

Medicine

Susmit

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# Chapter 1

## Cardiology

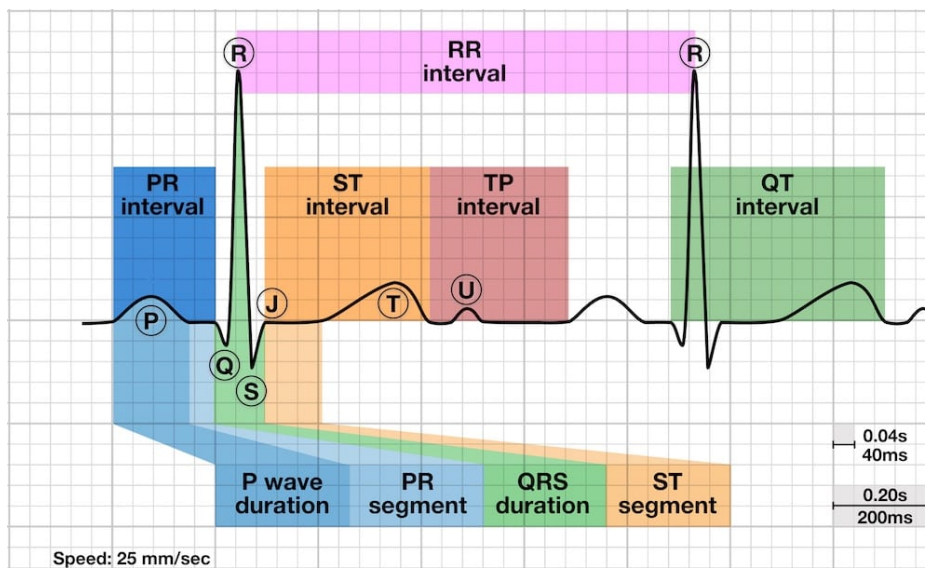
### 1.1 Presenting problems in CVS disease

#### 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  $> 2\text{mm}$
- Height  $> 1\text{mm}$
- Present in  $\geq 2$  leads
- Assocd with loss of R height ( $Q > R/4$ ; normally  $Q \leq R/4$ )
- Indicates *transmural* myocardial necrosis

### Segments vs intervals

- e.g. ST segment = end of S  $\rightarrow$  start of T
- PR interval = start of P  $\rightarrow$  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,  $V_1-V_6$

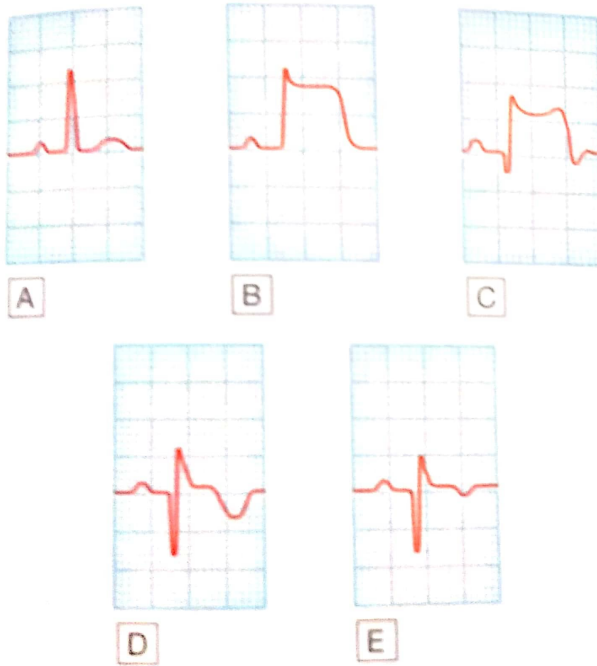
### Reciprocal changes

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

Site	Facing	Reciprocal
<i>Septal</i>	$V_1, V_2$	$V_7, V_8, V_9$
<i>Anterior</i>	$V_3, V_4$	None
<i>Lateral</i>	I, aVL, $V_5, V_6$	II, III, aVF
<i>Inferior</i>	II, III, aVF	I, aVL
<i>Posterior</i>	$V_7, V_8, V_9$	$V_1, V_2$

### 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
- $\beta$ -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

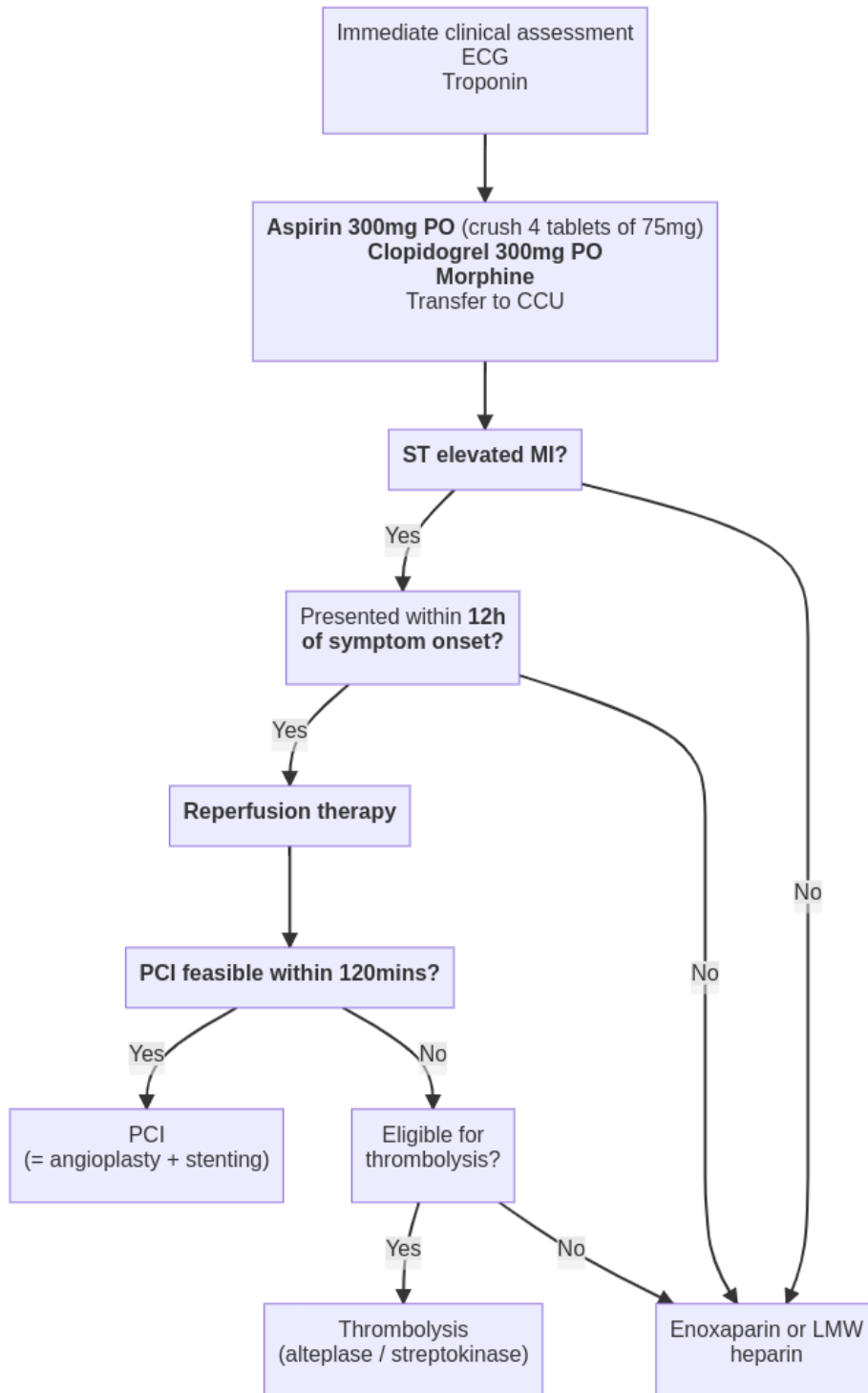
- **Rhythm control:**
  - Pharmacological cardioversion
    - \* Pt stable + no history of heart disease  $\rightarrow$  IV flecainide
    - \* Structural / ischaemic heart disease  $\rightarrow$  IV amiodarone
  - DC cardioversion if drugs fail
- **Rate control**
  - $\beta$ -blockers
  - Digoxin
  - 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  $\rightarrow \uparrow$  sebum
- oestrogen  $\rightarrow \downarrow$  sebum

- Sweat glands
  - innervated 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)  $\rightarrow$  prevent water loss from skin by oil layer
    - \* less preservatives  $\rightarrow$  less risk of allergy
- Emollients
  - Moisturise, lubricate, protect skin
  - *Vehicles without active drug*
- Glucocorticoids

### Phototherapy

- UVB
- Psoralen UVA
  - Psoralen:
    - \* natural photosensitiser from plant source
    - \* cross-link DNA strands on excitation with UVA
  - Cumulative exposure to PUVA  $\rightarrow \uparrow$  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- $\alpha$  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<sub>2</sub>*
  - 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** / **tinea**
    - \* *Trichophyton*
    - \* *Epidermophyton*
    - \* *Microsporum*
  - Yeast
- Deep: less common
  - Chromomycosis
  - Sporotrichosis

## 2.5 Scabies

### Agent

Caused by the mite *Sarcoptes scabiei 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, immunosuppression 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

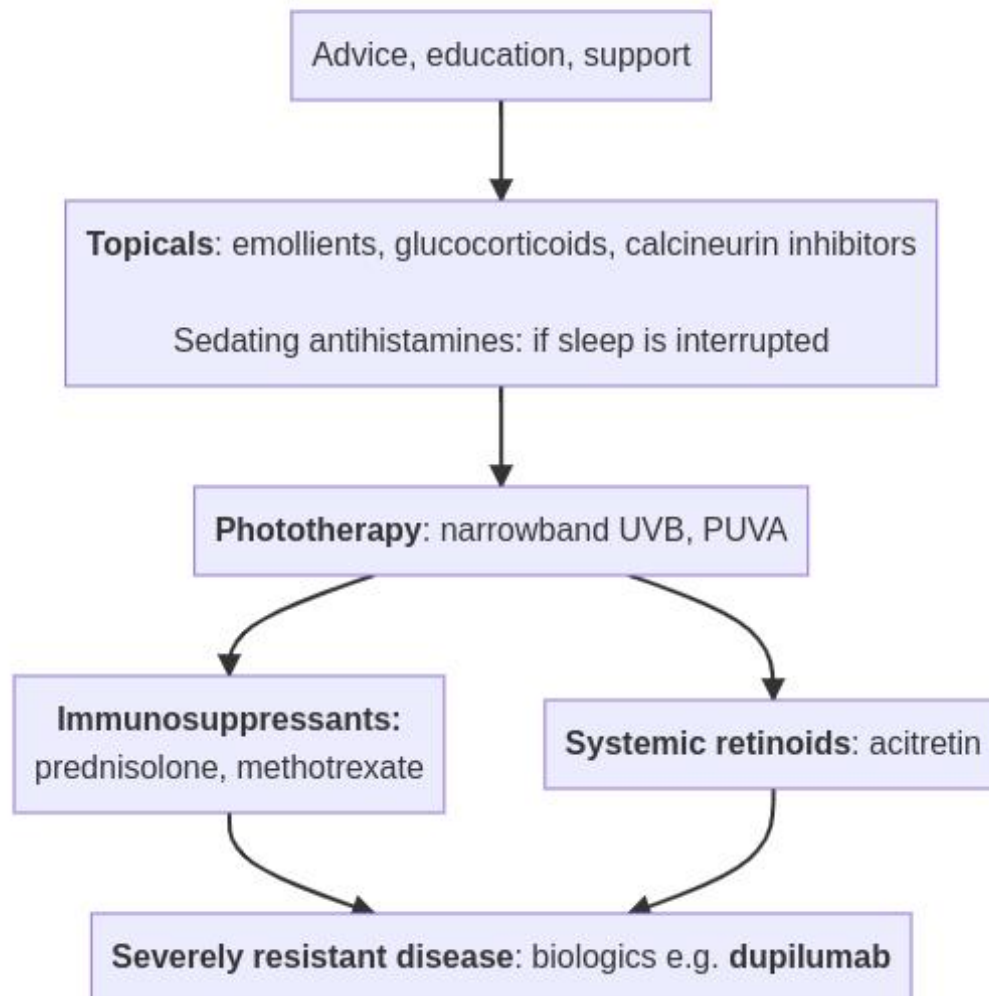
- Ill-defined erythema, oedema
- Papules, vesicles, bullae
- Exudation
- Scaling

#### 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

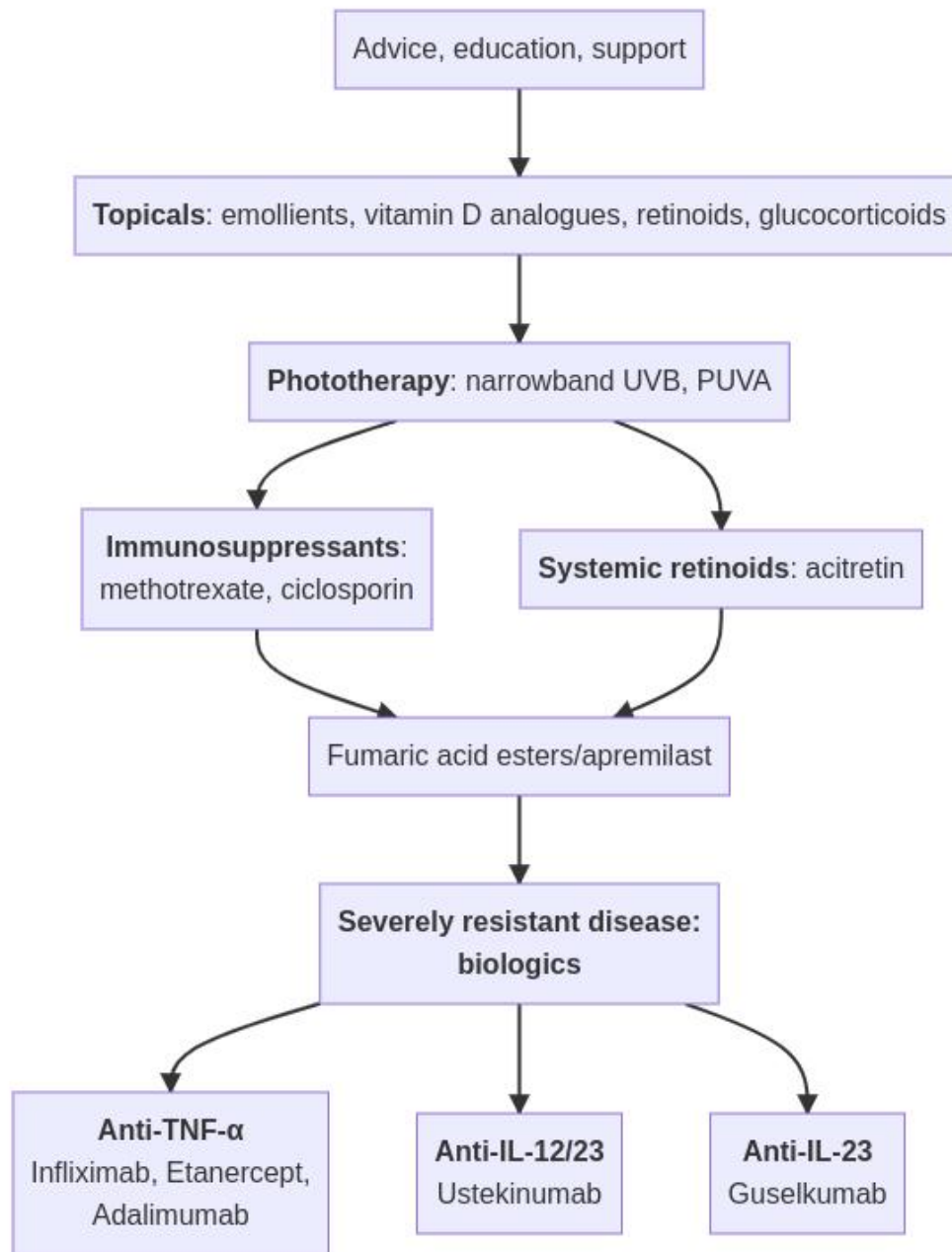
- **Sunlight**
- **Trauma**
- **Infection**
  - $\beta$ -haemolytic strep ↑ guttate psoriasis
  - HIV may initially present with severe psoriasis
- **Drugs**
  - Antimalarials
  - $\beta$ -blockers
  - Lithium
  - NSAIDs
- **Stress and anxiety**

### 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** psoriasis: generalised → medical emergency
- **Pustular** psoriasis

## Management of psoriasis



## Complications

- Psoriatic arthropathy
- Exfoliative dermatitis
- Secondary infection
- Hyperuricaemia and gout

## 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

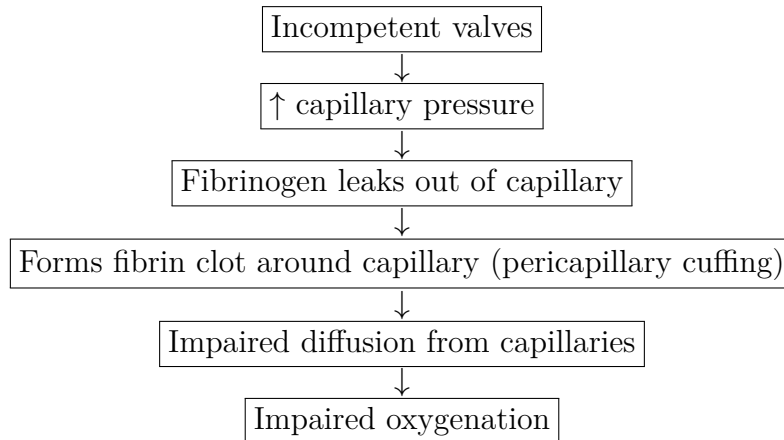
- **Endocrine**
  - Melasma/chloasma:
    - \* in pregnancy / some OCP users
    - \* discrete patches of facial pigmentation
  - Addison's disease
  - Cushing's syndrome
  - Nelson's syndrome
    - \* hyper-ACTH 2° to bilateral adrenalectomy for Cushing's
    - \* due to loss of -ve feedback from plasma cortisol
  - CKD
- **Drugs**
  - Amiodarone
  - Anti-cancers:
    - \* Bleomycin: Hodgkin's
    - \* Busulfan: CML
  - Chloroquine
  - 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  $\geq 2\text{L/day}$
- 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
- <sup>99</sup>Tc radiolabelled bisphosphonate used

#### DEXA (Dual Emission X-ray Absorptiometry)

- Measure BMD (bone mineral density)
  - $< -2.5$  → osteoporosis
  - Between -2.5 and -1 → osteopenia
  - $> 2.5$  → 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 oligoarthritis 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

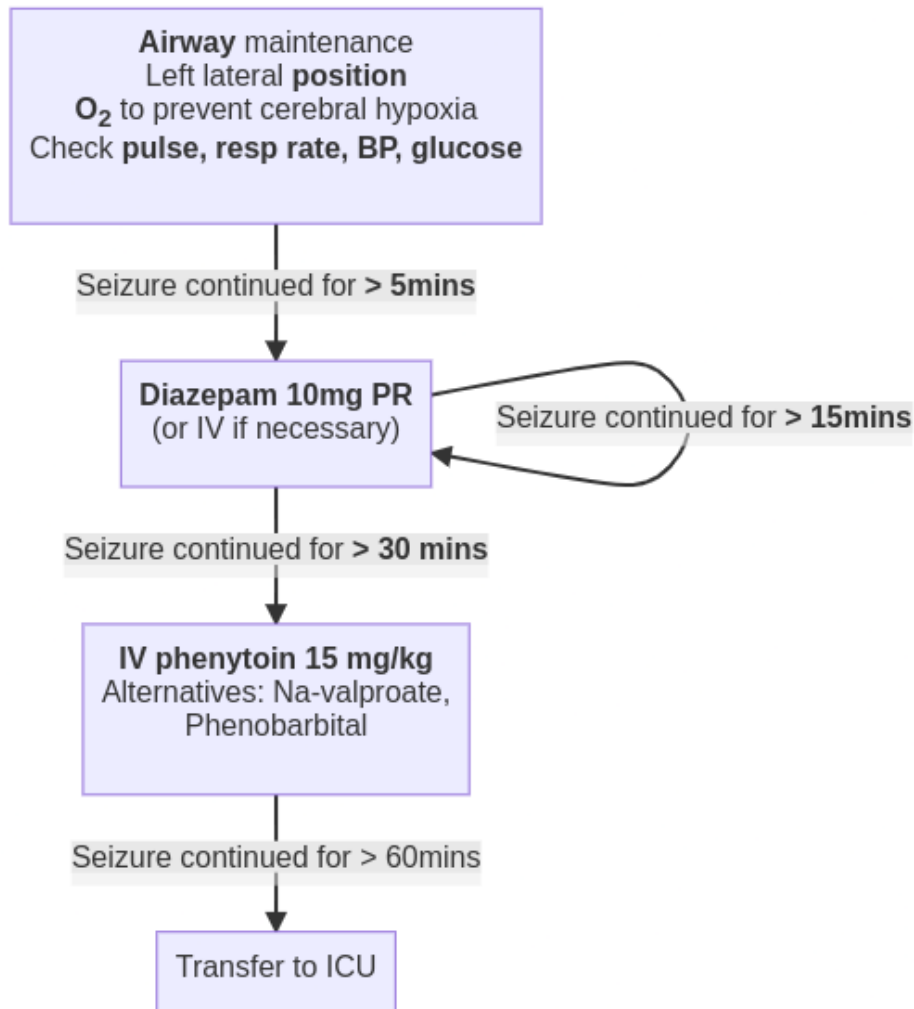
- **Status epilepticus**
- **Stroke** (if thrombo)
- **Subarachnoid haemorrhage**
- **Cord compression**
- **GBS**
- **Myasthenia gravis** (if bulbar and/or respiratory)

## 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)

## 5.5 Subarachnoid haemorrhage

### Causes

- Ruptured berry aneurysm (85%)
- Arterio-venous malformations

### Features

- Sudden severe “thunderclap” headache (often occipital)
- Vomiting
- High BP
- Neck stiffness
- May be loss of consciousness
- Photophobia

### Investigations

- CT scan: hyperdense material in the subarachnoid space
- Lumbar puncture: blood, xanthochromia

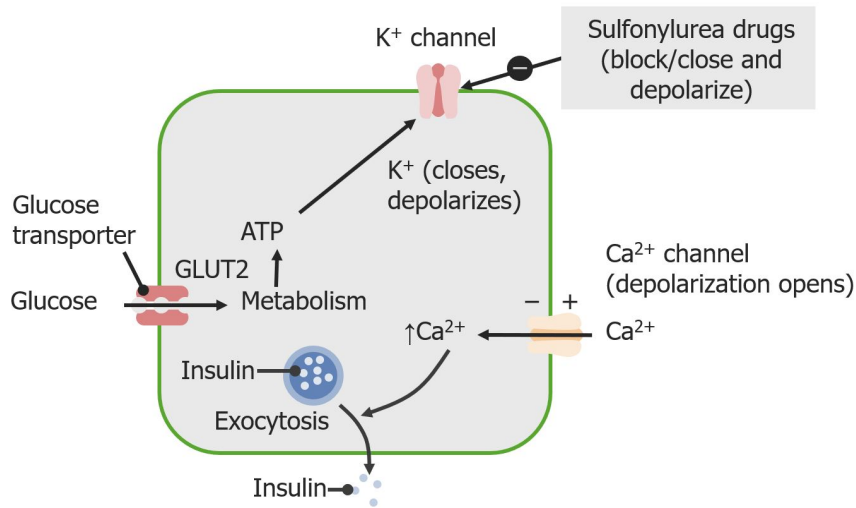
### Management

- **Nimodipine** 30-60mg IV for 5-14d, followed by 360mg oral for 7d
  - *prevents delayed ischaemia*
- Insertion of **Pt coils** into aneurysm
- **Surgical clipping** of the neck of the aneurysm
- Surgical removal if AVM

# Chapter 6

## Diabetes Mellitus

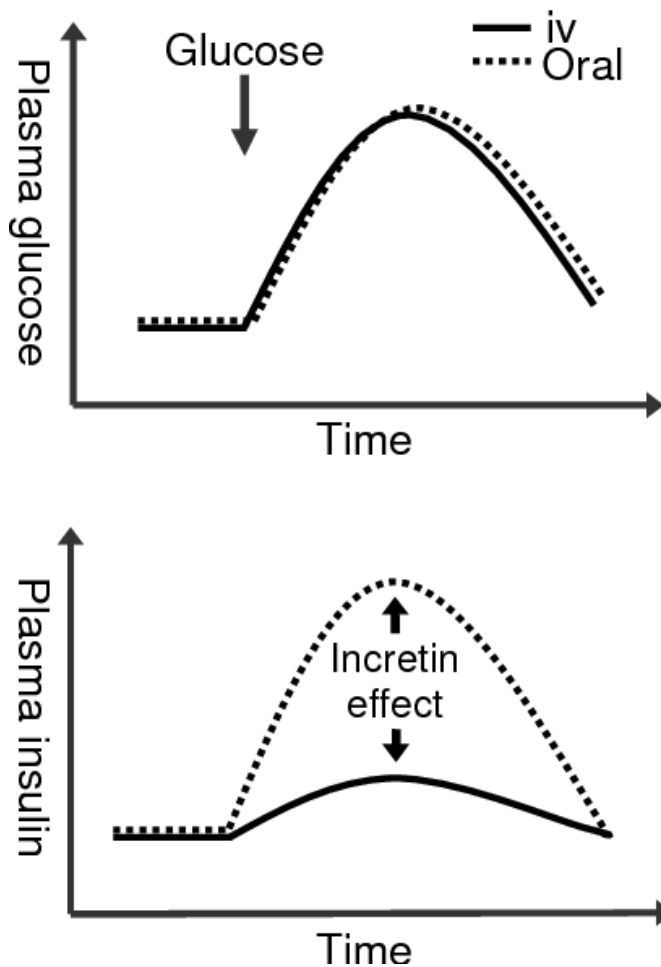
### 6.1 Mechanism of insulin secretion



### 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

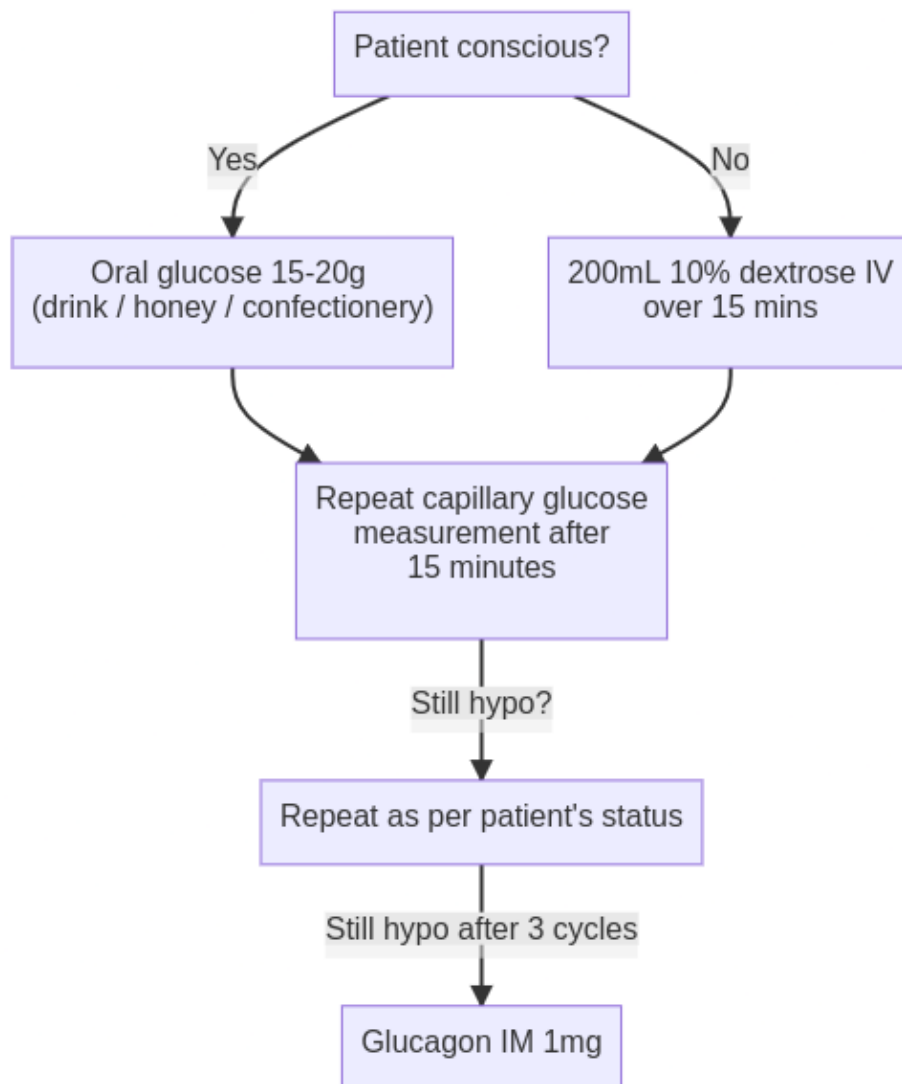
- **Establish IV access**
- **Volume replacement: 0.9% NaCl**
  - If systolic BP  $\geq$  90mmHg: 1L over 1h
  - Else:  $\frac{1}{2}$ L over 15mins  $\rightarrow$  reassess. If BP still  $<$  90mmHg, repeat.
- **Insulin therapy: IV 0.1 U/kg/h**
  - Corrects hyperglycaemia & acidosis
- **Monitor**
  - Every 1h:
    - \* capillary blood glucose and ketone
    - \* vitals: pulse, BP, resp rate, O<sub>2</sub> sat, urine output
  - Every 2h: Venous HCO<sub>3</sub><sup>-</sup> and K<sup>+</sup>
  - Every 4h: Serum electrolytes
- If K<sup>+</sup> is low, 40mmol/L KCl with normal saline

## 6.4 Hypoglycaemia

### Features

- **Autonomic**
  - Sweating
  - Trembling
  - Palpitations
- **Neuroglycopenic**
  - 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**

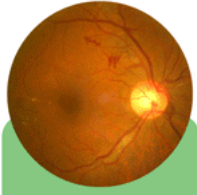

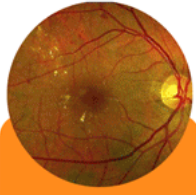


## 6.6 Oral Hypoglycaemic Agents

- **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  $\beta$ -cells → ↑ insulin secretion
  - **Side effects profile**
    - \* Wt gain
    - \* Hypoglycaemia
- **$\alpha$ -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- $\gamma$  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

## 6.7 Diabetic retinopathy

### Diabetic Retinopathy Classification

				
<b>No disease visible</b>	<b>Mild nonproliferative diabetic retinopathy (NPDR)</b>  Localized swelling of the small blood vessels in the retina (microaneurysms)	<b>Moderate NPDR</b>  Mild NPDR plus small bleeds (dot and blot haemorrhages), leaks (hard exudates) or closure (cotton wool spots) of small blood vessels.	<b>Severe NPDR</b>  Moderate NPDR plus further damage to blood vessels (interretinal hemorrhages, venous beading, intraretinal microvascular abnormalities).	<b>PDR</b>  New vessel formation or vitreous/preretinal hemorrhage or tractional retinal detachment

# 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
  - ↑ M/E ratio



- ↓ erythropoiesis
- ↑ leucopoiesis
- **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

# Chapter 9

## Nutritional diseases

### 9.1 Vitamins

#### B<sub>1</sub> (thiamin) deficiency

##### Functions of thiamin

- Cofactor in different pathways of aerobic metabolism of glucose
  - decarboxylation of pyruvate to acetyl-coA (so bridge between glycolysis and Krebs)
  - decarboxylation of  $\alpha$ -ketoglutarate to succinate in Krebs

##### Features

- For its pivotal role in aerobic glucose meta, the largest blow is dealt to the tissues most dependent on glucose - the **brain** and the **heart**.
- **Beri-beri**
  - **Dry:** Neurological beri-beri
    - \* Peripheral neuropathy
    - \* Wrist/foot drop
    - \* **Korsakoff's psychosis**
    - \* **Wernicke's encephalopathy**
  - **Wet:** Cardiac beri-beri (wet as it causes generalised oedema)
    - \* Biventricular failure
    - \* Generalised oedema
    - \* Pulmonary oedema

##### Treatment

- Wet and Wernicke's should be treated by IV vit-B and C mixture
- Korsakoff's: irreversible, nonresponsive to thiamin

## **B<sub>12</sub> deficiency**

### **Functions of B<sub>12</sub>**

- Recycles folate → essential for **cell division** (especially in RBC)
- **Myelination**

### **Features**

- Megaloblastic anaemia
- **Neurologic features**
  - Peripheral neuropathy
  - Autonomic neuropathy
  - Optic atrophy
  - Subacute combined degeneration of spinal cord