MMed and DCH Lectures

Weekly by Zoom

Prof Trevor Duke

MMed and DCH Lectures

Endocrine problems in children

September 7th, 2020

Prof Trevor Duke

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

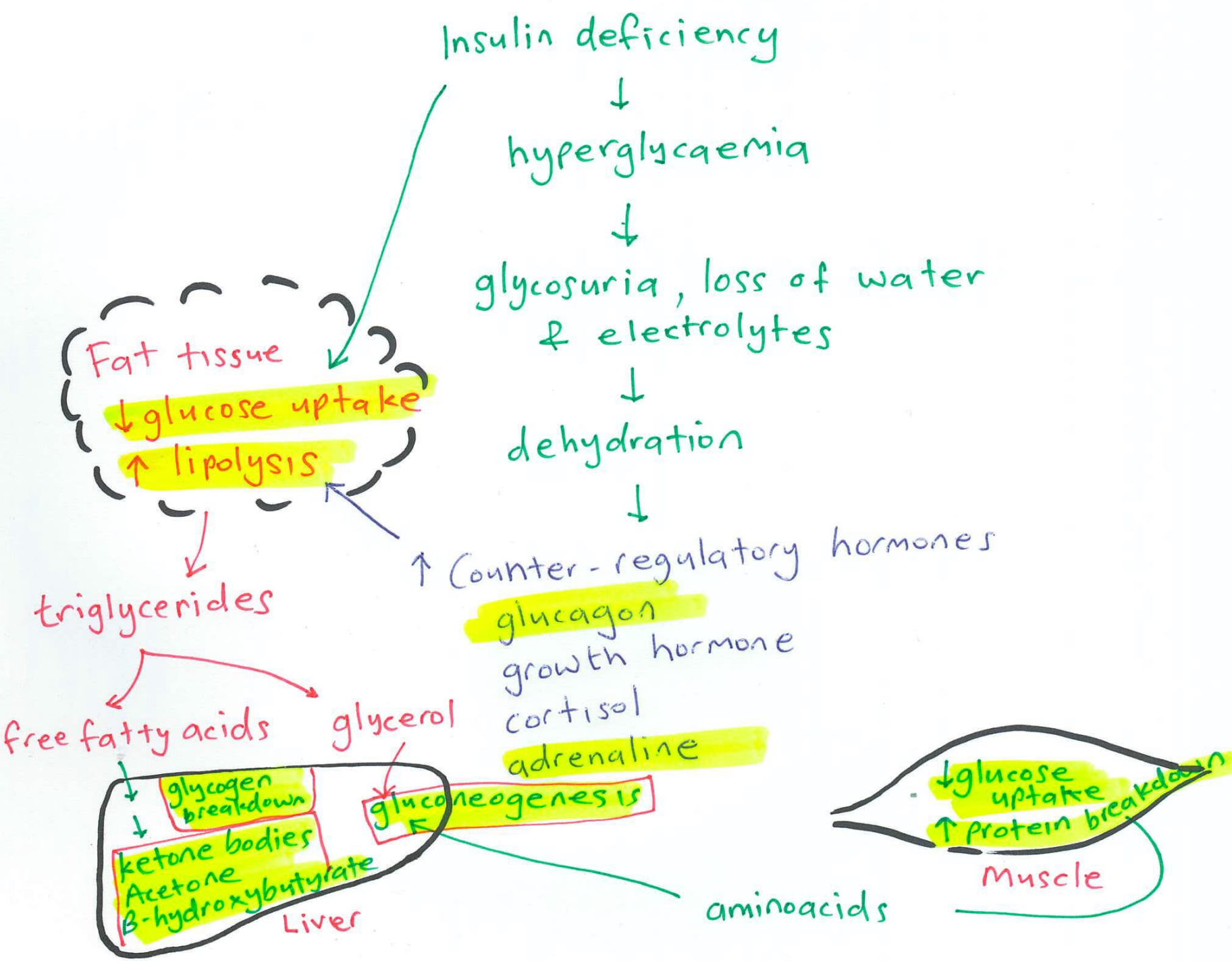
- Poorly compensated
- Anion gap?
  - (Na + K) - (Cl + HCO3) = 39.6
  - Normal anion gap 3-10 mmol/L
- What are the unmeasured anions?
- Lactate 3.3 mmol/L
- Ketonuria ++++
- Glucose ++++ (35 mmol/L in lab)

Diabetes

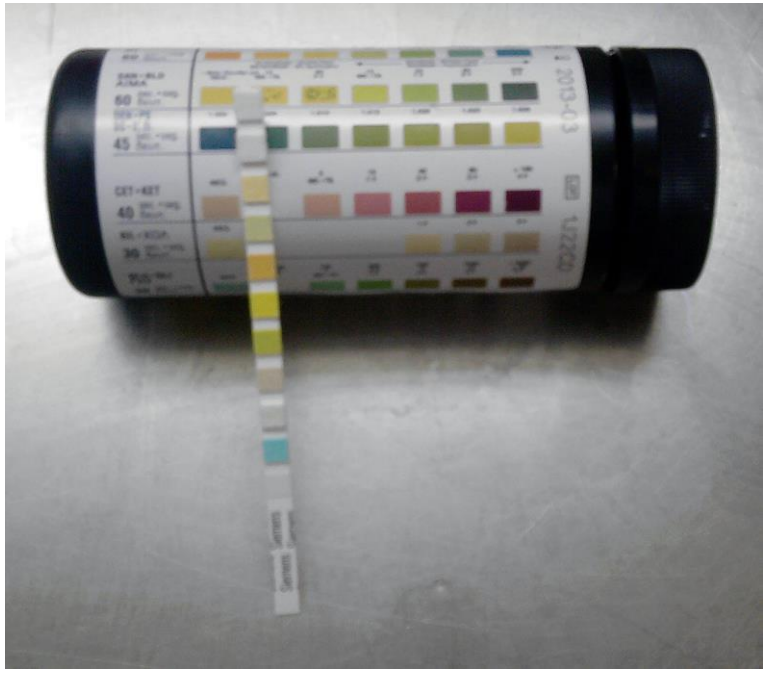
- Type I diabetes increasing around the world
- Cases reported in PNG since 2000.
- Type II diabetes increasing in children and adolescents (NZ / Polynesia)
- Clinical features
  - Weight loss
  - Thirst
  - Polyuria
  - Vomiting (ketosis)
  - Confusion, coma

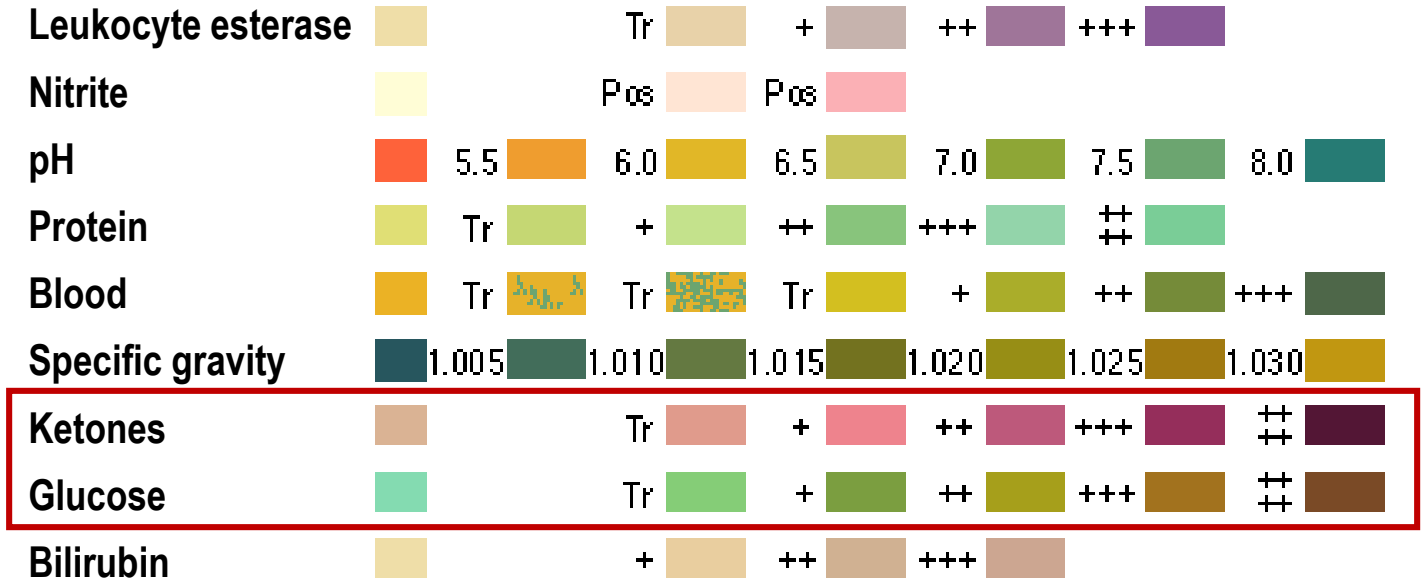
Insulin functions

- 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





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

Establishing children with type I diabetes on treatment

- 0.8-1 IU per kg per day
- 2 subcutaneous injections
- 2/3 of total daily dose in morning, 1/3 at night
- 2/3 of each dose as intermediate-acting insulin, 1/3 as short-acting insulin

7 y/o ♀ 20 kg Type 1 diabetes

1 unit /kg /day = 20 IU

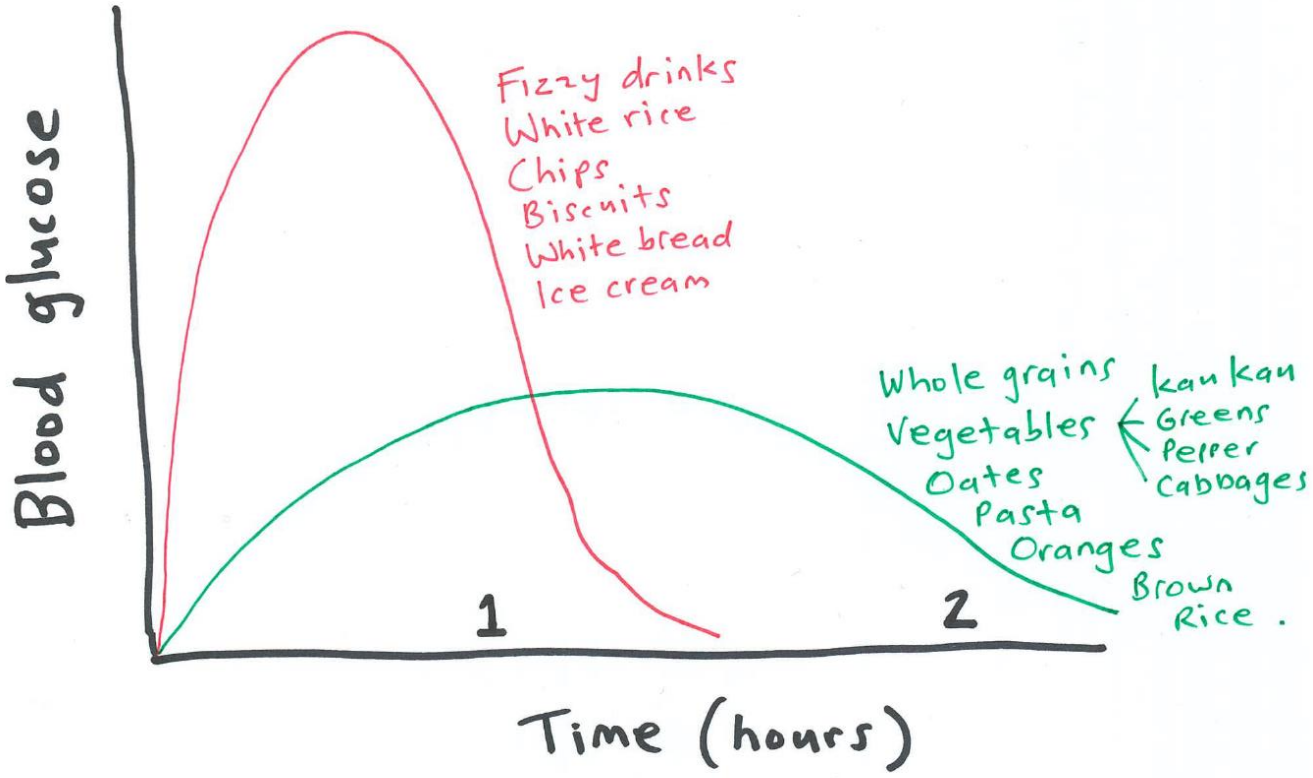
2/3 mane = 13 IU
- 9 IU intermed
- 4 IU actrapid

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%

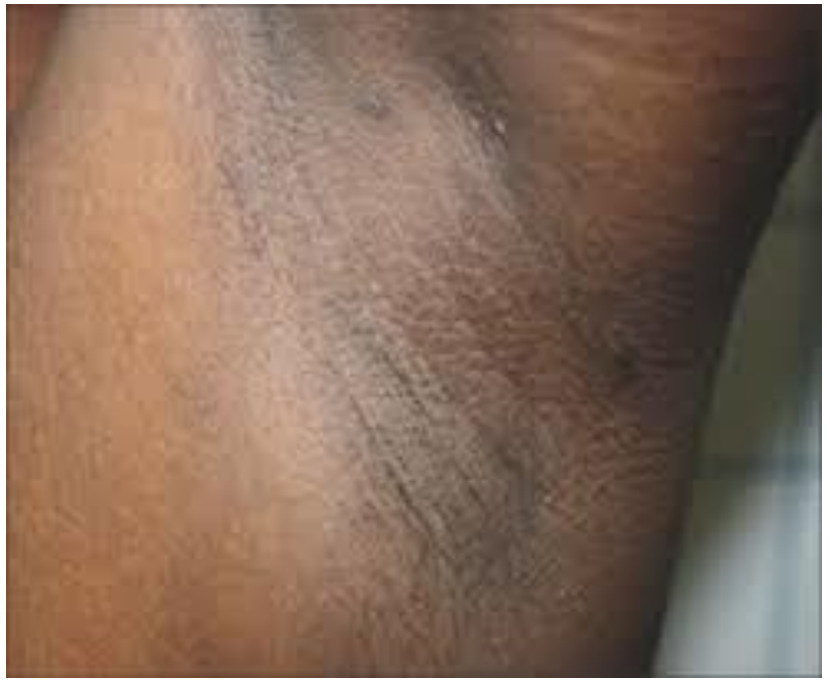


Risks

- 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)

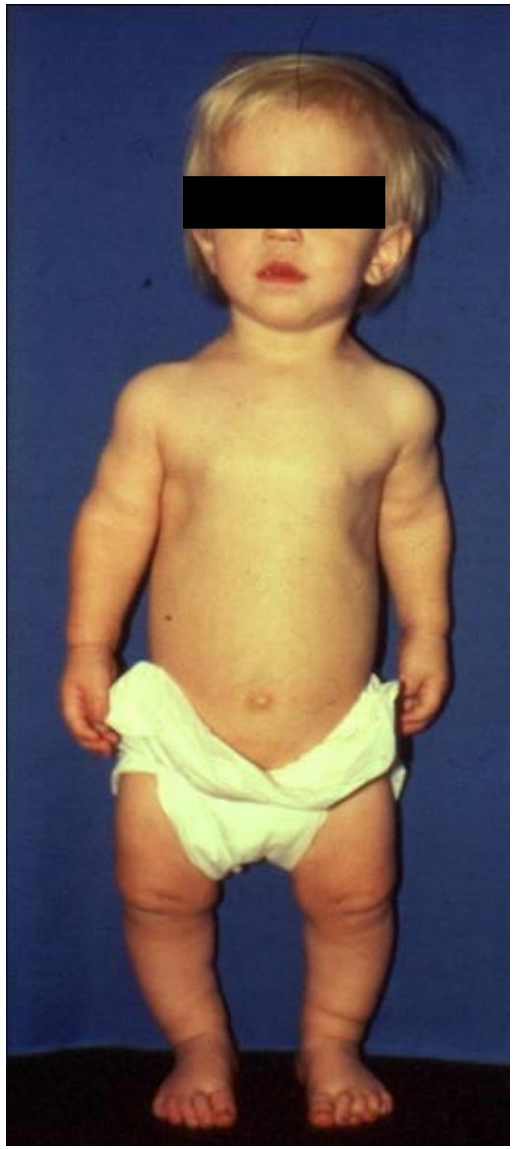
Fungal infection

Staph sepsis

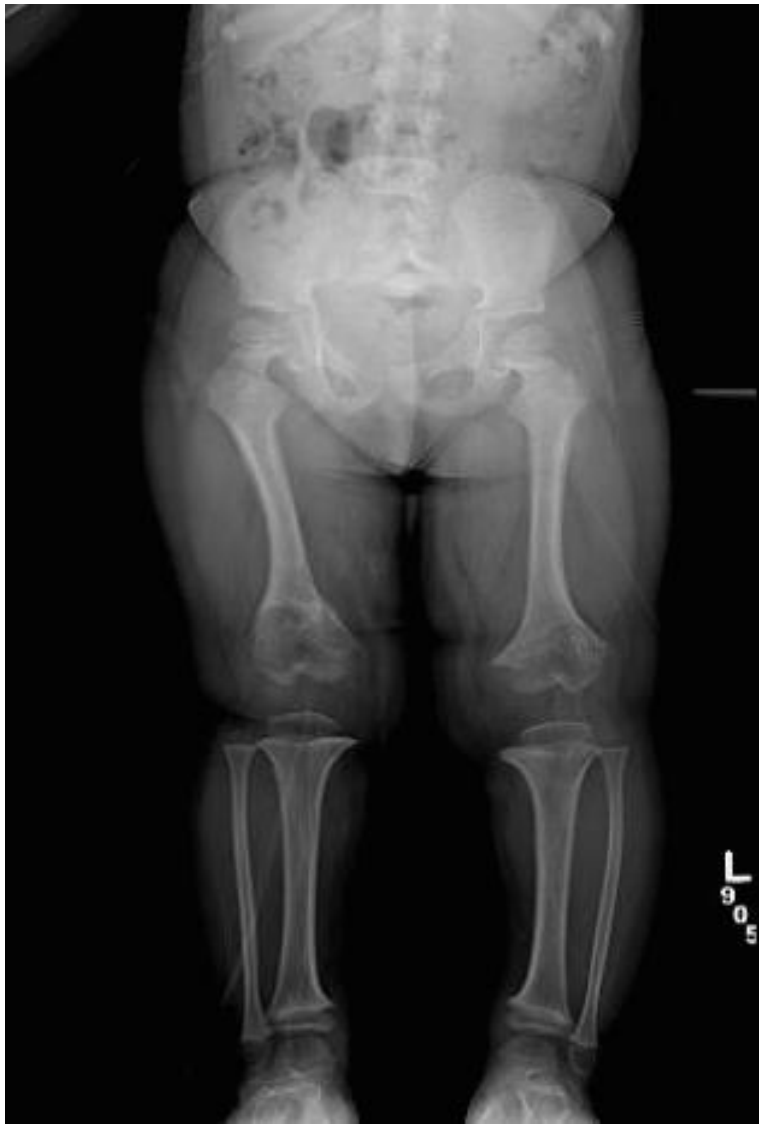
Lipoatrophy

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
  - Steroid exposure

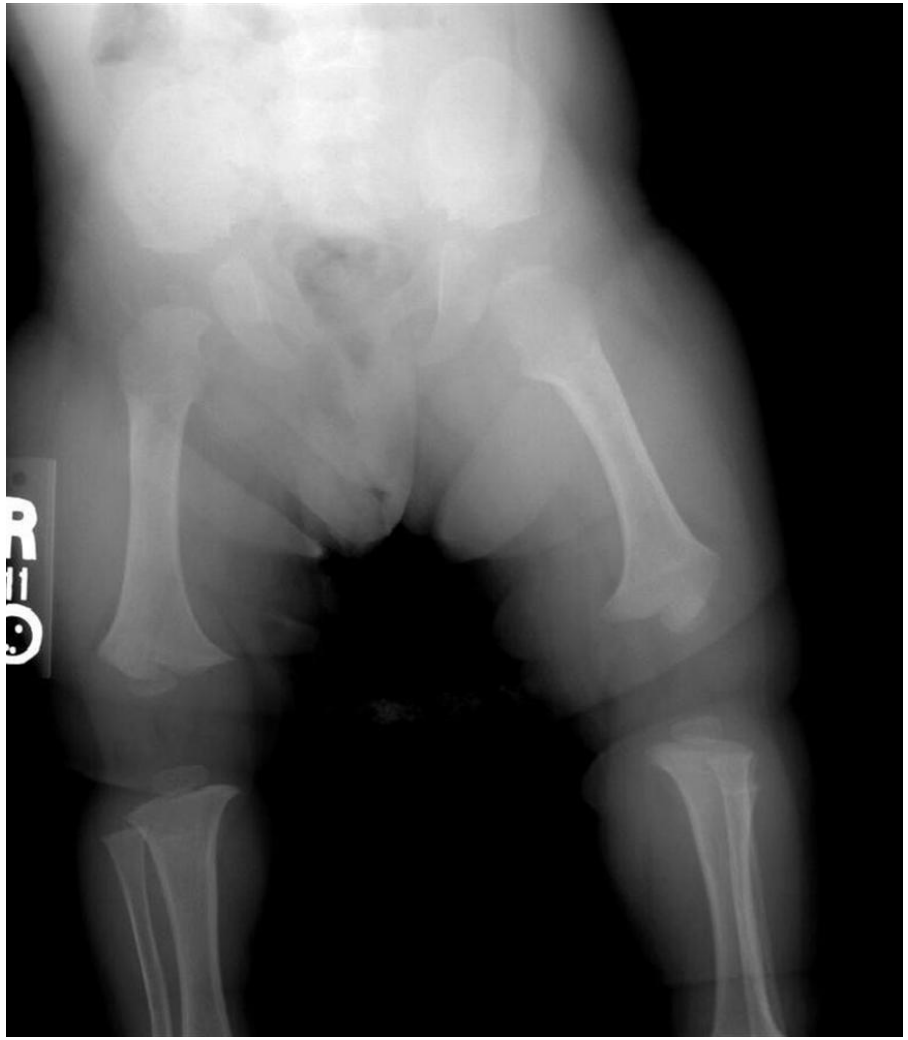


Large head, frontal bossing, small midface, flattened nasal bridge
Thoracic-lumbar kyphoscoliosis
Lumbar stenosis – cord compression
Foramen magnum stenosis



Achondroplasia

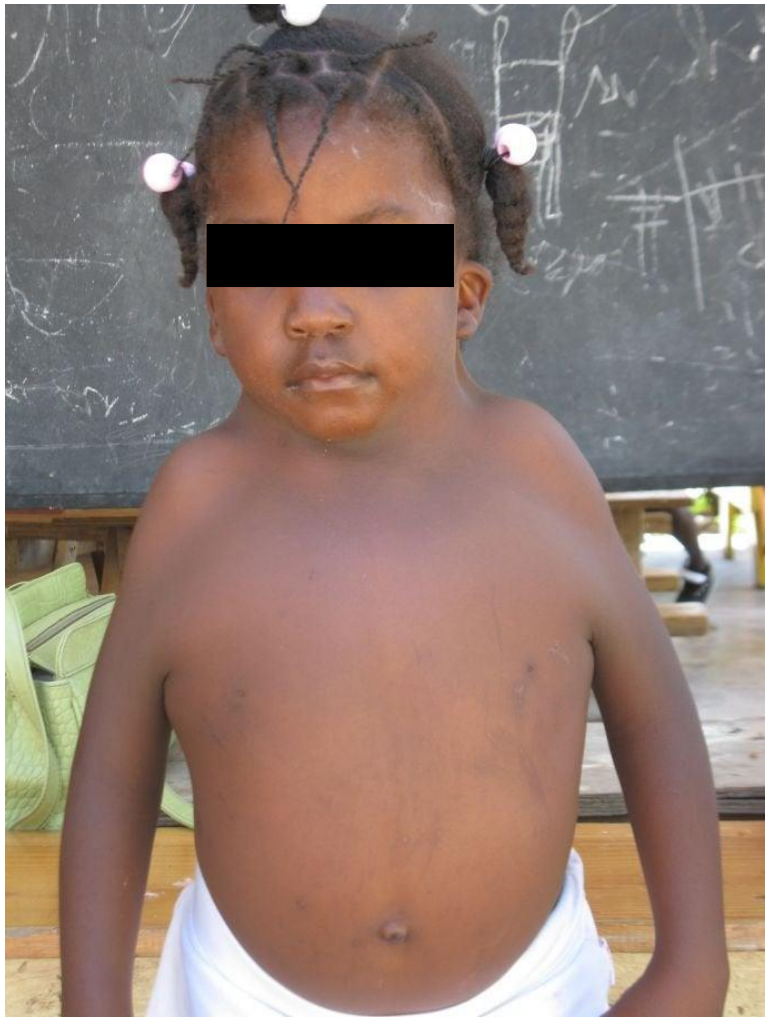
- Cartilage defect
- Mutation which inhibits chondrocyte proliferation in area of bone growth
- Normal intelligence
- Most children with achondroplasia will be healthy
- Recurrent otitis media
- Spinal cord compression
- Hydrocephalus
- Sleep apnoea

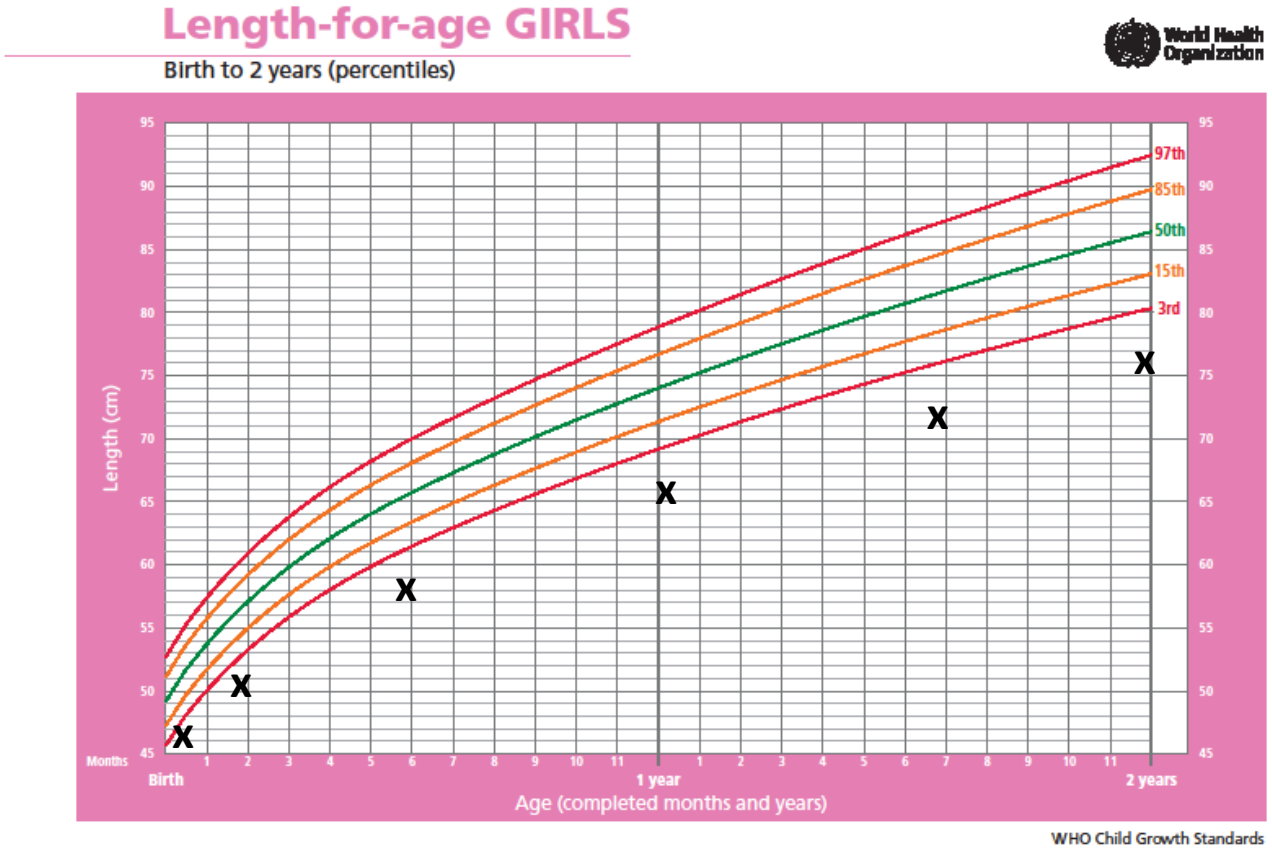


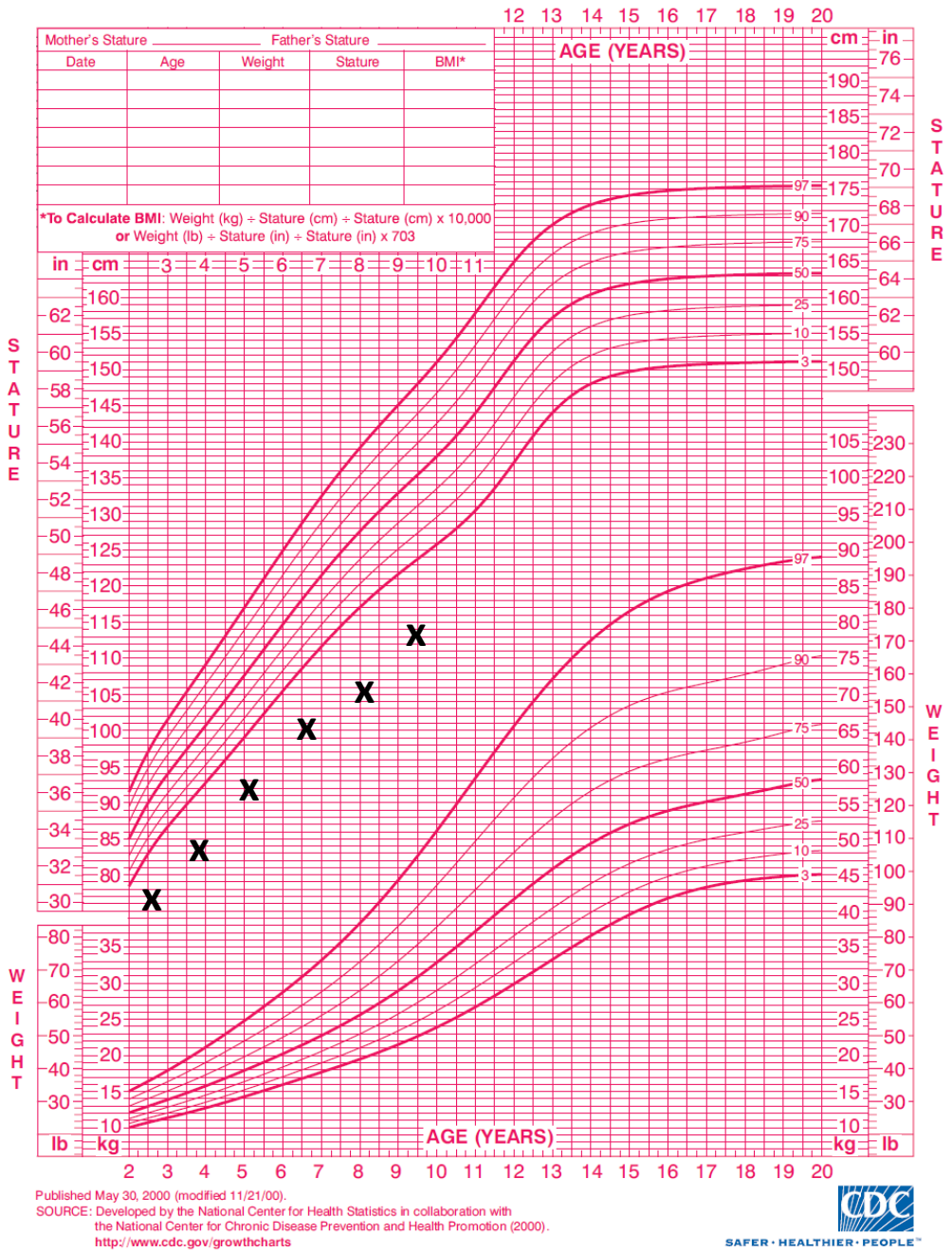
Clinical management of achondroplasia Arch Dis Child 2012;97:129–134

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)







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