Metabolic medicine

LIPIDS

Lipoproteins

1 Very low-density lipoprotein (VLDL)
   (a) Synthesised continuously by liver
   (b) Carries 60% triglycerides and some cholesterol
   (c) Enzymic degradation to intermediate density lipoprotein (IDL) and then LDL
2 Low-density lipoprotein (LDL)
   (a) Formed from IDL by hepatic lipase
   (b) Major carrier of cholesterol
   (c) Binds to, and levels regulated by feedback on to, hepatic LDL receptor
3 High-density lipoprotein (HDL)
   (a) Synthesised in gut wall and liver
   (b) Carries cholesterol from periphery to liver
   (c) Inverse association with ischaemic heart disease
4 Chylomicrons
   (a) Carry dietary lipid from gut to liver
   (b) Broken down by lipoprotein lipase in portal vessels to free fatty acids

Hyperlipidaemias

1 Can be primary or secondary

2 Atherosclerotic disease associated with high total cholesterol and LDL
3 HDL protective

Primary disorders

1 Familial hypercholesterolaemia
  (a) Autosomal dominant
    (i) Heterozygotes ≈ 1:500
    (ii) Homozygotes very rare
  (b) Around 400+ defects in LDL receptor known
  (c) Defect in the receptor means half-life of LDL in plasma is prolonged, leading to increased serum levels
  (d) Heterozygotes
    (i) Total cholesterol 9–15 mmol/l
    (ii) 6–8 times increased risk of IHD (MI at young age)
    (iii) Xanthelasma and tendon xanthoma
  (e) Homozygotes
    (i) Xanthomas in early childhood
    (ii) MI as child
  (f) Treat with diet and statins
2 Familial triglyceridaemia
  (a) AD
  (b) Plasma turbid
  (c) Associated with eruptive xanthomata, pancreatitis, retinal vein thrombosis, hepatosplenomegaly, lipaemia retinalis
  (d) Treat with diet and fibrates
3 Lipoprotein lipase deficiency
  (a) Rare
  (b) AR
  (c) Failure to break down chylomicrons
  (d) Raised triglycerides
4 Familial combined hyperlipidaemia
  (a) Elevated cholesterol and triglycerides
  (b) Prevalence 1:200
  (c) Main feature is atherosclerosis

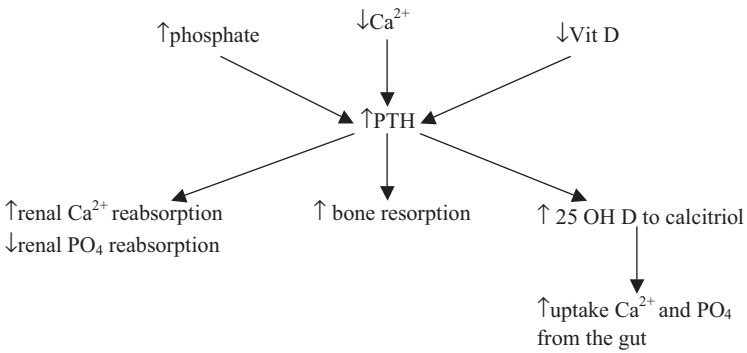
Causes of secondary hyperlipidaemia

1 Mainly raised cholesterol
  (a) Hypothyroidism

(b) Cholestasis
(c) Nephrotic syndrome
(d) Renal transplant

2 Mainly raised triglycerides
(a) Obesity
(b) Chronic alcohol excess
(c) Insulin resistance and diabetes
(d) Chronic liver disease
(e) Thiazide diuretics
(f) High-dose oestrogens

BONE AND MINERALS (FIG. 4)



Vitamin D

1 Mostly made in skin by action of UV light
2 25 – hydroxylated in liver
3 Hydroxylated again to 1,25-OH D (calcitriol) in kidney

Hypercalcaemia

1 Causes
(a) Primary hyperparathyroidism (adenoma of parathyroid gland)
(b) Malignancy – PTH-related protein and bone metastases, commonly breast, kidney, thyroid, squamous cell tumours
(c) Calcium intake (and milk-alkali syndrome)
(d) Vitamin D
(e) Tertiary hyperparathyroidism

(f) Hyperthyroidism
(g) Sarcoid – macrophages in lesions produce 1,25 vitamin D_3
(h) Thiazides
(i) Lithium
(j) Addison's
(k) Theophylline toxicity
(l) Phaeochromocytoma
(m) Familial hypocalciuric hypercalcaemia

2 Features
(a) As underlying condition, plus
(b) Lethargy, malaise and depression
(c) Polyuria and polydipsia
(d) Weakness
(e) Confusion and psychosis
(f) Constipation
(g) Peptic ulceration
(h) Nausea
(i) Renal stones
(j) Nephrocalcinosis
(k) Pseudogout
(l) Proximal myopathy
(m) Diabetes insipidus
(n) Pancreatitis

3 Treatment
(a) Aggressive rehydration
(b) Bisphosphonate (pamidronate)
(c) Frusemide
(d) Steroids

Hyperparathyroidism

1 Primary
(a) Single adenoma in > 80%
(b) Multiple in around 5%
(c) Commonest in women aged 40–60
(d) Carcinoma very rare
(e) Results in ↑ PTH, ↑ serum and urinary calcium, ↑ alkaline phosphatase and ↓ serum phosphate
(f) Causes increased osteoblasts and osteoclasts with woven osteoid and osteatitis fibrosa cystica

2 Secondary
   (a) Due to hypertrophy of glands in response to chronic hypocalcaemia (eg in renal failure)
3 Tertiary
   (a) Consequence of long-standing secondary hyperparathyroidism. Further gland hyperplasia raises calcium levels. Treatment is parathyroidectomy

Hypocalcaemia

1 Causes
   (a) Hypoparathyroidism (including pseudohypoparathyroidism)
   (b) Chronic renal failure
   (c) Low levels of vitamin D_3
   (d) Hyperphosphataemia
   (e) Hypomagnesaemia
   (f) Sepsis
   (g) Respiratory alkalosis
   (h) Calcium deposition (eg acute pancreatitis)
   (i) Carcinoma of prostate
2 Features
   (a) Muscle weakness
   (b) Neuromuscular excitability
   (c) Confusion, seizures
   (d) Tetany
   (e) Alopecia
   (f) Brittle nails
   (g) Cataracts
   (h) Dental hypoplasia
3 Treatment
   (a) Supplementation of calcium, vitamin D_3

Hypoparathyroidism

1 Causes
   (a) Parathyroidectomy (intentional and accidental)
   (b) Autoimmune
   (c) Receptor defect (pseudohyperparathyroidism)
   (d) Di George syndrome
2 Diagnosis (hypoparathyroidism)
   (a) ↓ Calcium, ↓ PTH

Pseudohypoparathyroidism

1 Receptor defect leading to resistance of target tissues to PTH
2 X-linked dominant
3 ↓ Calcium, ↑ PTH
4 Clinical features
  (a) Short stature
  (b) Round face
  (c) Short neck
  (d) Shortening of the metacarpals and metatarsals

Causes of hyperphosphataemia

1 Renal failure
2 Hypoparathyroidism
3 Acromegaly
4 Vitamin D excess
5 Overintake of phosphate
6 Tumour lysis syndrome

Causes of hypophosphataemia

1 Intravenous glucose
2 Deficiency during parenteral feeding
3 Recovery phase of DKA
4 Primary hyperparathyroidism
5 Renal tubular disease
6 Vitamin D deficiency
7 Alcohol withdrawal

Osteomalacia/rickets

Decreased mineralisation of osteoid
1 Causes
  (a) Calciopenic
    (i) Vitamin D deficiency
    (ii) Impaired calcium metabolism
  (b) Phosphopenic
    (i) Proximal renal tubular disease
2 Clinical features
  (a) Pain
  (b) Deformity

(c) Fractures
(d) Proximal myopathy
(e) Raised alkaline phosphatase

Paget's disease

1 Increased bone turnover with abnormal new bone turnover
2 Causes pain, deformity, arthritis, nerve compression, fractures, sarcoma
3 ↑↑ ALP
4 Calcium only raised with immobility
5 Diagnosis – clinical, typical X rays or bone scan
6 Treatment: analgesia and bisphosphonates

Magnesium

Hypomagnesaemia

1 Usually associated with low Ca^{2+} and low K^{+}
2 Associated with ventricular arrhythmias, fits, tetany and paraesthesiae

Causes

1 Renal loss
  (a) Loop/thiazide diuretics
  (b) Alcohol
  (c) DKA
  (d) Volume expansion
  (e) Hypercalcaemia
2 Loop of Henle disorder
  (a) Acute tubular necrosis
  (b) Post obstruction diuresis
  (c) Renal transplant
3 Nephrotoxic drugs
  (a) Aminoglycosides
  (b) Cisplatin
  (c) Ciclosporin
  (d) Amphotericin
4 GI loss
  (a) High-volume diarrhoea
  (b) Malabsorption

   (c) Other small bowel disease
   (d) Acute pancreatitis
5 Primary renal magnesium wasting
   (a) Rare familial condition

Hypermagnesaemia

1 Causes
   (a) Magnesium infusion
   (b) Magnesium enema
   (c) Oral magnesium overdose
   (d) Renal failure
   (e) Adrenal insufficiency
   (f) Milk-alkali syndrome
   (g) Theophylline toxicity
   (h) Lithium
2 Treat with iv calcium if symptomatic

Copper

1 50% of amount ingested is absorbed
2 Transported to liver by albumin
3 Binds with globulin to form caeruloplasmin

Wilson's disease

1 Autosomal recessive
2 Gene on chromosome 13
3 Abnormality of caeruloplasmin formation, hence accumulation of copper in body
4 Features: acute/chronic hepatitis, cirrhosis, Kayser–Fleischer rings, CNS symptoms, arthropathy, RTA.
5 Diagnosis: low caeruloplasmin, high urinary copper, liver biopsy, KF rings
6 Treatment: penicillamine (copper chelator), liver transplant

Iron

1 4 g in normal human body, two-thirds in haemoglobin
2 20 mg/day in normal diet; only 10% absorbed
3 Fe^{2+} more readily absorbed than Fe^{3+}
4 Transferrin one-third saturated normal

5 Ferritin increased in iron overload (NB: acute-phase protein), decreased in deficiency
6 Plasma iron varies ++

Haemochromatosis

1 Autosomal recessive
2 Commoner, more severe in men
3 Gene on chromosome 6
4 Features: micronodular cirrhosis chondrocalcinosis, pseudogout, skin bronzing, diabetes, cardiomyopathy, arrhythmias
5 Diagnosis: raised serum iron and ferritin. Transferrin > 45% saturated. Liver biopsy
6 Treatment: venesection, desferrioxamine

Causes of secondar y iron overload

1 Multiple transfusions
2 Alcoholic cirrhosis
3 Chronic hepatitis B/C
4 Beta-thalassaemia
5 Aplastic anaemia
6 Sideroblastic anaemia

Acid–base homoeostasis (Table 46)

Table 46

	pH	pCO_2	HCO_3
Metabolic acidosis	N or ↓	↓	↓↓
Metabolic alkalosis	N or ↑	Slight ↑	↑↑
Respiratory acidosis	N or ↓	↑↑	↑
Respiratory alkalosis	N or ↑	↓↓	Slight ↓

$H^+ + HCO_3 \leftrightarrow H_2O + CO_2$
Anion gap = $\{[Na^+] + [K^+]\} - \{[CL^-]+[HCO_3^-]\}$ = 10–18 mmol/l

Metabolic acidosis

1 Normal anion gap
  (a) Direct loss of bicarbonate (↑ chloride)

    (i) Diarrhoea
    (ii) Pancreatic fistulae
    (iii) Ureterosigmoidostomy
    (iv) RTA (see page ??)
    (v) Acetazolamide
  (b) Ingestion of acidifying agents
    (i) Ammonium chloride
2 High anion gap
  (a) DKA
  (b) Lactic acidosis
  (c) Renal failure
  (d) Salicylate poisoning
  (e) Methanol poisoning
  (f) Ethylene glycol poisoning

Respiratory acidosis

1 Hypoventilation leading to increased CO_2 and acidosis
2 Causes
  (a) COPD
  (b) Severe asthma
  (c) Obesity
  (d) Neuromuscular disorders leading to hypoventilation
    (i) Guillain–Barré
    (ii) MND
    (iii) Myasthenia gravis
    (iv) Muscular dystrophy
    (v) Flail chest
    (vi) Severe kyphoscoliosis
  (e) Muscle relaxants

Respiratory alkalosis

1 Hyperventilation leading to low CO_2 levels and alkalosis
2 Causes
  (a) Psychogenic
  (b) Pulmonary disease
  (c) Altitude
  (d) Right to left shunt
  (e) CO poisoning
  (f) Salicylates

(g) Acute liver failure

Metabolic alkalosis

1 Vomiting
2 Potassium depletion
3 Hyperaldosteronism
4 Rapid diuresis
5 Fulminant hepatic failure
6 Milk-alkali syndrome
7 Forced alkaline diuresis

Lactic acidosis

1 Type A
   (a) Poor tissue perfusion with or without hypoxia
      (i) Exercise
      (ii) Post epileptic seizure
      (iii) Shock
      (iv) Severe hypoxia
2 Type B
   (a) Administration of drugs or metabolic disturbance leading to increased production of lactate
      (i) Metformin
      (ii) Alcohol
      (iii) Recovery from DKA
      (iv) Liver failure
      (v) Paracetamol poisoning
      (vi) Thiamine deficiency

Osmolar gap

1 Normally gap between serum osmolality and calculated osmolality is < 10
2 If the value is greater then this suggests another osmotically active substance in the blood
3 Calculated with formula
   (a) $2(Na^+ + K^+)$ + urea + glucose
4 Causes of raised osmolar gap
   (a) Methanol
   (b) Ethylene glycol

(c) Diethylene glycol
(d) Ethanol

Porphyrias

1 Hereditary defects of enzymes involved in haem synthesis pathway
2 Overproduction of intermediates – porphyrins
3 Several different types; most important are
4 Acute intermittent porphyria
  (a) Autosomal dominant
  (b) Rare, commoner in females
  (c) Due to low levels of porphobilinogen deaminase in liver
  (d) Presents in youth
  (e) Increased urinary porphobilinogen in attack; urine turns dark red after standing
  (f) Clinical features
    (i) Severe abdominal pain
    (ii) Neuropsychiatric symptoms
    (iii) Vomiting
    (iv) Hypertension
    (v) Tachycardia
    (vi) Motor polyneuropathy
  (g) Commonly precipitated by hepatic enzyme-inducing drugs, eg alcohol, phenytoin, oral contraceptives, sulphonamides, rifampicin, benzodiazepines
  (h) Treatment of attacks
    (i) High-carbohydrate diet
    (ii) Haematin
    (iii) Opiate analgesia
    (iv) Fluid restriction for hyponatraemia
    (v) Conservative management of seizures, as antiepileptics can precipitate attacks
5 Porphyria cutanea tarda
  (a) Chronic hepatic condition
  (b) Many patients drink excessive alcohol
  (c) Autosomal dominant and acquired
  (d) Reduced hepatic uroporphyrinogen decarboxylase
  (e) Accumulation of uroporphyrinogen (raised in urine)
  (f) Many have evidence of iron overload and require venesection
  (g) Photosensitive bullous rash main feature

Amino acid metabolism disorders (Table 47)

[See Table 47, overleaf]

Deficiencies

Protein–energy malnutrition

1 Undernutrition
   (a) Weight 60–80% of standard for age, no oedema
2 Marasmus
   (a) Deficient in protein and calories
   (b) Weight < 60% of standard, no oedema
3 Kwashiorkor
   (a) Solely due to protein deficiency
   (b) Weight 60–80% of standard, oedema present
   (c) Fatty liver often seen

Vitamin deficiencies (Table 48)

[See Table 48, overleaf]

DISORDERS OF SODIUM AND WATER HOMOEOSTASIS

Sodium is regulated by volume receptors. In health, water is adjusted to maintain a normal osmolarity and, in the absence of abnormal osmotically active solutes, a normal sodium. Therefore, disturbances of sodium concentration are caused by disturbances of water balance.

Causes of hyponatraemia – with normal extracellular water

1 Pseudohyponatraemia
   (a) Hyperlipidaemia
   (b) Hyperproteinaemia
2 Abnormal ADH release
   (a) Hypothyroidism
   (b) Severe potassium depletion
3 ADH-like substances
   (a) Oxytocin
   (b) DDAVP

Table 47

Condition	Genetics	Clinical features	Diagnosis	Management
Cystinosis	Autosomal recessive; short arm of 17	Lymphadenopathy, growth retardation, Fanconi syndrome, renal failure	Measure cystine content of neutrophils	Dialysis, renal transplant Death usual
Cystinuria	AR	Renal stones	Urinary cystine/stone analysis	Fluids, penicillamine, alkalisation of urine
Homocystinuria	AR	Osteoporosis, arterial thrombosis, downward dislocation of lens, mental retardation	Cyanide-nitroprusside test – raised urinary homocysteine	Methionine restriction Supplements of cystine and pyridoxine
Alkaptonuria	AR	Arthritis, disc calcification, pigmentation of ears	Clinical; urine darkens on standing	Symptomatic for arthritis
Phenylketonuria	AR	Mental retardation, irritability, eczema, decreased pigmentation	Guthrie screening test perinatally	Dietary restriction of phenylalanine Tyrosine supplements
Oxalosis	AR	Renal stones/calcification, bone, cardiac and arterial disease	Urinary oxalate increased; may need liver biopsy	Pyridoxine, treat renal failure, fluids

Table 48

Vitamin	Cause of deficiency	Consequence of deficiency
A	Protein–energy malnutrition	Night blindness, dry corneas, keratomalacia
B_1 (thiamine)	Alcoholism, dietary restriction	Dry beri beri: Wernicke–Korsakoff, polyneuropathy Wet beri-beri: high output cardiac failure
B_2 (riboflavin)	Protein–energy malnutrition	Glossitis, angular stomatitis
Niacin	Alcoholism, isoniazid, carcinoid syndrome	Pellagra – **d**ermatitis, **d**iarrhoea, **d**ementia and **d**eath
B_6 (pyridoxine)	Hydralazine, isoniazid	Peripheral neuropathy, glossitis
B_{12} (cyanocobalamin)	Pernicious anaemia, gastrectomy, ileal disease, vegans	Macrocytic anaemia, subacute combined degeneration of the cord
C	Dietary deficiency	Scurvy: gingivitis, bleeding, joint swelling
D	Renal failure, dietary	Osteomalacia, rickets
E	Fat malabsorption, abetalipoproteinaemia	Spinocerebellar degeneration
K	Biliary obstruction, antibiotic therapy	Bleeding diathesis

4 Unmeasured osmotically active substances stimulating osmotic ADH release
   (a) Glucose
   (b) Alcohol
   (c) Mannitol
5 Syndrome of inappropriate ADH secretion (SIADH)*
6 Stress
   (a) Surgery
   (b) Nausea

Causes of hyponatraemia – with decreased extracellular volume

1 Kidney
   (a) Osmotic diuresis (hyperglycaemia, severe uraemia)
   (b) Diuretics
   (c) Adrenocortical insufficiency
   (d) Tubulointerstitial disease
   (e) Unilateral renal artery stenosis
   (f) Recovery post ATN
2 Gastrointestinal
   (a) Vomiting
   (b) Diarrhoea
   (c) Haemorrhage
   (d) Fistula
   (e) Obstruction

Causes of hyponatraemia – with increased extracellular volume

1 Oliguric renal failure
2 Heart failure
3 Liver failure
4 Hypoalbuminaemia

Causes of hypernatraemia

1 Dehydration
2 Iatrogenic (administration of hypertonic sodium solution)
3 Diabetes insipidus
4 Osmotic diuresis

(a) Total parenteral nutrition
(b) Hyperosmolar diabetic coma

Causes of SIADH

1 Malignancy
   (a) Bronchus, bladder, prostate, pancreas
   (b) Lymphoma
   (c) Ewing's sarcoma
   (d) Mesothelioma
   (e) Thymoma
2 Pulmonary disorders
   (a) Pneumonia
   (b) Abscess
   (c) TB
   (d) PEEP
   (e) Asthma
3 Central nervous system
   (a) Encephalitis
   (b) Meningitis
   (c) Trauma
   (d) Subarachnoid haemorrhage
   (e) Guillain-Barré syndrome
   (f) Hydrocephalus
   (g) Acute psychosis
   (h) Acute intermittent porphyria
4 Drugs
   (a) Opiates
   (b) Carbamazepine
   (c) Oxytocin
   (d) Chlorpropamide
   (e) Phenothiazines
   (f) TCAs
   (g) Cytotoxics (vincristine, cyclophosphamide)
   (h) Rifampicin
   (i) Porphyria (drug induced)

Causes of diabetes insipidus

1 Cranial (reduced secretion of ADH)
   (a) Idiopathic

   (b) Familial (eg DIDMOAD syndrome)
   (c) Craniopharyngioma
   (d) Infiltrative processes of hypothalamus
      (i) Sarcoidosis
      (ii) Histiocytosis X
   (e) Trauma
   (f) Pituitary surgery
   (g) Lymphocytic hypophysitis
   (h) Dysgerminomas
2 Nephrogenic (reduced action of ADH)
   (a) Primary
      (i) Childhood onset
      (ii) X-linked/dominant
      (iii) Tubular receptor abnormality
   (b) Secondary
      (i) Hypercalcaemia
      (ii) Hypokalaemia
      (iii) Renal disease
      (iv) Chronic pyelonephritis
      (v) APKD
      (vi) Post obstruction
      (vii) Sarcoidosis
      (viii) Drugs
         (1) Lithium
         (2) Demeclocycline (used to treat SIADH)
         (3) Amphotericin
         (4) Glibenclamide

Causes of polyuria

1 Excessive intake
   (a) Beer drinking
   (b) Primary polydipsia (lesion of hypothalamus)
   (c) Psychogenic polydipsia
2 Osmotic diuresis
   (a) Diabetes mellitus
   (b) CRF
3 ARF (diuretic phase)
4 Diuretics
5 Diabetes insipidus (cranial and nephrogenic)

6 Hypokalaemia
7 Hypercalcaemia
8 Obstructive uropathy
9 Tubulointerstitial disease

Investigation of polyuria

1 Record fluid intake
2 Record urine volume (if ,3l/24 hrs and normal biochemistry excludes significant abnormality)
3 Blood glucose, U&E, calcium
4 Urinalysis
5 Early morning urine osmolality
6 Water deprivation test
   (a) To identify the cause of polyuria and/or polydipsia
   (b) Hourly urine and plasma osmolality measured until 3% of bodyweight lost
   (c) Injection of DDAVP (synthetic ADH)

Interpretation of water deprivation test (Table 49)

Table 49

	Initial plasma osmolality	Final urine osmolality (mmol/kg)	Urine osmolality post DDAVP (mmol/kg)	Final plasma ADH
Normal	Normal	> 600	> 600	High
Cranial DI	High	< 300	> 600	Low
Nephrogenic DI	High	< 300	< 300	High
Primary polydipsia	Low	300–400 (approx.)	400 (approx.)	Moderate
Partial cranial DI	High	300–400	400–600	Relatively low

POTASSIUM

Potassium is the major intracellular ion. Excretion of potassium is increased by aldosterone.

Causes of hypokalaemia

1 Decreased intake
  (a) Oral (uncommon except in starvation)
  (b) Parenteral
1 Redistribution into cells
  (a) Metabolic alkalosis
  (b) Insulin
  (c) Alpha-adrenergic antagonists
  (d) Beta-adrenergic agonists
  (e) Vitamin B_{12} or folic acid when correcting megaloblastic anaemia
  (f) Total parenteral nutrition (TPN)
  (g) Hypokalaemic periodic paralysis
  (h) Pseudohypokalaemia
  (i) Hypothermia
2 Increased excretion
  (a) Gastrointestinal
    (i) Purgative abuse
    (ii) Vomiting
    (iii) Villous adenoma
    (iv) Severe diarrhoea
    (v) Ileostomy/uterosigmoidostomy
    (vi) Fistulae
  (j) Renal
    (i) Thiazides
    (ii) Loop diuretics
    (iii) Renal tubular damage
    (iv) Mineralocorticoid excess
      (1) Primary hyperaldosteronism (Conn's)
      (2) Secondary hyperaldosteronism
      (3) Apparent mineralocorticoid excess
        (a) Liquorice
        (b) Carbenoxolone
      (4) Cushing's syndrome
    (v) Bartter's syndrome
    (vi) Renal tubular acidosis type 1 and 2

Hyperkalaemia

1 Causes
  (a) Spurious
    (i) Haemolysis
    (ii) Delayed separation of serum
    (iii) Contamination
    (iv) Excessive intake (parenteral, oral)
  (b) Decreased excretion
    (i) Acute oliguric renal failure
    (ii) Chronic renal failure
    (iii) Mineralocorticoid deficiency (Addison's disease)
    (iv) Hypoaldosteronism
    (v) Drugs
      (1) Spironolactone
      (2) Amiloride
      (3) Triamterene
      (4) ACE inhibitors
      (5) NSAIDs
      (6) Ciclosporin
  (c) Redistribution
    (i) Acidosis
    (ii) Rhabdomyolysis
    (iii) Tumour lysis syndrome
    (iv) Digoxin poisoning
2 ECG changes
  (a) Tenting of T waves
  (b) Reduction in size of P waves
  (c) Increase in PR interval
  (d) Widening QRS complexes
  (e) Disappearance of P waves
  (f) Further QRS widening
  (g) Sinusoidal waveform
3 Treatment
  (a) IV calcium gluconate (stabilises cardiac membranes)
  (b) IV insulin and dextrose
  (a) Calcium resonium
  (b) Frusemide
  (c) Salbutamol nebulisers
  (d) Dialysis