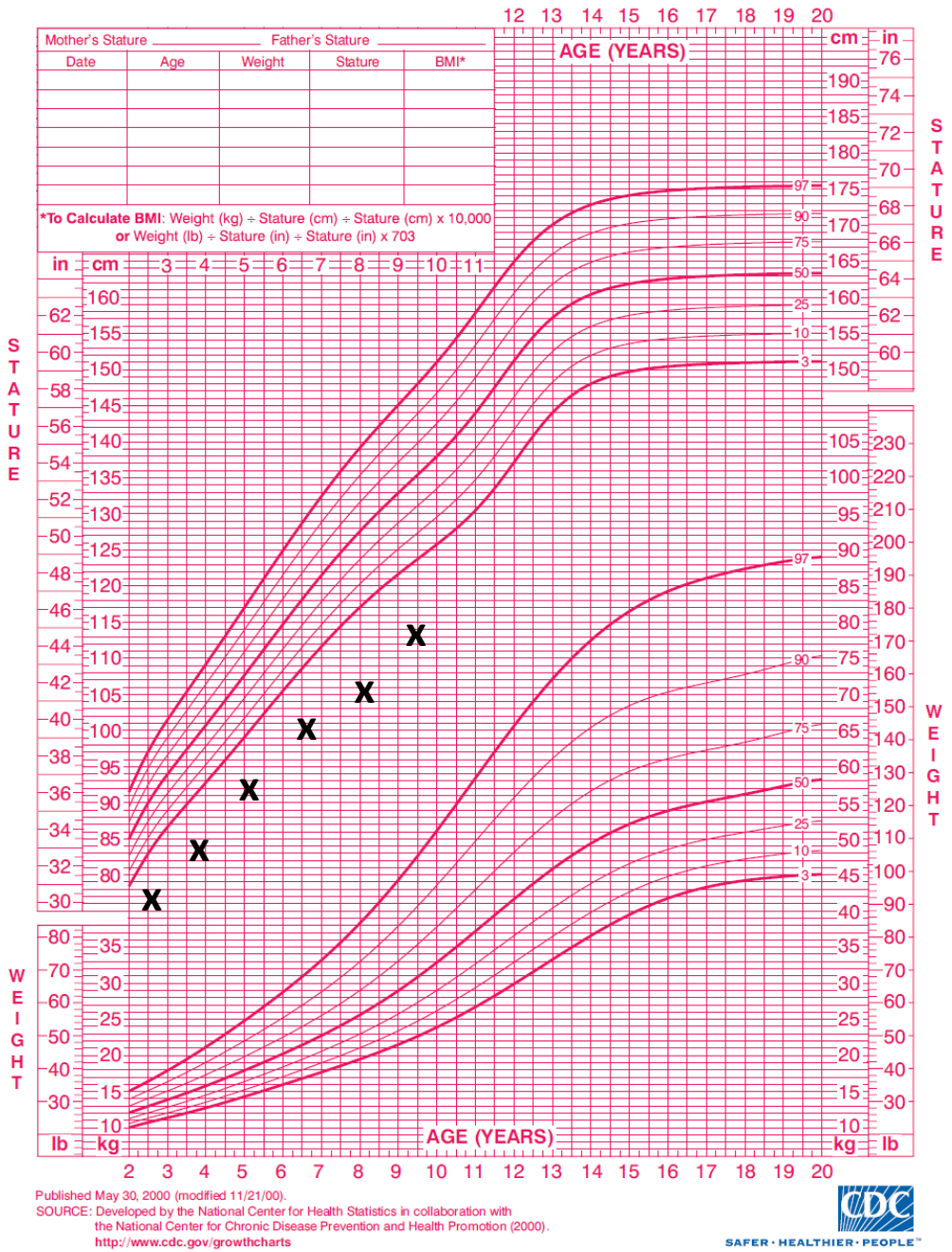
Diagnosis

- Primary hypothyroidism: High TSH, low free T4
- Subclinical hypothyroidism - High TSH, normal free T4 or total T4
- Central hypothyroidism - Low (or “normal” TSH), low free T4

Treatment

- Begin replacement therapy with levothyroxine before the 30th day of life
- Goal: to maintain T4 at >8 µg/dL, and TSH between 0.5 and 2.0 mU/L (mean normal range)





Constitutional short stature / Inherited
Genetic / syndromic cause
Intrauterine influences
Hormonal / endocrine