Medicine

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Contents

Chapter 1

Cardiology

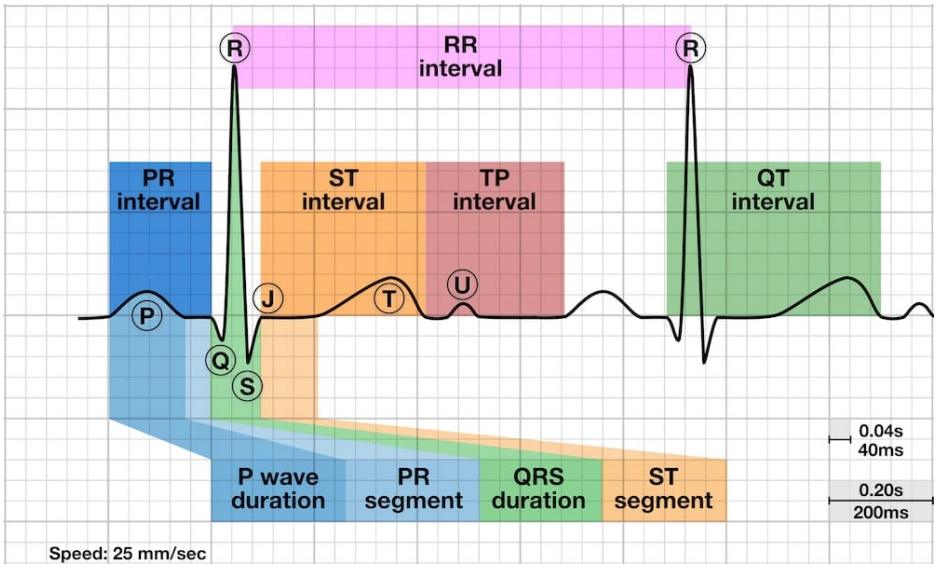
1.1 Presenting problems in CVS disease

Features of benign murmur

- Soft
- Midsystolic
- Heard at left sternal edge
- No radiation
- No other cardiac abnormalities

1.2 ECG

Anatomy of an ECG



Abnormalities of components

Pathological Q

- Depth > 2mm
- Height > 1mm
- Present in ≥ 2 leads
- Assocd with loss of R height (Q > R/4; normally Q ≤ R/4)
- **Indicates *transmural* myocardial necrosis**

Segments vs intervals

- e.g. ST segment = end of S → start of T
- PR interval = start of P → start of R

ST segment elevation

- Normal: upto 1mm in limb leads, upto 2mm in chest leads
- **Causes**
  - **STEMI: convexity** upwards
  - **Acute periCArditis:**: **conCAvity** upwards
- **Indicates ongoing myocardial injury**

Myocardial infarction

A somewhat interesting physiological explanation on how the changes arise

Sites of infarction based on lead

- Septal: V_1, V_2
- Anterior: V_3, V_4
- Lateral: I, aVL, V_5, V_6
- Extensive anterior: V_1-V_6
- Anterolateral: I, aVL, V_1-V_6

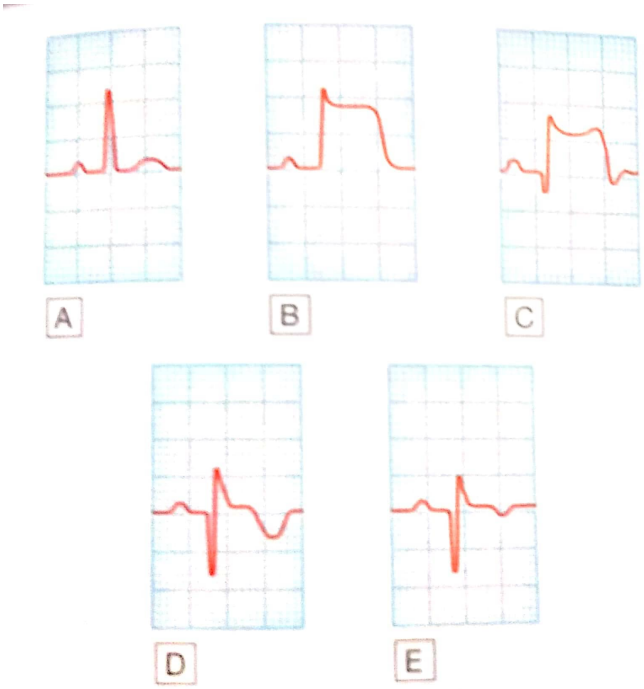
Reciprocal changes

- Acute STEMI in some surface of the heart → ST elevation in corresponding leads, and ST depression in reciprocal leads

Site	Facing	Reciprocal
Septal	V1, V2	V7, V8, V9
Anterior	V3, V4	None
Lateral	I, aVL, V5, V6	II, III, aVF
Inferior	II, III, aVF	I, aVL
Posterior	V7, V8, V9	V1, V2

Basic pathophys of STEMI

- Occurs due to proximal **complete occlusion of major coronary artery**



A. Before the onset of infarction
↓
B. In acute phase, ST elevation
↓
C. Progressive loss of R and deepening Q
↓
D. Resolution of ST elevation; fully developed pathological Q; T inversion
↓
E. In old infarcts, T-wave inversion may or may not persist

- ST elevation resolves after a few days

NSTEMI

- **Partial occlusion of major** or **complete occlusion of minor** coronary artery
- *Subendocardial/partial-thickness MI* → **no pathological Q**
- **ST depression + T inversion** in chest leads

1.3 Coronary Artery Disease

- Diseases arising due to narrowing of the lumen of one or more coronary arteries and the resulting ischaemia/infarction of the myocardium or the conductive system.
- **Types**:
  - Stable angina: Fixed atheromatous stenosis
  - Unstable angina:
    - dynamic obstruction
    - due to plaque rupture/erosion with thrombosis
  - MI
  - Heart failure
  - Arrhythmia
  - Sudden cardiac death
    - ventricular arrhythmia
    - asystole
    - massive MI

1.4 Arrhythmias

Classification according to ECG morphology

- **Narrow complex**: QRS $<$ 120ms (3 small sqs)
  - Sinus tachycardia
  - Atrial fibrillation (irregular narrow complex tachycardia)
  - Atrial flutter
  - AV Nodal Re-entry Tachycardia (AVNRT aka SVT)
- **Broad complex**: QRS $>$ 120ms (3 small sqs)
  - Ventricular tachycardia
  - AV Re-entry Tachycardia (AVRT e.g. Wolff-Parkinson-White syndrome)
    - Abnormal band of conductive tissue connecting atria and ventricles (accessory pathway)

Management of SVT

- Carotid sinus massage or
- Valsalva manoeuvre
- If the manoeuvre fails,

  - Adenosine (3-12mg IV) or
  - Rate-limiting CCB (Verapamil 5mg IV) or
  - β-blocker

- If haemodynamic state compromised, DC cardioversion
- Recurrent SVT $\rightarrow$ catheter ablation

1.5 Atrial fibrillation

Causes

- **Cardiac**
  - CAD (including acute MI)
  - Mitral stenosis (MS; rheumatic mitral valve disease)
  - Hypertension
  - Cardiomyopathy
- **Non-cardiac**
  - Thyrotoxicosis
  - Pulmonary embolism
  - Pneumonia
  - Alcoholism

Investigations

- ECG
- Echo: to see valvular condition
- Thyroid function test: to exclude thyrotoxicosis

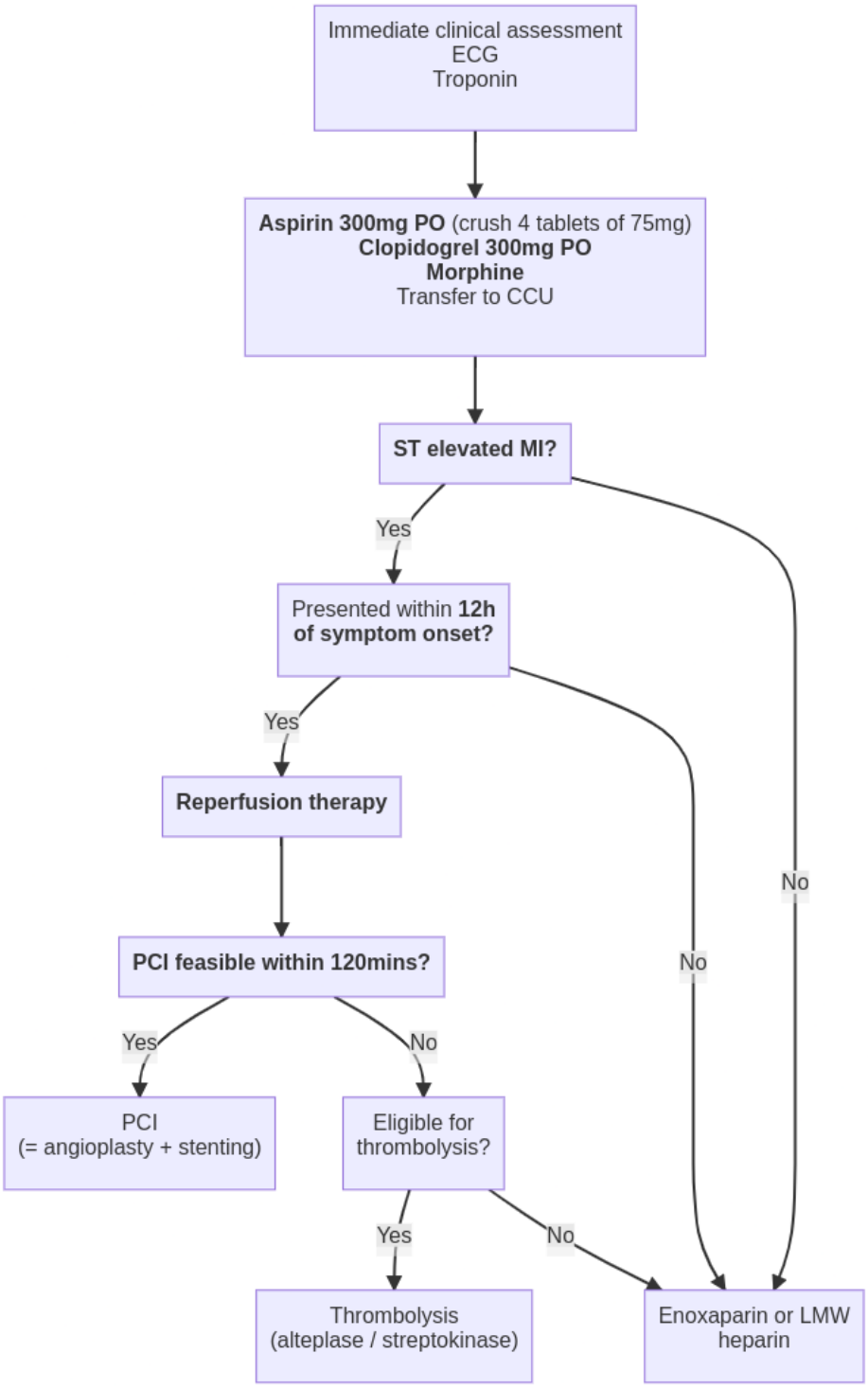
Management of AF

- **Rhythm control**:
  - Pharmacological cardioversion
    - Pt stable + no history of heart disease $\rightarrow$ IV flecainide
    - Structural / ischaemic heart disease $\rightarrow$ IV amiodarone
  - DC cardioversion if drugs fail
- **Rate control**
  - β-blockers
  - Digoxin
  - Rate-limiting CCB: verapamil / diltiazem
- **Thromboprophylaxis:**
  - Oral Warfarin
  - Target INR: 2.0-3.0

- Reduces risk of stroke by $\frac{2}{3}$
- Start 4wks before cardioversion, continue till 3mo after successful cardioversion

1.6 Myocardial Infarction

Management of acute MI



Chapter 2

Dermatology

2.1 Anatomy and physiology

- Layers of skin:
  - Epidermis: further layered into (from out→in)
    - corneum
    - lucidum
    - granulosum
    - spinosum
    - basale
  - Dermis: contains
    - blood vessels
    - nerves
    - pilosebaceous units (hair follicle + sebaceous gland)
  - Subcutis: adipose

Epidermal appendages

- Hair follicles:
  - phases of growth
    - anagen:
      - active growth
      - lasts years in scalp hairs
    - catagen:
      - transitional
      - lasts days (in scalp)
    - telogen:
      - resting
      - lasts months (in scalp)
- Sebaceous glands
  - usually *associated with a hair follicle*

  - androgens → ↑ sebum
  - oestrogen → ↓ sebum
- Sweat glands
  - innerved by *sympathetic cholinergic* fibres

2.2 Principles of management of skin disease

Topical treatments

- Ointments vs Creams
  - Ointments preferred to creams for dry skin (e.g. chronic eczema) as
    * more hydrating
      · 80% oil + 20% water in ointments (vs 50-50 for creams) → prevent water loss from skin by oil layer
    * less preservatives → less risk of allergy
- Emollients
  - Moisturise, lubricate, protect skin
  - *Vehicles without active drug*
- Gluocorticoids

Phototherapy

- **UVB**
- **Psoralen UVA**
  - Psoralen:
    * natural photosensitiser from plant source
    * cross-link DNA strands on excitation with UVA
  - Cumulative exposure to PUVA → ↑ risk of SCC, so reserved for UVB resistance
- Uses
  - Psoriasis
  - Atopic eczema
  - Vitiligo
  - Chronic urticaria

Systemics

- Antihistamines
- **Retinoids**
  - *Anti-inflammatory*
  - Promote *differentiation of skin cells*

  - **Teratogenic**
    * must be prescribed with robust contraception
    * females must have negative pregnancy test before, during, and after therapy

- **Immunosuppressants**
  - Glucocorticoids e.g. prednisolone
  - Methotrexate
  - Azathioprine

Biologics

- Biological *inhibitors* of *proinflammatory cytokines*
- **TNF-α inhibitors**
  - Infliximab
  - Etanercept
- **Interleukin inhibitors**
  - Ustekinumab: IL-12, 23
  - Guselkumab: IL-23
  - Secukinumab: IL-17
- *Rituximab*:
  - Binds to CD20 $\rightarrow$ cause ADCC of B cells
  - As terminally differentiated plasma cells don't have CD20 they're safe
  - Use: pemphigus vulgaris

Non-surgical therapy

- **Cryo**
  - *Liquid* N_2
  - Causes cell membrane destruction $\rightarrow$ death
- Laser
- PDT / photodynamic therapy

2.3 Skin cancers

Classification

- Non-melanoma skin cancer (NMSC): most common
  - SCC
  - BCC
- Melanoma
  - Less common
  - More metastatic risk $\rightarrow$ cause of most skin cancer deaths

2.4 Fungal infections

Types

- Superficial
  - Dermatophytes: aka **ringworm / tineasis**
    - *Trichophyton*
    - *Epidermophyton*
    - *Microsporum*
  - Yeast
- Deep: less common
  - Chromomycosis
  - Sporotrichosis

2.5 Scabies

Agent

Caused by the mite *Sarcoptis scabies hominis*

Diagnosis

- Identify the skin burrow
- Visualize the mite by dermatoscope / extracting with a needle

Treatment

- Affected + all asymptomatic family members / physical contacts
- Topical permethrin / malathion
  - 2 applications
  - 1 wk apart
  - Whole body, except head
- Oral Ivermectin:
  - Single dose
  - For poor adherence, immunosuppresion or heavy infestation

2.6 Acne

- *Chronic inflammation* of *pilosebaceous* units

Pathogenesis

Key components are:

- ↑ Sebum production
- Colonisation of pilosebaceous ducts by *Propionibacterium acnes*
- Occlusion of pilosebaceous ducts

Features

- Hallmark: **comedone**
- Greasiness of skin

Management

- **Mild disease**
  - Topical Benzoyl peroxide
  - Topical Retinoids
  - Topical antibiotics
    - Erythromycin
    - Clindamycin
- **Moderate disease**: topical *plus*
  - Systemic tetracycline
  - Oestrogen containing OCP
  - Isotretinoin: if inadequate response to topical+systemic therapy for 6 months
- **Severe disease**
  - Isotretinoin 0.5-1 mg/kg for 4 months:
    - Reduce sebum secretion and follicle colonisation
    - Teratogen
    - Pregnancy must be avoided during treatment *and* within 2 mo of drug cessation
  - Systemic glucocorticoid (with isotretinoin)
  - If unable to use isotretinoin
    - UVB phototherapy
    - PDT

2.7 Eczemas

- Seborrhoeic dermatitis is associated with *Malassezia* yeasts

Features

Most types have the following clinical features:

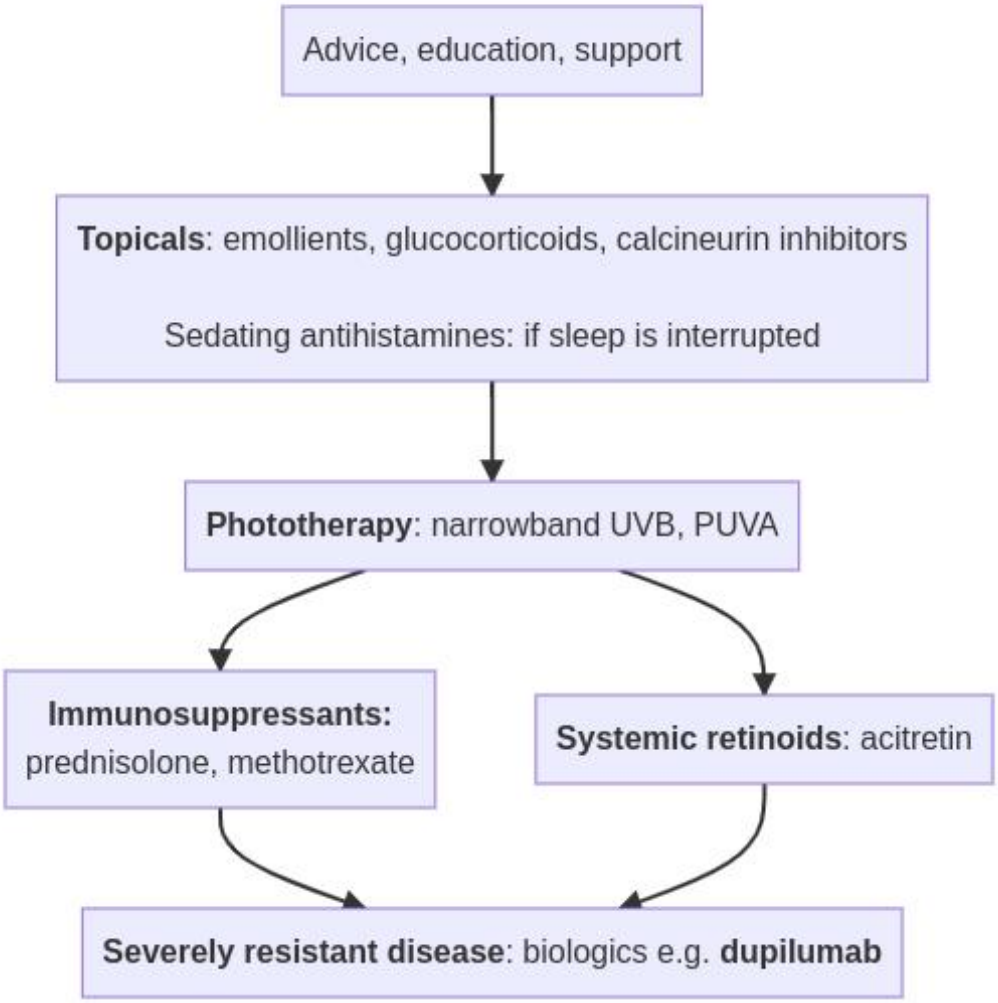
Acute

- Ill-defined erythema, oedema
- Papules, vesicles, bullae
- Exudation
- Scaling

Chronic

- Above features
- Lichenification
  - Skin thickening with pronounced skin markings, 2° to chronic scratching
  - Fissures
  - Dyspigmentation

Management of eczema



2.8 Psoriasis

- Chronic inflammatory hyperproliferative skin disease
- **Characteristics**
  - **Well-defined erythematous scaly plaques**
  - Affecting **extensor surfaces, scalp, nails**

Histological features

- Keratinocyte hyperproliferation + abnormal differentiation → nucleated stratum corneum cells (transit time from basale to corneum reduced to 5 from 28 → keratinocytes reach the surface while immature)
- Inflammation with Th-1 and Th-17 infiltration
- Tortuosity of dermal capillaries and release of VEGF

Exacerbating factors

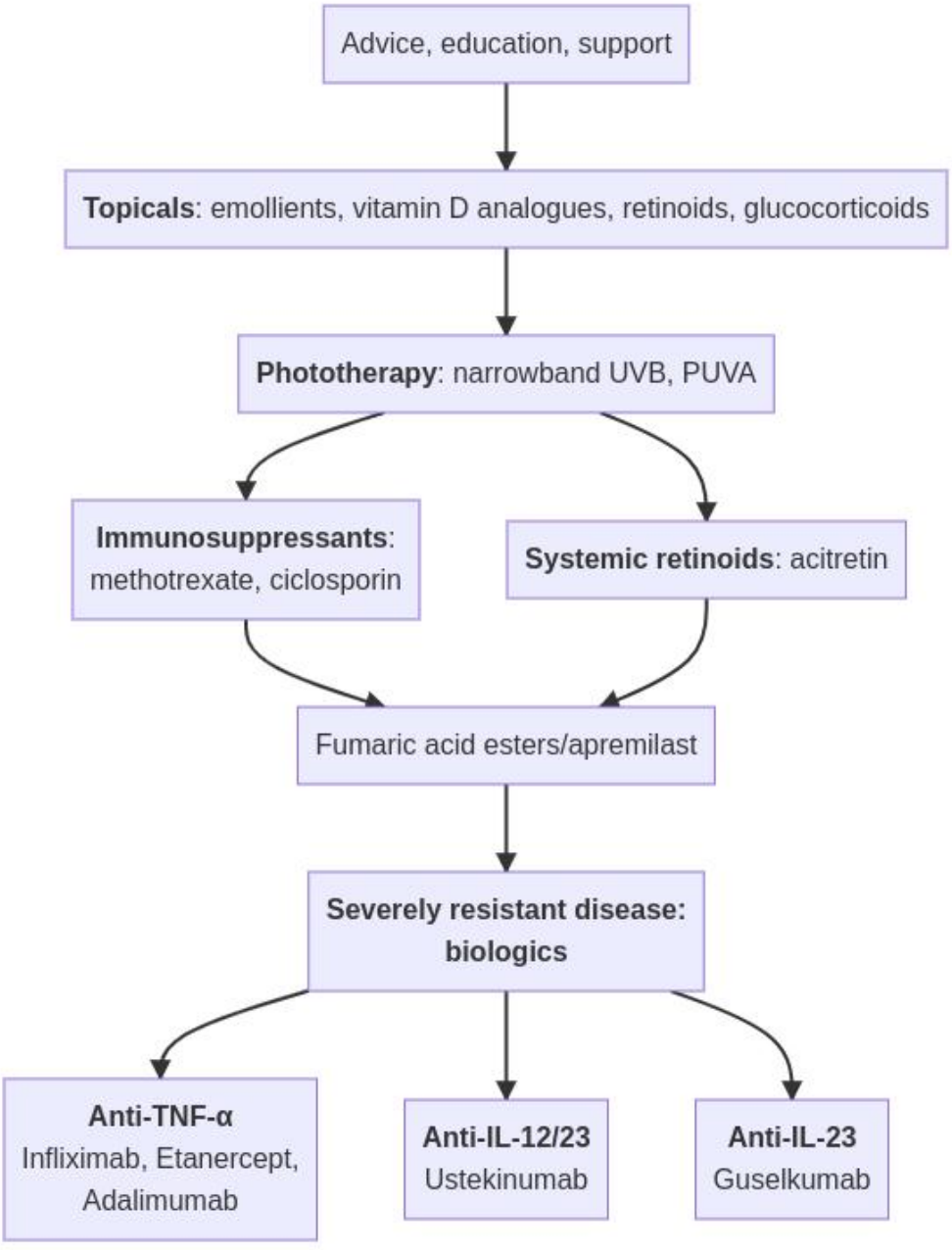
- **Sunlight**
- **Trauma**
- **Infection**
  - β-haemolytic strep ↑ guttate psoriasis
  - HIV may initally present with severe psoriasis
- **Drugs**
  - Antimalarials
  - β-blockers
  - Lithium
  - NSAIDs
- **Stress and anxiety**

Clinical types

- **Plaque** psoriasis:
  - most common
  - well-demarcated erythematous plaques
  - silver-white scales in untreated
    - bleed on scraping (due to dilated vessels underneath) → **Auspitz sign**
  - **Sites**
    - extensor surfaces
      - elbows
      - knees
      - lower back
    - scalp
    - nails

- **Guttate** psoriasis:
  - follows *Strep* throat
  - common in children/adolescent
  - UVB highly effective
  - may herald the onset of plaque psoriasis in adulthood
- **Erythrodermic** sporiasis: generalised → medical emergency
- **Pustular** psoriasis

Management of psoriasis



2.9 Hypopigmentation

Causes

- Vitiligo
- Albinism
- Pityriasis alba
- Pityriasis versicolor

Vitiligo

- **Acquired**
- Cell-mediated **autoimmune destruction of melanocytes**
- Loss of melanocytes → hypopigmented patches

Albinism

- **Autosomal recessive**
- **Reduced melanin production** by **normal number of melanocytes**
- ↑↑ risk of sunburn, skin cancer

2.10 Hyperpigmentation

Causes

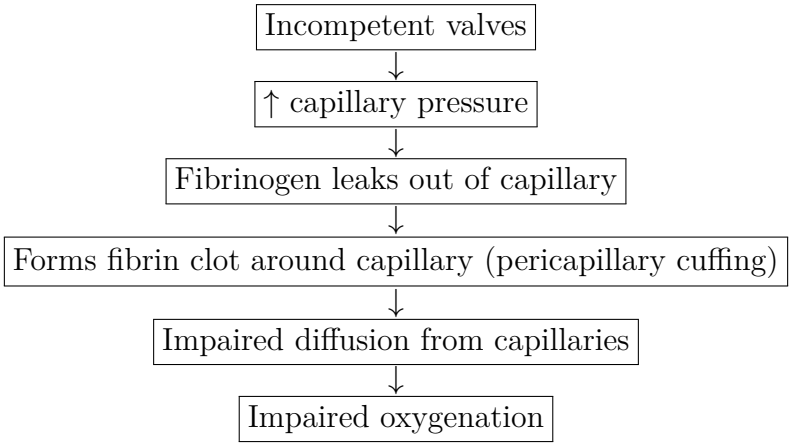
- **Endocrine**
  - Melasma/chloasma:
    - in pregnancy / some OCP users
    - discrete patches of facial pigmentation
  - Addison's disease
  - Cushing's syndrome
  - Nelson's syndrome
    - hyper-ACTH 2° to bilateral adrenalectomy for Cushing's
    - due to loss of -ve feedback from plasma cortisol
  - CKD
- **Drugs**
  - Amiodarone
  - Anti-cancers:
    - Bleomycin: Hodgkin's
    - Busulfan: CML
  - Choroquine
  - Psoralens

2.11 Pseudorandom factoids

SPF (sun protection factor)

- $\frac{\text{UV dose for producing erythema with sunscreen}}{\text{UV dose for producing erythema without sunscreen}}$

Mechanism of venous ulceration



Chapter 3

Nephrology

3.1 UTI

Definition

Presence of $> 10^5$ organisms/mL in a mid-stream sample of urine.

Features

- **LUTI**: cystitis/urethritis
  - Frequency
  - Urgency
  - Dysuria (burning urethral pain during micturition)
  - Haematuria
  - Strangury (intense desire to pass more urine after voiding, due to spasm of inflamed bladder wall)
- **UUTI**: acute pyelonephritis
  - Fever with chills and rigor
  - Vomiting
  - Loin pain
  - Renal angle tenderness

Commonly involved pathogens

- *E. coli*: 75%
- *Proteus*
- *Pseudomonas*
- *Streptococci*
- *Staph. epidermidis*

Investigations

- Dipstick test for nitrites, leucocyte esterase, and glucose

  - Most urinary pathogens (e.g. *E. coli, Proteus* etc) reduce nitrate to nitrite
  - UTI → Neutrophils in urine → leucocyte esterase

- Microscopy for WBC and organisms
- Urine culture

Treatment

Cystitis

- **1st choice**
  - **Trimethoprim** (200mg bds 3 days)
  - **Nitrofurantoin** (50mg qds 3 days)
- **Pregnancy**
  - Nitrofurantoin (50mg qds 7 days)
  - Cefalexin (250mg qds 7 days)
- Avoid trimethoprim during pregnancy, and nitrofurantoin at term

Pyelonephritis

- **1st choice**
  - **Cefalexin** (1g qds 14 days)
  - **Ciprofloxacin** (500mg bds 7 days)
- Hospitalise if no response within 24h

Epididymo-orchitis

- *1st choice*: Ciprofloxacin

Acute prostatitis

- *1st choice*: Trimethoprim

Prophylactic measures in women with recurrent UTI

- Fluid intake $\geq$ 2L/day
- Regular complete bladder evacuation
- Emptying the bladder before and after intercourse
- Good personal hygiene
- Continuous prophylactic trimethoprim (100mg) and nitrofurantoin (50 mg) at night

Chapter 4

Rheumatology

4.1 Investigations of musculoskeletal disease

Joint fluid aspiration

- Normal:
  - Amount small
  - Viscosity high
  - Colourless / pale yellow
- Inflammation:
  - Amount raised
  - Viscosity lowered (due to enzymatic degradation of hyaluronan & aggrecan)
  - Turbid (due to neutrophils)
- Crystal-induced arthropathies
  - Crystals seen by polarised light microscopy
  - Urate crystals → long, needle shaped, -ve birefringence
  - Ca pyrophosphate crystals → small, rhomboid, +ve birefringence ### Bone scintigraphy
- Dx of metastatic bone disease and Paget's
- $^{9}9$Tc radiolabelled bisphosphonate used

DEXA (Dual Emission X-ray Absorptiometry)

- Measure BMD (bone mineral density)
  - $<$ -2.5 → osteoporosis
  - Between -2.5 and -1 → osteopoenia
  - $>$ 2.5 → high bone mass (most common cause osteoarthritis)

Immunology

- **RF**

  - Antibody to Fc fragment of human Ig
  - 70% sensitive for RA (if nodules & extra-articular manifestations then 100% sensitive); specificity poor
  - **RF +ve diseases**
    * Rheumatoid arthritis
    * Sjogren's syndrome
    * SLE
    * Old age (> 65)

- **ACPA**
  - Antibody to peptides in which arginine has been converted to citrulline by peptidylarginine deiminase, an enzyme abundant in inflamed synovium.
  - 70% sensitive, >95% specific for RA

- **ANA** (antinuclear antibodies)
  - 100% sensitive for SLE but poor specificity
  - **ANA +ve diseases**
    * SLE
    * Sjogren's
    * Systemic sclerosis
    * Rheumatoid arthritis

- **Complement C3**
  - Active SLE $\rightarrow \downarrow$ C3 (due to consumption of C3 by immune complexes)

4.2 Seropositive vs Seronegative arthritis

- Seropositive: RF+ inflammatory arthritis
  - Rheumatoid arthritis
  - SLE

- Seronegative: RF- inflammatory arthritis
  - Ankylosing spondylitis
  - Reactive arthritis
  - Psoriatic arthropathy

4.3 Osteoarthritis

- Characterised by
  - degeneration of articular cartilage
  - subchondral osteosclerosis
  - osteophyte formation at joint margin
  - enlargement of affected joint

- Sites

  - hips
  - knees
  - PIPs
  - DIPs
  - cervical and lumbar spine

- Investigations:
  - X-ray of affected joint: findings described above in characteristics
  - MRI spine if spine OA + suspected root compression / spinal stenosis

- Treatment
  - Conservative:
    * Wt loss
    * Exercise
    * NSAIDs
    * Intraarticular glucocorticoids
  - Surgical: if refractory
    * Total joint replacement
    * Osteotomy

4.4 Spondyloarthropathies

- Asymmetrical oligoarthrites associated with HLA-B27 and typically involving the spine
  - Ankylosing spondylitis
  - Reactive arthritis
  - Psoriatic arthropathy
  - Axial spondyloarthritis
  - Entropathic spondyloarthritis (arthritis associated with IBD)

- Common features:
  - Asymmetric oligoarthritis
  - Sacroilitis
  - Enthesitis (inflammation where tendon attaches to bone)

Reactive arthritis

- "Reactive" to certain infections e.g. *Chlamydia, Campylobacter Salmonella, Shigella.*
- **Reiter's syndrome**:
  - Triad of *can't see, can't pee, can't bend the knee*
    * **Conjunctivitis**
    * **Urethritis**
    * **Reactive arthritis**
  - Due to *Chlamydia*

Chapter 5

Neurology

5.1 Raised ICP

- Normal ICP = **5-15 mmHg**

Causes

- **ICSOL**
  - Intracranial haemorrhage
  - Tumours e.g. glioma
  - Brain abscess
- **Hydrocephalus**: blockade of CSF circulation
  - Obstructive / non-communicating
  - Communicating
- **Cerebral oedema** e.g. meningoencephilitis
- **Venous sinus obstruction** e.g. cerebral venous thrombosis

Features

- **Headache**
- **Vomiting**
- **Diplopia / blurred vision**: Due to *6th nerve palsy*
  - 6th nerve palsy due to
    - stretching of the long, slender nerve
    - compression against petrous temporal bone
- **Papilloedema**
- **Bradycardia**
- **Hypertension**
- **Depressed consciousness**

Management

- According to cause:
  - Mass lesion → surgical decompression
  - Hydrocephalus → *ventriculoperitoneal shunt* operation
  - Oedema → glucocorticoids
- Supportive:
  - Head elevation
  - Fluid balance
  - BP control
  - Diuretics: mannitol

5.2 Neurological emergencies

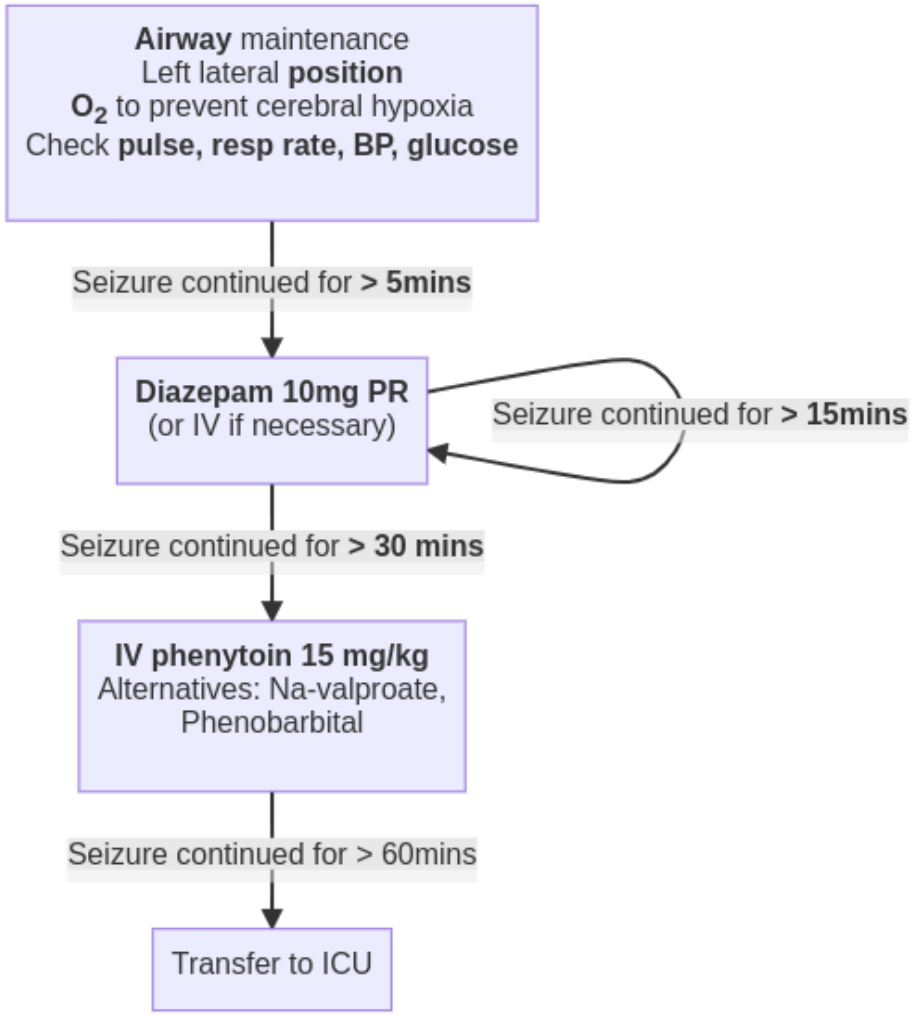
- **Status epilepticus**
- **Stroke** (if thrombo)
- **Subarachnoid haemorrhage**
- **Cord compression**
- **GBS**
- **Myasthenia gravis** (if bulbar and/or respiratory)

5.3 Status epilepticus

Definition

Continuous or recurrent **seizures** for $\geq$ **30 mins without gain of consciousness** in between.

Management



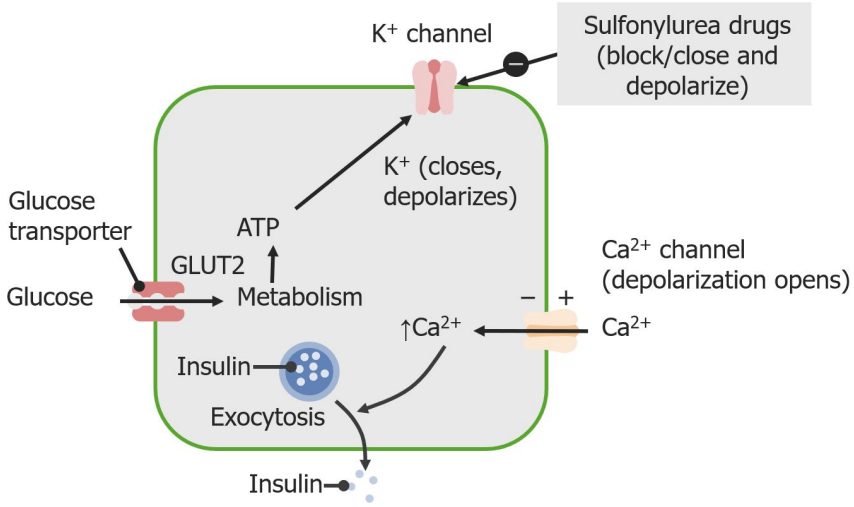
5.4 All jerks root values

- Biceps: C5
- Supinator: C6
- Triceps: C7
- Finger (aka Hoffmann test): C8
- Knee: L3, L4
- Ankle: S1, S2
- Plantar: S1 (technically not a jerk since it's a superficial reflex)

Chapter 6

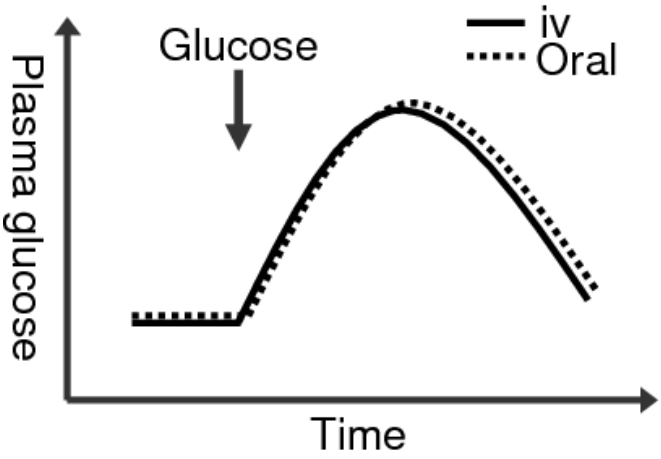
Diabetes Mellitus

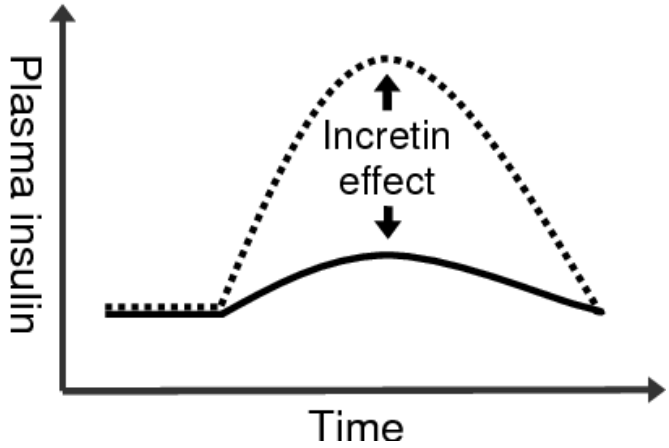
6.1 Mechanism of insulin secretion



6.2 Incretin effect

For the same glucose load applied orally and IV, the oral load stimulates more insulin secretion (because oral load → release of gut peptides GLP-1 and GIP → ↑ insulin secretion).





6.3 Diabetic ketoacidosis (DKA)

- **Medical emergency**
- Cause of death
  - Children: cerebral oedema
  - Adults:
    - **Hypokalaemia**
    - ARDS
    - Comorbidities: acute MI, sepsis, pneumonia
- **Cardinal biochemical features**
  - Hyperglycaemia → osmotic diuresis → dehydration, dyselectrolytaemia
  - Hyperketonaemia:
    - Insulin deficiency + elevated catecholamines → unrestrained lipolysis to make FFA → hepatic ketogenesis
  - Metabolic acidosis

Clinical features

- **Symptoms**

  - Polyuria, thirst
  - Weakness
  - Nausea, vomiting
  - Abdominal pain
  - Blurred vision
- **Signs**
  - Dehydration
  - Hypotension
  - Tachycardia
  - Air hunger / Kussmaul breathing (deep and sighing breathing)
  - Acetone breath
  - Delirium, drowsiness, coma

Management

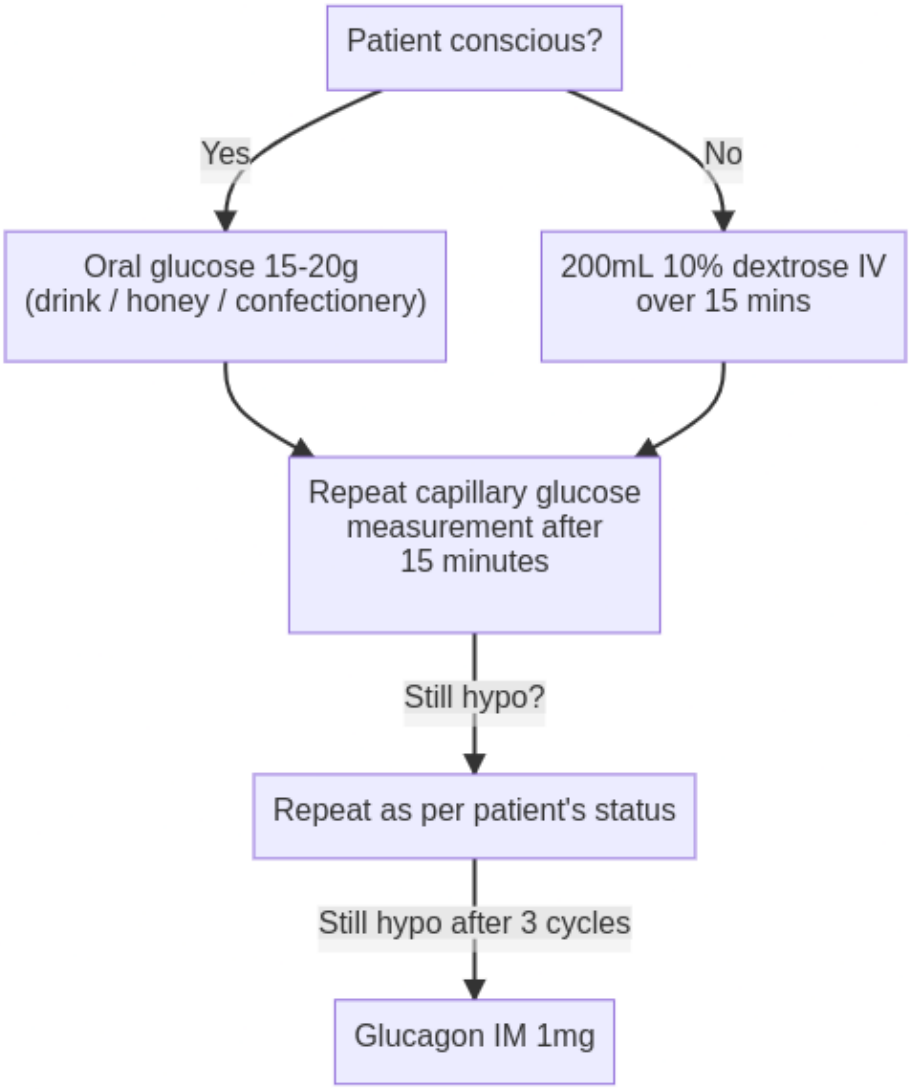
- **Establish IV access**
- **Volume replacement: 0.9% NaCl**
  - If systolic BP $\geq$ 90mmHg: 1L over 1h
  - Else: $\frac{1}{2}$L over 15mins $\rightarrow$ reassess. If BP still $<$ 90mmHg, repeat.
- **Insulin therapy**: **IV** 0.1 U/kg/h
  - Corrects hyperglycaemia & acidosis
- **Monitor**
  - Every 1h:
    - capillary blood glucose and ketone
    - vitals: pulse, BP, resp rate, O_2 sat, urine output
  - Every 2h: Venous HCO_3^- and K^+
  - Every 4h: Serum electrolytes
- If K^+ is low, 40mmol/L KCl with normal saline

6.4 Hypoglycaemia

Features

- **Autonomic**
  - Sweating
  - Trembling
  - Palpitations
- **Neuroglycopoenic**
  - Delirium
  - Drowsiness
  - Speech difficulty
  - Incoordination

Management



- Oral fast-acting carbohydrate (10-15g) e.g. glucose drink / confectionery / honey to buccal mucosa
- Repeat capillary glucose measurement 10-15mins later
  - If still hypo, repeat upto 3 cycles
  - Still hypo after 3 cycles → glucagon 1mg IM

6.5 Insulin therapy

Indications

- Type I DM
- Type II DM not controlled by OHA
- DIP / GDM
- DKA
- Hyperkalaemia

Preparations

- **Rapid-acting** (rapid=LAG-less)
  - Lispro
  - Aspart
  - Glulisine
- **Short-acting:** soluble/regular insulin
- **Intermediate-acting:** Isophane (I for I)
- **Long-acting**
  - Glargine (gLARGE-in)
  - Detemir Route of administration: **subcutaneous**

6.6 Oral Hypoglycaemic Agents

- **Biguanides**: Metformin
  - Insulin *sensitiser*
  - **Mechanism of action**
    - ↓ hepatic glucose production (gluconeogenesis and glycogenolysis)
    - ↑ gut glucose uptake & utilisation
    - weak inhibitor of mitochondrial respiration → ↑ AMP, ↓ ATP → ↑ glucose uptake utilisation etc.
  - **Side effects profile**
    - Weight neutral
    - Non-hypoglycaemic
    - *Lactic acidosis*
- **Sulphonylureas**: Glibenclamide, Gliclazide, Glimepiride
  - Insulin *secretagogue*
  - **Mechanism of action:** Block K^+ channel in β-cells → ↑ insulin secretion
  - **Side effects profile**
    - Wt gain
    - Hypoglycaemia
- **α-glucosidase inhibitors:** Acarbose

  - **Mechanism of action**: delay absorption of carbs
  - **Side effects profile**
    * Non-hypoglycaemic
    * Flatulence
    * Bloating
    * Diarrhoea

- **Incretin-based therapies:**
  - **DPP-4 inhibitors:** Gliptins
    * **MoA**
      · DPP-4: breaks down GLP-1 & GIP → inhibit incretin effect
  - **GLP-1 receptor agonists:** Exenatide, liraglutide

- **Thiazolidinediones:** Pioglitazone
  - **Mechanism of action**
    * PPAR-γ agonist → enhance action of insulin
  - **Side effects profile**
    * Non-hypoglycaemic
    * Wt gain (increase fat cells)

- **SGLT-2 inhibitors:** empagliflozin, dapagliflozin
  - **MoA:** inhibit reabsorption of glucose in renal tubules → 25% of filtered glucose excreted
  - Resulting glycosuria can lead to genital fungal infections
  - Empagliflozin → 35% reduced mortality in heart failure

Chapter 7

Gastrointestinal diseases

7.1 Weight loss

Causes

- **Endocrine**
  - DM (more in type I)
  - Thyrotoxicosis
  - Addison's
- **GI**
  - Any cause of dysphagia e.g.
    - Stroke
    - MS
    - Ca oesophagus
    - Achalasia cardia
    - Plummer-Vinson syndrome (oesophageal webs+IDA)
  - Malabsorption syndrome
    - IBD
    - Chronic pancreatitis (due to enzyme insufficiency)
    - Coeliac disease
- **Malignancies**
- **Chronic infection**
  - TB
  - AIDS
- **Psychological**
  - Depression
  - Anorexia nervosa
  - Bulimia nervosa
  - Alcoholism

Chapter 8

Haematology

8.1 Chronic myeloid leukaemia (CML)

Defining characteristic: **Philadelphia chromosome**

- Shortened chr22 by *reciprocal translocation* with chr9
- Results in **BCR-ABL fusion gene**
- BCR-ABL codes for a **tyrosine kinase** which influences cell proliferation and survival

Features

- Wt loss
- Lethargy
- Abdominal discomfort
- Splenomegaly
- Hepatomegaly

Phases

- Chronic
- Accelerated
- Blastic crisis

Investigations

- CBC: anaemia, leucocytosis
- PBF: full range of granulocytic precursors, from *myeloblasts* to *mature neutrophils*. Predominant: neutrophils and myelocytes. Myeloblasts $< 10\%$.
- Bone marrow examination: hypercellular marrow with increased myeloid precursors
- Chromosome analysis to detect Ph chromosome

Management

Chronic phase

- **1st line: Tyrosine kinase inhibitors (TKIs):**
  - **Imatinib**
  - **Dasatinib**
  - **Nilotinib**
  - normalise blood count within a month, complete cytogenetic response (disappearance of Ph chr) within 6 months in 90% patients. Resample bone marrow at 6mo to confirm. Thereafter monitor 3-monthly by RT-PCR for BCR-ABL mRNA transcripts.
- **Allogeneic HSC transplant:** if TKI fails
- **Hydroxycarbamide**
- **Interferon:** in pregnancy