Hypertension

The practical definition of hypertension is 'the level of BP at which the benefits of treatment outweigh the costs and hazards'.

Blood pressure values are determined ***by mechanical, hormonal and environmental factors***. Systemic BP rises with age, and the incidence of cardiovascular disease (particularly stroke and coronary artery disease) is closely related to average BP at all ages, even when BP readings are within the so-called "normal range".

The cardiovascular risks associated with BP depend upon the combination of risk factors in an individual, such as;

- age,
- gender,
- weight,
- physical activity,
- smoking,
- family history,
- serum cholesterol,
- diabetes mellitus and
- pre-existing vascular disease.

18.85 Definition of hypertension

Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
BP		
Optimal	< 120	< 80
Normal	< 130	85
High normal	130–139	85–89
Hypertension		
Grade 1 (mild)	140–159	90–99
Grade 2 (moderate)	160–179	100–109
Grade 3 (severe)	≥ 180	> 110
Isolated systolic hypertension		
Grade 1	140–159	< 90
Grade 2	≥ 160	< 90

Aetiology

In more than 95% of cases, a specific underlying cause of hypertension cannot be found. Such patients are said to have essential hypertension. The pathogenesis is not clearly understood.

In about 5% of cases, hypertension can be shown to be a consequence of a specific disease or abnormality leading to sodium retention and/or peripheral vasoconstriction secondary hypertension.

18.86 Causes of secondary hypertension

Alcohol

Obesity

Pregnancy (pre-eclampsia)

Renal disease (Ch. 17)
- Parenchymal renal disease, particularly glomerulonephritis
- Renal vascular disease
- Polycystic kidney disease

Endocrine disease (Ch. 20)
- Phaeochromocytoma
- Cushing's syndrome
- Primary hyperaldosteronism (Conn's syndrome)
- Glucocorticoid-suppressible hyperaldosteronism
- Hyperparathyroidism
- Acromegaly
- Primary hypothyroidism
- Thyrotoxicosis
- Congenital adrenal hyperplasia due to 11-β-hydroxylase or 17-α-hydroxylase deficiency
- Liddle's syndrome (p. 441)
- 11-β-hydroxysteroid dehydrogenase deficiency

Drugs
- e.g. Oral contraceptives containing oestrogens, anabolic steroids, corticosteroids, NSAIDs, carbenoxolone, sympathomimetic agents

Coarctation of the aorta (p. 632)

Many factors may contribute to its development, including:

- renal dysfunction,
- Peripheral resistance vessel tone,
- endothelial dysfunction,
- autonomic tone,
- insulin resistance and
- neurohumoral factors.

Hypertension is more common in some ethnic groups, particularly African Americans and Japanese, and approximately 40–60% is explained by genetic factors.

Important environmental factors include

- a high salt intake,
- heavy consumption of alcohol,
- obesity,
- lack of exercise and
- impaired intrauterine growth.

There is little evidence that 'stress' causes hypertension.

Approach to newly diagnosed hypertension

Hypertension is predominantly an asymptomatic condition and the diagnosis is usually made at routine examination or when a complication arises. A BP check is advisable every 5 years in adults.

The objectives of the initial evaluation of a patient with high BP readings are:

- to obtain accurate, representative BP measurements
- to identify contributory factors and any underlying cause (secondary hypertension)
- to assess other risk factors and quantify cardiovascular risk
- to detect any complications (target organ damage) that are already present
- to identify comorbidity that may influence the choice of antihypertensive therapy.

These goals are attained by:

- ✓ a careful history,
- ✓ clinical examination and
- ✓ some simple investigations.

Measurement of blood pressure

Measurements should be made to the nearest 2 mmHg, in the sitting position with the arm supported, and repeated after 5 minutes' rest if the first recording is high

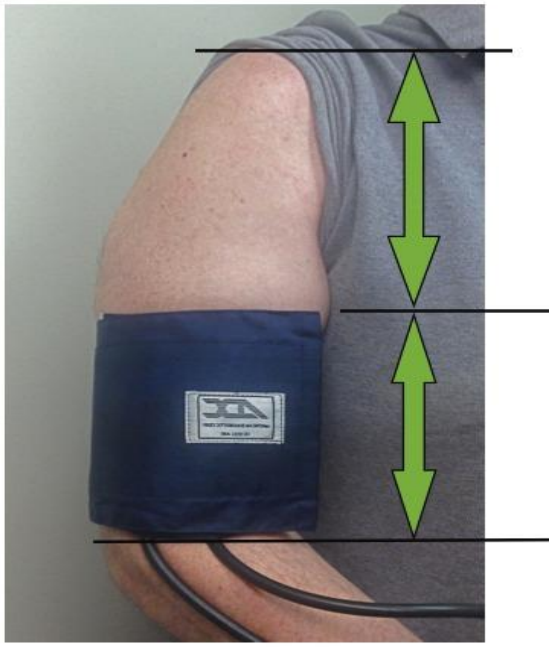
To avoid spuriously high readings in obese subjects, the cuff should contain a bladder that encompasses at least two-thirds of the arm circumference.

18.87 How to measure blood pressure

- Use a machine that has been validated, well maintained and properly calibrated
- Measure sitting BP routinely, with additional standing BP in elderly and diabetic patients and those with possible postural hypotension
- Remove tight clothing from the arm
- Support the arm at the level of the heart
- Use a cuff of appropriate size (the bladder must encompass more than two-thirds of the arm)
- Lower the pressure slowly (2 mmHg per second)
- Read the BP to the nearest 2 mmHg
- Use phase V (disappearance of sounds) to measure diastolic BP
- Take two measurements at each visit

This cuff is the right size around the arm, but it's too narrow for the length of the arm.

It should be 2/3 the length from elbow to shoulder



History

Family history, lifestyle (exercise, salt intake, smoking habit) and other risk factors should be recorded. A careful history will identify those patients with drug- or alcohol-induced hypertension and may elicit the symptoms of other causes of secondary hypertension, such as pheochromocytoma-***Small vascular tumor of adrenal medulla causing irregular secretion of epinephrine and norepinephrine, leading to attacks of raised blood pressure, palpitations, and headache*** **-** (paroxysmal headache, palpitation and sweating) or complications such as coronary artery disease (e.g. angina, breathlessness).

Examination

Radio-femoral delay (coarctation of the aorta; see Fig.18.97, p. 632), enlarged kidneys (polycystic kidney disease), abdominal bruits (renal artery stenosis) and the characteristic facies and habitus of Cushing's syndrome are all examples of physical signs that may help to identify causes of secondary hypertension

Examination may also reveal features of important risk factors, such as central obesity and hyperlipidemia (tendon xanthomas and so on). Most abnormal signs are due to the complications of hypertension.

Nonspecific findings include:

1- left ventricular hypertrophy (apical heave),
2- accentuation of the aortic component of the second heart sound, and a fourth heart sound.
3- Abnormal optic fundi
4- generalized atheroma
5- aortic aneurysm or
6- peripheral vascular disease

Target organ damage

The adverse effects of hypertension on the organs can often be detected clinically.

Blood vessels

In larger arteries (> 1 mm in diameter), the internal elastic lamina is thickened, smooth muscle is hypertrophied and

fibrous tissue is deposited. The vessels dilate and become tortuous, and their walls become less compliant.
In smaller arteries (< 1 mm), hyaline arteriosclerosis occurs in the wall, the lumen narrows and aneurysms may develop. Widespread atheroma develops and may lead to coronary and cerebrovascular disease, *particularly if other risk factors (e.g. smoking, hyperlipidaemia, diabetes) are present*.
These structural changes in the vasculature often perpetuate and aggravate hypertension by increasing peripheral vascular resistance and reducing renal blood flow, thereby activating the renin–angiotensin–aldosterone axis (p. 547).
Hypertension is a major risk factor in the pathogenesis of aortic aneurysm and aortic dissection.

Central nervous system
Stroke is a common complication of hypertension and may be due to cerebral hemorrhage or infarction. Carotid atheroma and TIAs (**transient ischemic attacks**) are more common in hypertensive patients. Subarachnoid hemorrhage is also associated with hypertension.
Hypertensive encephalopathy is a rare condition characterized by high BP and neurological symptoms, including transient disturbances of speech or vision, paresthesia, isorientation, fits and loss of consciousness. Papilledema is common.
A CT scan of the brain often shows hemorrhage in and around the basal ganglia; however, the neurological deficit is usually reversible if the hypertension is properly controlled.

Retina
The optic fundi reveal a gradation of changes linked to the severity of hypertension; fundoscopy can, therefore, provide an indication of the arteriolar damage occurring elsewhere
*((The **fundus** of the eye is the interior surface of the eye opposite the lens and includes the retina, **optic** disc, macula, fovea, and posterior pole))*

.....To be continued

Hypertension

Heart

High BP places a pressure load on the heart and may lead to left ventricular hypertrophy. The excess cardiac mortality and morbidity associated with hypertension are largely due to a higher incidence of coronary artery disease.

Severe hypertension can cause left ventricular failure in the absence of coronary artery disease, particularly when renal function, and therefore sodium excretion, are impaired.

Kidneys

Long-standing hypertension may cause proteinuria and progressive renal failure by damaging the renal vasculature.

Malignant or 'accelerated' phase Hypertension

This rare condition is characterized by accelerated microvascular damage with necrosis in the walls of small arteries and arterioles ('fibrinoid necrosis') and by intravascular thrombosis.

The diagnosis is based on evidence of high BP and rapidly progressive end organ damage, such as:-

1- retinopathy (grade 3 or 4),
2- renal dysfunction (especially proteinuria)
3- and/or hypertensive encephalopathy
4- Left ventricular failure may occur
5- and, if this is untreated, death occurs within months

Investigations

All hypertensive patients should undergo a limited number of investigations.

18.89 Hypertension: investigation of all patients

- Urinalysis for blood, protein and glucose
- Blood urea, electrolytes and creatinine
  N.B. Hypokalaemic alkalosis may indicate primary hyperaldosteronism but is usually due to diuretic therapy
- Blood glucose
- Serum total and HDL cholesterol
- Thyroid function tests
- 12-lead ECG (left ventricular hypertrophy, coronary artery disease)

(HDL = high-density lipoprotein)

Additional investigations are appropriate in selected patients

18.90 Hypertension: investigation of selected patients

- Chest X-ray: to detect cardiomegaly, heart failure, coarctation of the aorta
- Ambulatory BP recording: to assess borderline or 'white coat' hypertension
- Echocardiogram: to detect or quantify left ventricular hypertrophy
- Renal ultrasound: to detect possible renal disease
- Renal angiography: to detect or confirm presence of renal artery stenosis
- Urinary catecholamines: to detect possible phaeochromocytoma (p. 781)
- Urinary cortisol and dexamethasone suppression test: to detect possible Cushing's syndrome (p. 773)
- Plasma renin activity and aldosterone: to detect possible primary aldosteronism (p. 780)

Management

Quantification of cardiovascular risk

The sole objective of antihypertensive therapy is to reduce the incidence of adverse cardiovascular events, particularly:

a- coronary artery disease,
b- stroke and
c- heart failure

Threshold for intervention

Systolic BP and diastolic BP are both powerful predictors of cardiovascular risk.

Patients with diabetes or cardiovascular disease are at particularly high risk and the threshold for initiating antihypertensive therapy is therefore lower (≥ 140/90 mmHg) in these patient groups. The thresholds for treatment in the elderly are the same as for younger patients

Hypertension in old age:

• **Prevalence**: affects more than half of all people over the age of 60 yrs (including isolated systolic hypertension).

• **Risks**: hypertension is the most important risk factor for MI, heart failure and stroke in older people.

• **Benefit of treatment**: absolute benefit from therapy is greatest in older people (at least up to age 80 yrs).

• **Target BP**: similar to that for younger patients.

• **Tolerance of treatment**: antihypertensives are tolerated as well as in younger patients.

• **Drug of choice**: low-dose thiazides but, in the presence of coexistent disease (e.g. gout, diabetes), other agents may be more appropriate.

Treatment targets

The optimum BP for reduction of major cardiovascular events has been found to be ***139/83 mmHg***, & even lower in patients with diabetes mellitus. Moreover, reducing BP below this level causes no harm. Patients taking antihypertensive therapy require follow-up at 3-monthly intervals to:

- monitor BP,
- minimize side-effects and
- reinforce lifestyle advice.

Non-drug therapy

Appropriate lifestyle measures may obviate the need for drug therapy in patients with borderline hypertension.

- ✓ Correcting obesity,
- ✓ reducing alcohol intake,
- ✓ restricting salt intake,
- ✓ taking regular physical exercise and
- ✓ increasing consumption of fruit and vegetables can all lower BP.
- ✓ Moreover, quitting smoking,

- ✓ eating oily fish and
- ✓ adopting a diet that is low in saturated fat, ***may produce further reductions in cardiovascular risk***

Antihypertensive drugs

Thiazide and other diuretics; The mechanism of action of these drugs is incompletely understood and it may take up to a month for the maximum effect to be observed. An appropriate daily dose is 2.5 mg bendroflumethiazide or 0.5 mg cyclopenthiazide. More potent loop diuretics, such as furosemide (40 mg daily) or bumetanide (1 mg daily), have few advantages over thiazides in the treatment of hypertension, unless there is substantial renal impairment or they are used in conjunction with an ACE inhibitor.

ACE inhibitors; ACE inhibitors (e.g. enalapril 20 mg daily, ramipril 5–10 mg daily or lisinopril 10–40 mg daily) inhibit the conversion of angiotensin I to angiotensin II and are usually well tolerated.

They should be used with particular care in patients with impaired renal function or renal artery stenosis because they can reduce the filtration pressure in the glomeruli and precipitate renal failure.

Calcium channel antagonists; The dihydropyridines (e.g. amlodipine 5–10 mg daily, nifedipine 30–90 mg daily) are effective and usually well-tolerated antihypertensive drugs that are particularly useful in older people.

Side-effects include flushing, palpitations and fluid retention.

Beta-blockers; These are no longer used as first-line antihypertensive therapy, except in patients with another indication for the drug (e.g. angina). Metoprolol, atenolol, and bisoprolol preferentially block cardiac β-adrenoceptors, as opposed to the β2-adrenoceptors that mediate vasodilatation and bronchodilatation.

Labetalol and carvedilol; are combined β- and α-adrenoceptor antagonists which are sometimes more effective

than pure β-blockers. Labetalol can be used as an infusion in malignant phase hypertension.

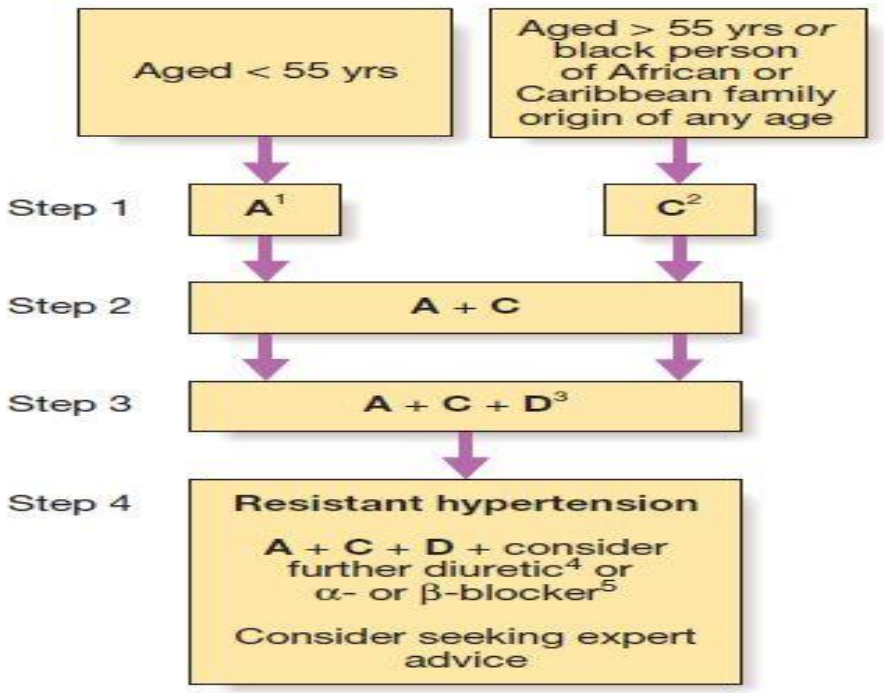
Other drugs. A variety of vasodilators may be used. These include the α1-adrenoceptor antagonists (α-blockers), such as:

- ✓ prazosin
- ✓ indoramin and
- ✓ doxazosin

and drugs that act directly on vascular smooth muscle, such as hydralazine and minoxidil.
Side-effects include first-dose and postural hypotension, headache, tachycardia and fluid retention. Minoxidil also causes increased facial hair and is therefore unsuitable for female patients.

Choice of antihypertensive drug

Trials that have compared thiazides, calcium antagonists, ACE inhibitors and angiotensin receptor blockers have not shown consistent differences in outcome, efficacy, side-effects or quality of life. Beta-blockers, which previously featured as first-line therapy in guidelines, have a weaker evidence base.
Although some patients can be treated with a single antihypertensive drug, a combination of drugs is often required to achieve optimal BP control.



1A = ACE inhibitor or consider angiotensin II receptor blocker (ARB)
2C = calcium channel blocker
3D = thiazide-type diuretic

Combination therapy may be desirable for other reasons; for example, low-dose therapy with two drugs may produce fewer unwanted effects than treatment with the maximum dose of a single drug. Some drug combinations have complementary or synergistic actions; for example, thiazides increase activity of the renin–angiotensin system, while ACE inhibitors block it.

Emergency treatment of accelerated phase or malignant hypertension

In accelerated phase hypertension, lowering BP too quickly may compromise tissue perfusion (due to altered autoregulation) and can cause cerebral damage, including occipital blindness, and precipitate coronary or renal insufficiency.

Even in the presence of cardiac failure or hypertensive encephalopathy, a controlled reduction to a level of about 150/90 mmHg over a period of 24–48 hours is ideal.
Bed rest and oral drug therapy, in most patients, can bring BP under control and avoid parenteral therapy.

Refractory hypertension

The common causes of treatment failure in hypertension are

1- non-adherence to drug therapy,
2- inadequate therapy, and
3- failure to recognize an underlying cause, such as renal artery stenosis or pheochromocytoma.

Adjuvant drug therapy

• *Aspirin*. Antiplatelet therapy is a powerful means of reducing cardiovascular risk but may cause bleeding, particularly intra-cerebral hemorrhage, in a small number of patients.
• *Statins*. Treating hyperlipidemia can produce a substantial reduction in cardiovascular risk.

Lec.3 **GENERAL MEDICINE**

Dr.Anas Hammad

Ischemic Heart Diseases

The RA receives deoxygenated blood from the superior and inferior venae cavae and discharges blood to the RV, which in turn pumps it into the pulmonary artery. Blood passes through the pulmonary arterial and alveolar capillary bed, where it is oxygenated, then drains through the pulmonary veins into the LA. Blood then passes into the LV, which pumps it into the Aorta.

Systemic and locally released vasoactive substances influence tone; vasoconstrictors include noradrenaline (norepinephrine), angiotensin II and endothelin-1, whereas adenosine, bradykinin, prostaglandins and nitric oxide are vasodilators. Resistance to blood flow rises with viscosity and is mainly influenced by the haematocrit.

Coronary blood vessels receive sympathetic and parasympathetic innervation. While;

- ***stimulation of a-adrenoceptors causes vasoconstriction*** and
- ***stimulation of β2-adrenoceptors causes vasodilatation***,

the predominant effect of sympathetic stimulation in coronary arteries is vasodilatation.

Parasympathetic stimulation also causes modest dilatation of normal coronary arteries. Because of these homeostatic mechanisms that regulate vessel tone, narrowing or stenosis in a coronary artery does not limit flow, even during exercise, until the cross-sectional area of the vessel is reduced by at least **70%**.

Cardiac output, BP and pulse rate change with respiration as the result of changes in blood flow to the right and left heart.

Investigation of Cardiovascular Disease

Several investigations may be required in the diagnosis of cardiac disease and assessment of its severity. Basic tests, such as electrocardiography, chest X-ray and echocardiography, can be performed in an outpatient clinic or at the bedside, whereas more complex procedures such as cardiac catheterisation, radionuclide imaging, computed tomography (CT) and magnetic resonance imaging (MRI) require specialized facilities.

16.4 Common indications for echocardiography

- Assessment of left ventricular function
- Diagnosis and quantification of severity of valve disease
- Identification of vegetations in endocarditis
- Identification of structural heart disease in atrial fibrillation, cardiomyopathies or congenital heart disease
- Detection of pericardial effusion
- Identification of structural heart disease or intracardiac thrombus in systemic embolism

Cardiac biomarkers

Several biomarkers are available that can be measured in peripheral blood to assess myocardial dysfunction and ischaemia.

- ✓ **Brain natriuretic peptide;** (BNP) is a peptide hormone of 32 amino acids with diuretic properties. It is secreted by the LV as a 108-amino acid prohormone, which is cleaved to produce active BNP, and an inactive 76-amino acid N-terminal fragment (NT-proBNP). Circulating levels are elevated in conditions associated with LV systolic dysfunction.
  Generally, NT-proBNP is measured in preference to BNP since it has a longer half-life. Measurements of NT-proBNP are indicated for the diagnosis of LV dysfunction and to assess prognosis and response to therapy in patients with heart failure
- ✓ **Cardiac troponin;** Troponin I and troponin T are structural cardiac muscle proteins that are released during myocyte damage and necrosis, and represent the cornerstone of the diagnosis of acute myocardial infarction, so that elevated plasma troponin concentrations may be observed in conditions other than acute MI, such as pulmonary embolus, septic shock and pulmonary oedema.

Functional Anatomy and Physiology

The atria are thin-walled structures that act as priming pumps for the ventricles, which provide most of the energy required to maintain the circulation.
The ventricles are thick-walled structures, adapted to circulating blood through large vascular beds under pressure. The LV myocardium is normally around 10 mm thick because it pumps blood at a higher pressure than the RV.
Normally, the heart occupies less than 50% of the transthoracic diameter in the frontal plane, as seen on a chest X-ray.

Coronary circulation

The left main and right coronary arteries arise from the left and right sinuses of the aortic root, distal to the aortic valve (Fig.1). Within **2.5 cm** of its origin, the left main coronary artery divides into the left anterior descending artery (LAD), which runs in the anterior interventricular groove, and the left circumflex artery (CX), which runs posteriorly in the atrioventricular groove.

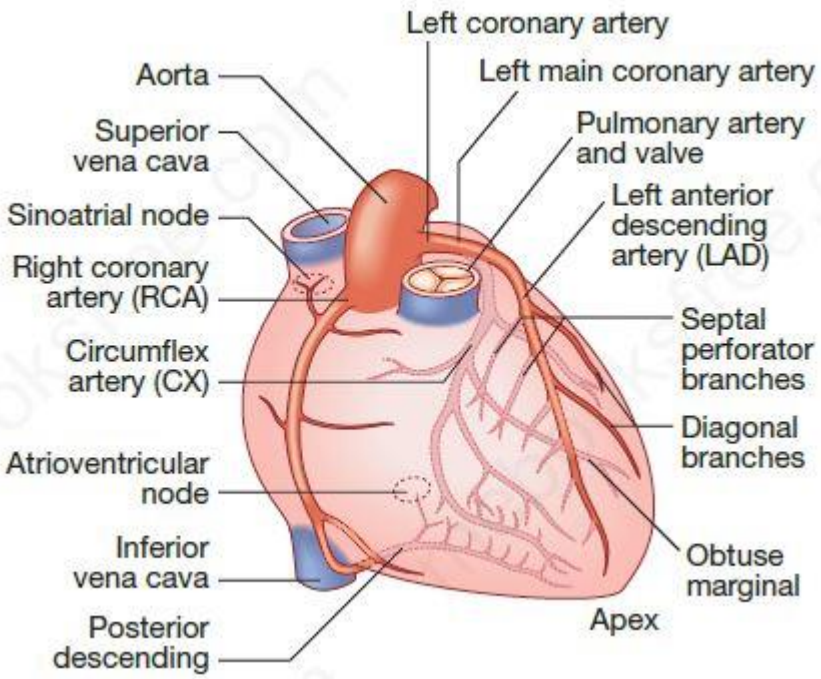


Fig.1:The coronary arteries, anterior view

The LAD gives branches to supply the anterior part of the septum (septal perforators) and the anterior, lateral and apical walls of the LV. The CX gives marginal branches that supply the lateral, posterior and inferior segments of the LV. The right coronary artery (RCA) runs in the right atrioventricular groove,giving branches that supply the RA, RV and inferoposterior aspects of the LV.

The RCA supplies the sinoatrial (SA) node in about 60% of individuals and the AV node in about 90%. Proximal occlusion of the RCA therefore often results in sinus bradycardia and may also cause AV nodal block.

The posterior descending artery runs in the posterior interventricular groove and supplies the inferior part of the interventricular septum. This vessel is a branch of the RCA in approximately 90% of people **(dominant right system)** and is supplied by the CX in the remainder **(dominant left system)**. ***The coronary anatomy varies greatly from person to person and there are many normal variants***.

The venous system follows the coronary arteries but drains into the coronary sinus in the atrioventricular groove, and then to the RA. An

extensive lymphatic system drains into vessels that travel with the coronary vessels and then into the thoracic duct.
Abrupt occlusion of the RCA, due to coronary thrombosis, ***results in*** infarction of the inferior part of the LV and often the RV. Abrupt occlusion of the LAD or CX ***causes*** infarction in the corresponding territory of the LV, ***and occlusion of the left main coronary artery is usually fatal***.
The venous system follows the coronary arteries but drains into the coronary sinus in the atrioventricular groove, and then to the RA. An extensive lymphatic system drains into vessels that travel with the coronary vessels and then into the thoracic duct.

Coronary artery disease

Coronary artery disease (CAD) is the most common form of heart disease and the single most important cause of premature death in Europe, the Baltic states, Russia, North and South America, Australia and New Zealand. By 2020, it is estimated that it will be the major cause of death in all regions of the world. However, in Eastern Europe and much of Asia, the rates of CAD are rapidly rising. Disease of the coronary arteries is almost always due to atheroma and its complications, particularly thrombosis (Box-2).

Clinical problem	Pathology
Stable angina	Ischaemia due to fixed atheromatous stenosis of one or more coronary arteries
Unstable angina	Ischaemia caused by dynamic obstruction of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Myocardial infarction	Myocardial necrosis caused by acute occlusion of a coronary artery due to plaque rupture or erosion with superimposed thrombosis
Heart failure	Myocardial dysfunction due to infarction or ischaemia
Arrhythmia	Altered conduction due to ischaemia or infarction
Sudden death	Ventricular arrhythmia, asystole or massive myocardial infarction

Box-2: Coronary artery disease: clinical manifestations and pathology.

Stable angina

Angina pectoris is the symptom complex caused by transient myocardial ischaemia and constitutes a clinical syndrome rather than a disease. It may occur whenever there is an imbalance between myocardial oxygen supply and demand.

Coronary atheroma is by far the most common cause of angina, although the symptom may be a manifestation of other forms of heart disease, particularly aortic valve disease and hypertrophic cardiomyopathy

Clinical features

The history is the most important factor in making the diagnosis. Stable angina is characterized by:

- ✓ central chest pain,
- ✓ discomfort or breathlessness caused by exertion or other forms of stress, and is relieved by rest

Activities precipitating angina;

Common

• Physical exertion
• Cold exposure
• Heavy meals
• Intense emotion

Uncommon

• Lying flat (decubitus angina)
• Vivid dreams (nocturnal angina)

Investigations

1- Resting ECG
2- Exercise ECG

Management: general measures

The management of angina pectoris involves:

• a careful assessment of the likely extent and severity of arterial disease
• the identification and control of risk factors such as smoking, hypertension and hyperlipidaemia
• the use of measures to control symptoms
• Identification of high-risk patients for treatment to improve life expectancy.

Symptoms alone are a poor guide to the extent of coronary artery disease. An algorithm for the investigation and treatment of patients with stable angina is shown in Figure 2

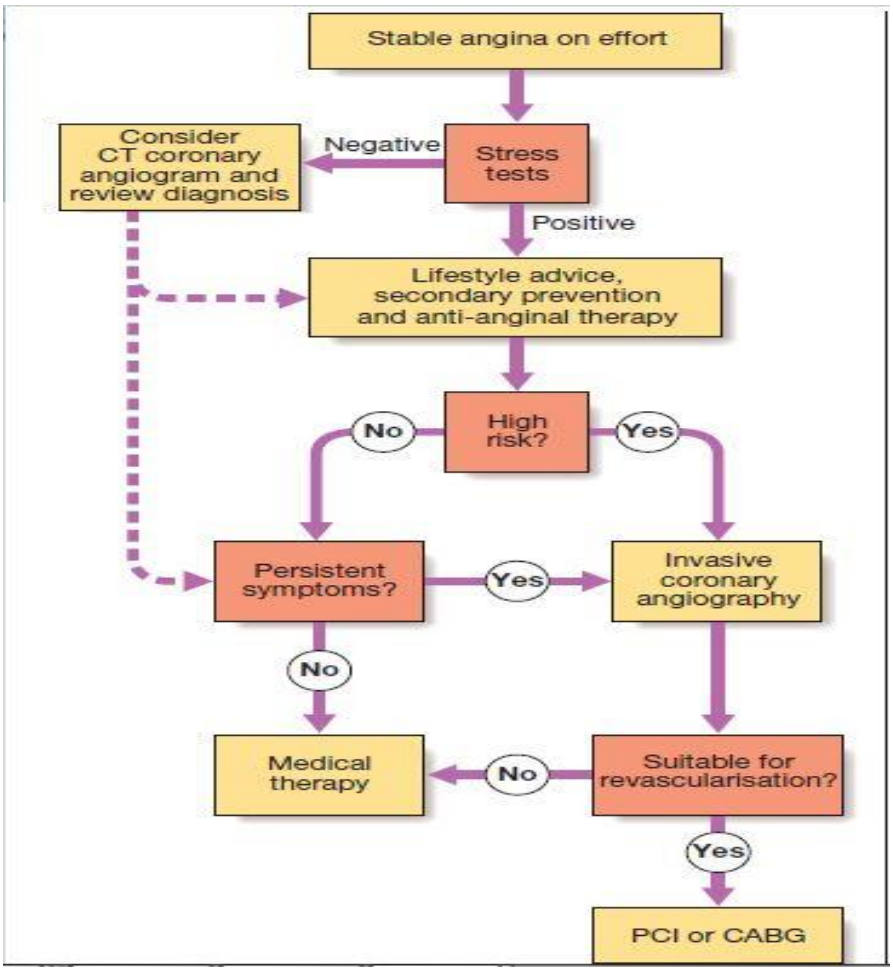


Fig. 2 A scheme for the investigation and treatment of stable angina on effort. The selection of percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) depends upon patient choice, coronary artery anatomy and extent of coronary artery disease. In general, left main stem and three-vessel coronary artery disease should be treated by CABG surgery.

THANK YOU

Lec.4 **GENERAL MEDICINE**

Dr.Anas Hammad

Ischemic Heart Diseases

Box-3 Advice to patients with stable angina

- Do not smoke
- Aim for ideal body weight
- Take regular exercise (exercise up to, but not beyond, the point of chest discomfort is beneficial and may promote collateral vessels)
- Avoid severe unaccustomed exertion, and vigorous exercise after a heavy meal or in very cold weather
- Take sublingual nitrate before undertaking exertion that may induce angina

Antiplatelet therapy

Low-dose ***(75 mg) aspirin*** reduces the risk of adverse events such as MI and should be prescribed for all patients with coronary artery disease indefinitely. ***Clopidogrel (75 mg daily)*** is an equally effective antiplatelet agent that can be prescribed if aspirin causes troublesome dyspepsia or other side-effects.

Anti-anginal drug treatment

Five groups of drug are used to help relieve or prevent the symptoms of angina:

1- nitrates,
2- β-blockers,
3- calcium antagonists,
4- potassium channel activators and,
5- an I_f channel antagonist (Ivabradine is a selective sinus node inhibitor which decreases resting heart rate. It is licensed for the treatment of chronic stable angina in patients with normal sinus rhythm, who have a contraindication or intolerance for beta blockers).

Although each of these anti-anginal drugs is superior to placebo in relieving the symptoms of angina, there is little evidence that one group is more effective than another. It is conventional to start therapy with

low-dose aspirin, a statin, sublingual GTN and a β-blocker, and then add a calcium channel antagonist or a long-acting nitrate later, if needed.

The goal is the control of angina with minimum side-effects and the simplest possible drug regimen. There is little evidence that prescribing multiple anti-anginal drugs is of benefit, and revascularization should be considered if an appropriate combination of two or more drugs fails to achieve an acceptable symptomatic response.

Percutaneous coronary intervention vs medical therapy in stable angina

'PCI is more effective than medical therapy in alleviating angina pectoris and improving exercise tolerance but does not reduce mortality. It carries risks of procedure-related MI, emergency CABG and repeat procedures for re-stenosis.'

Angina with normal coronary arteries

Approximately **10%** of patients who report stable angina on effort will ***have angiographically normal coronary arteries***. Many of these patients are women and the mechanism of their symptoms is often difficult to establish. It is important to review the original diagnosis and explore other potential causes.

Coronary artery spasm

Vasospasm in coronary arteries may coexist with atheroma (*degeneration of the walls of the arteries caused by accumulated fatty deposits and scar tissue, and leading to restriction of the circulation and a risk of thrombosis*), especially in unstable angina; in less than 1% of cases, vasospasm may occur without angiographically detectable atheroma. This is sometimes known as variant angina, and may be accompanied by spontaneous and transient ST elevation on the ECG ***(Prinzmetal's angina)***.

Syndrome X

The constellation of typical angina on effort, objective evidence of myocardial ischaemia on stress testing, and angiographically normal coronary arteries is sometimes known as ***syndrome X***.
This disorder is poorly understood but carries a good prognosis and may respond to treatment with anti-anginal therapy.

Acute coronary syndrome

Acute coronary syndrome is a term that encompasses both unstable angina and myocardial infarction (MI). It is characterised by new-onset or rapidly worsening angina (crescendo angina), angina on minimal exertion or angina at rest in the absence of myocardial damage.
In contrast, MI occurs when symptoms occur at rest and there is evidence of myocardial necrosis, as demonstrated by an elevation in cardiac troponin or creatine kinase-MB isoenzyme.

The culprit lesion is usually a complex ulcerated or fissured atheromatous plaque with adherent platelet-rich thrombus and local coronary artery spasm In acute MI, occlusive thrombus is almost always present at the site of rupture or erosion of an atheromatous plaque. The thrombus may undergo spontaneous lysis over the course of the next few days, although, by this time, irreversible myocardial damage has occurred. Without treatment, the infarct-related artery remains permanently occluded in 20–30% of patients. The process of infarction progresses over several hours.

Clinical features of acute coronary
Syndromes
Symptoms

- Prolonged cardiac pain: chest, throat, arms, epigastrium or back
- Anxiety and fear of impending death
- Nausea and vomiting
- Breathlessness
- Collapse/syncope

Physical signs

- Signs of sympathetic activation: pallor, sweating, tachycardia
- Signs of vagal activation: vomiting, bradycardia
- Signs of impaired myocardial function
  - Hypotension, oliguria, cold peripheries
  - Narrow pulse pressure
  - Raised JVP
  - Third heart sound
  - Quiet first heart sound
  - Diffuse apical impulse
  - Lung crepitations
- Signs of tissue damage: fever
- Signs of complications: e.g. mitral regurgitation, pericarditis

Sudden death, from ventricular fibrillation or asystole, may occur immediately and often within the first hour. If the patient survives this

most critical stage, the liability to dangerous arrhythmias remains, but diminishes as each hour goes by.
The development of cardiac failure reflects the extent of myocardial ischaemia and is the major cause of death in those who survive the first few hours.

Immediate management: the first 12 hours

Patients should be admitted urgently to hospital because there is a significant risk of death or recurrent myocardial ischaemia during the early unstable phase, and appropriate medical therapy can reduce the incidence of these by at least 60%.
If there are no complications, the patient can be mobilised from the second day and discharged after 3–5 days.

Secondary prevention drug therapy

Aspirin and clopidogrel

Low-dose aspirin therapy reduces the risk of further infarction and other vascular events by approximately 25% and should be continued indefinitely if there are no unwanted effects. Clopidogrel should be given in combination with aspirin for at least 3 months. If patients are intolerant of long-term aspirin, clopidogrel is a suitable alternative.

Beta-blockers

Continuous treatment with an oral β-blocker reduces long-term mortality by approximately 25% among the survivors of acute MI

ACE inhibitors

Several clinical trials have shown that long-term treatment with an ACE inhibitor (e.g. enalapril 10 mg twice daily or ramipril 2.5–5 mg twice daily) can;

1- counteract ventricular remodelling,
2- prevent the onset of heart failure,
3- improve survival,
4- reduce recurrent MI and
5- avoid rehospitalisation.

Coronary revascularization

Prevention

There are several ways you can help reduce your risk of developing coronary heart disease (CHD), such as lowering your blood pressure and cholesterol levels. There are a number of ways you can do this, which are discussed below;

- Eat a healthy, balanced diet.
- Be more physically active.
- Keep to a healthy weight.

- Give up smoking.
- Reduce your alcohol consumption.
- Keep your blood pressure under control.
- Keep your diabetes under control.
- Take any prescribed medication.
- The importance of regular exercise.

Late management of Ml

Risk stratification and further investigation

I-Lifestyle modification

• Diet (weight control, lipid-lowering, 'Mediterranean diet')
• Cessation of smoking
• Regular exercise

II-Secondary prevention drug therapy

• Antiplatelet therapy (aspirin and/or clopidogrel)
• β-blocker
• ACE inhibitor/ARB
• Statin
• Additional therapy for control of diabetes and hypertension
• Mineralocorticoid receptor antagonist

Devices

• Implantable cardiac defibrillator (high-risk patients)

(ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker)

THANK YOU

Lec.5 **GENERAL MEDICINE**
Stage: Fourth
Dr.Anas Hammad

Infective Endocarditis

Infective Endocarditis
-Definition
-Clinical Features
-Investigations
-Diagnosis
-Prevention infective endocarditis,

Infective endocarditis is caused by microbial infection of a heart valve, the lining of a cardiac chamber or blood vessel, or by a congenital anomaly. Both native and prosthetic valves can be affected. streptococci and Staphylococci are the most common causes of infective endocarditis but other organism may be involved (rickettsia, chlamydia or fungus).

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Pathophysiology

Infection tends to occur at sites of endothelial damage because they attract deposits of platelets and fibrin that are vulnerable to colonisation by blood-borne organisms. Staphylococcal endocarditis of the tricuspid valve is a common complication of intravenous drug use. Infective endocarditis typically occurs at sites of pre-existing endocardial damage, but infection with particularly virulent or aggressive organisms such as *Staphylococcus aureus* can cause endocarditis in a previously normal heart.

Endocarditis in old age

- Symptoms and signs: may be non-specific, with delirium, weight loss, malaise and weakness, and the diagnosis may not be suspected.
- Common causative organisms: often enterococci (from the urinary tract) and *Streptococcus gallolyticus* subsp. *gallolyticus* (from a colonic source).
- Morbidity and mortality: much higher.

Clinical features

Endocarditis can take either an ***acute*** or a more insidious '***subacute***' form. The subacute form may abruptly develop acute life-threatening complications, such as valve disruption or emboli. The clinical pattern is influenced by the following:

1- the type of organism
2- the site of infection,
3- prior antibiotic therapy
4- and the presence of a valve or shunt prosthesis.

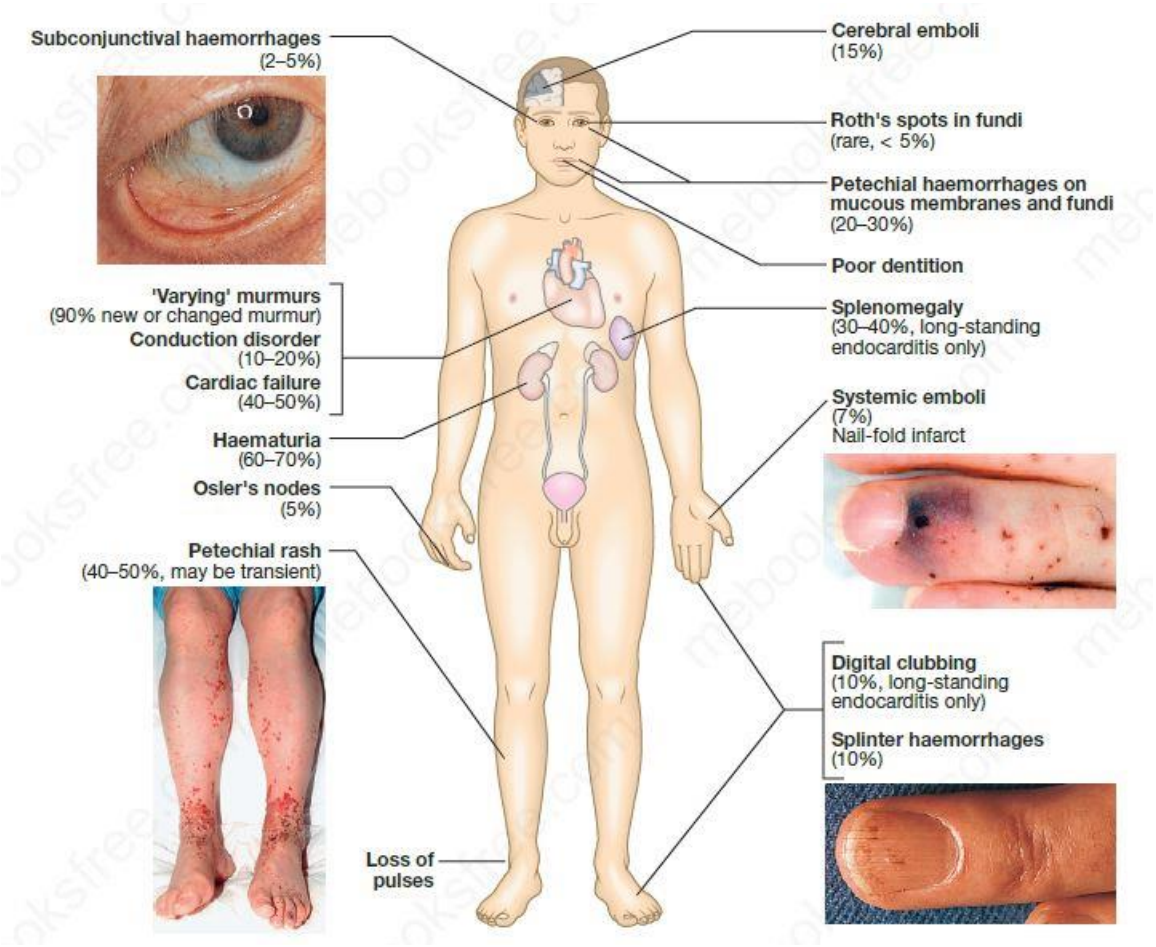

Fig.-1: Clinical features that may be present in endocarditis

Diagnosis of infective endocarditis

The Duke criteria for diagnosis of infective endocarditis are as the following:

Major criteria

Positive blood culture

- Typical organism from two cultures
- Persistent positive blood cultures taken > 12 hrs. apart
- Three or more positive cultures taken over > 1 hr.

Endocardial involvement

- Positive echocardiographic findings of vegetations
- New valvular regurgitation

Minor criteria

- Predisposing valvular or cardiac abnormality
- Intravenous drug misuse
- Pyrexia ≥ 38°C
- Embolic phenomenon
- Vasculitic phenomenon
- Blood cultures suggestive: organism grown but not achieving major criteria
- Suggestive

**Modified Duke criteria. Patients with two major, or one major and three minor, or five minor have definite endocarditis. Patients with one major and one minor, or three minor have possible endocarditis.*

Prevention

Until recently, antibiotic prophylaxis was routinely given to people at risk of infective endocarditis undergoing interventional procedures. However, as this has not been proven to be effective and the link between episodes of infective endocarditis and interventional procedures has not been demonstrated, antibiotic prophylaxis is no longer offered routinely.

Lec.6 **GENERAL MEDICINE**
Stage: Fourth
Dr.Anas Hammad

Valvular heart diseases

-Definition
-Clinical Features
-Mitral valve stenosis, regurgitation
-Aortic valve stenosis, regurgitation

The heart valves allow forward movement of blood through the cardiac chambers when they are open and prevent backward flow when they are closed. Diseased valve may become narrowed, obstructing forward flow, or become leaky, causing backward flow or regurgitation.
Breathlessness is a common ***symptom of valve disease***, and acute severe breathlessness may be a presenting ***symptom of valve failure***.
The causes of acute valve failure are shown below:

1- *Aortic regurgitation*

- Aortic dissection
- Infective endocarditis

2- *Mitral regurgitation*

- Papillary muscle rupture due to acute myocardial infarction
- Infective endocarditis
- Rupture of chordae due to myxomatous degeneration

3- *Prosthetic valve failure*

- Mechanical valves: fracture, jamming, thrombosis, dehiscence
- Biological valves: degeneration with cusp tear

While the principal causes of valve disease are as following:

1- Valve regurgitation

- Congenital
- Acute rheumatic carditis
- Chronic rheumatic carditis
- Infective endocarditis
- Cardiac failure ((Causes dilatation of the valve ring))
- Syphilitic aortitis

- Traumatic valve rupture
- Senile degeneration
- Damage to chordae and papillary muscles

2- Valve stenosis

- Congenital
- Rheumatic carditis
- Senile degeneration

Mitral valve disease

Mitral stenosis

There are three causes for mitral stenosis;

1- Rheumatic origin
2- Heavy calcification of the valve in older people
3- Congenital mitral stenosis (rare form)

Clinical features

The physical signs of mitral stenosis are often found before symptoms develop and their recognition is of particular importance in pregnancy. Effort-related dyspnoea is usually the dominant symptom. Typically, exercise tolerance diminishes very slowly over many years until symptoms eventually occur at rest. Acute pulmonary oedema or pulmonary hypertension can lead to haemoptysis. Fatigue is a common symptom due to a low cardiac output. Thromboembolism is a common complication, especially in patients with AF.

16.77 Clinical features of mitral stenosis

Clinical feature	Cause
Symptoms	
Breathlessness	Pulmonary congestion, low cardiac output
Fatigue	Low cardiac output
Oedema, ascites	Right heart failure
Palpitation	Atrial fibrillation
Haemoptysis	Pulmonary congestion, pulmonary embolism
Cough	Pulmonary congestion
Chest pain	Pulmonary hypertension
Thromboembolism	Atrial stasis and atrial fibrillation
Signs	
Atrial fibrillation	Atrial dilatation
Mitral facies	Low cardiac output
Auscultation:	
Loud first heart sound, opening snap	Pressure gradient across the valve
Mid-diastolic murmur	
Crepitations	Left heart failure
Pulmonary oedema	
Pleural effusions	
Right ventricular heave, loud P_2	Pulmonary hypertension

Investigations

Doppler echocardiography is the investigation of choice for evaluation of suspected mitral stenosis. Cardiac catheterisation may also be required if surgery or valvuloplasty is being considered.

16.78 Investigations in mitral stenosis

ECG

- Right ventricular hypertrophy: tall R waves in V_1–V_3
- P mitrale or atrial fibrillation

Chest X-ray

- Enlarged left atrium and appendage
- Signs of pulmonary venous congestion

Echo

- Thickened immobile cusps
- Reduced valve area
- Enlarged left atrium
- Reduced rate of diastolic filling of left ventricle

Doppler

- Pressure gradient across mitral valve
- Pulmonary artery pressure
- Left ventricular function

Cardiac catheterisation

- Coronary artery disease
- Pulmonary artery pressure
- Mitral stenosis and regurgitation

Mitral regurgitation

Rheumatic disease is the principal cause in countries where rheumatic fever is common but elsewhere, including in the UK, other causes are more important. Mitral regurgitation may also follow mitral valvotomy or valvuloplasty.

16.80 Causes of mitral regurgitation

- Mitral valve prolapse
- Dilatation of the left ventricle and mitral valve ring (e.g. coronary artery disease, cardiomyopathy)
- Damage to valve cusps and chordae (e.g. rheumatic heart disease, endocarditis)
- Ischaemia or infarction of the papillary muscle
- Myocardial infarction

Clinical Features

Symptoms and signs depend on the underlying cause and how suddenly the regurgitation develops (Box 16.81). Chronic mitral regurgitation produces a symptom complex that is similar to that of mitral stenosis but sudden-onset mitral regurgitation usually presents with acute pulmonary oedema.

16.81 Clinical features of mitral regurgitation

Clinical feature	Cause
Symptoms	
Breathlessness	Pulmonary congestion
Fatigue	Low cardiac output
Oedema, ascites	Right heart failure
Palpitation	Atrial fibrillation
Signs	
Atrial fibrillation	Atrial dilatation
Displaced apex beat	Cardiomegaly
Auscultation:	
Apical pansystolic murmur	Regurgitation of blood from left ventricle to left atrium
Soft S1	Valve does not close properly
Apical S3	Rapid flow of blood into left ventricle
Crepitations	Left heart failure
Pulmonary oedema	Left heart failure
Pleural effusions	Left heart failure
Right ventricular heave	Pulmonary hypertension
Raised jugular venous pressure	Right heart failure
Oedema	Right heart failure

Investigations

Echocardiography is a pivotal investigation. The severity of regurgitation can be assessed by Doppler and information may also be gained on papillary muscle function and valve prolapse. An ECG should be performed and commonly shows AF, as a consequence of atrial dilatation. Cardiac catheterisation is indicated when surgery is being considered.

16.82 Investigations in mitral regurgitation

ECG

- Left atrial hypertrophy
- Atrial fibrillation

Chest X-ray

- Enlarged left atrium
- Enlarged left ventricle
- Pulmonary venous congestion
- Pulmonary oedema (if acute)

Echo

- Dilated left atrium, left ventricle
- Dynamic left ventricle (unless myocardial dysfunction predominates)
- Structural abnormalities of mitral valve

Doppler

- Detects and quantifies regurgitation

Cardiac catheterisation

- Dilated left atrium, dilated left ventricle, mitral regurgitation
- Pulmonary hypertension
- Coexisting coronary artery disease

Medical management

16.83 Medical management of mitral regurgitation

- Diuretics
- Vasodilators if hypertension is present
- Digoxin if atrial fibrillation is present
- Anticoagulants if atrial fibrillation is present

Aortic valve disease

Aortic stenosis

There are several causes of aortic stenosis but the age at which patients present can give a clue to the most likely diagnosis. In congenital aortic stenosis, obstruction is present from birth or becomes apparent during infancy.

16.84 Causes of aortic stenosis

Infants, children, adolescents

- Congenital aortic stenosis
- Congenital subvalvular aortic stenosis
- Congenital supravalvular aortic stenosis

Young adults to middle-aged

- Calcification and fibrosis of congenitally bicuspid aortic valve
- Rheumatic aortic stenosis

Middle-aged to elderly

- Senile degenerative aortic stenosis
- Calcification of bicuspid valve
- Rheumatic aortic stenosis

Clinical features

Aortic stenosis is commonly picked up in asymptomatic patients at routine clinical examination but the three cardinal symptoms are angina, breathlessness and syncope.

16.85 Clinical features of aortic stenosis

Symptoms

- Mild or moderate stenosis: usually asymptomatic
- Exertional dyspnoea
- Angina
- Exertional syncope
- Sudden death
- Episodes of acute pulmonary oedema

Signs

- Ejection systolic murmur
- Slow-rising carotid pulse
- Thrusting apex beat (left ventricular pressure overload)
- Narrow pulse pressure
- Signs of pulmonary venous congestion

Investigations

Echocardiography is a pivotal investigation in patients suspected of having aortic stenosis. It can demonstrate restricted valve opening and Doppler assessment permits calculation of the systolic gradient across the aortic valve, from which the severity of stenosis can be assessed.

16.86 Investigations in aortic stenosis

ECG

- Left ventricular hypertrophy
- Left bundle branch block

Chest X-ray

- May be normal; sometimes enlarged left ventricle and dilated ascending aorta on postero-anterior view, calcified valve on lateral view

Echo

- Calcified valve with restricted opening, hypertrophied left ventricle

Doppler

- Measurement of severity of stenosis
- Detection of associated aortic regurgitation

Cardiac catheterisation

- Mainly to identify associated coronary artery disease
- May be used to measure gradient between left ventricle and aorta

16.87 Aortic stenosis in old age

- **Incidence**: the most common form of valve disease affecting the very old.
- **Symptoms**: a common cause of syncope, angina and heart failure in the very old.
- **Signs**: because of increasing stiffening in the central arteries, low pulse pressure and a slow rising pulse may not be present.
- **Trans-catheter aortic valve implantation (TAVI)**: a good option in older individuals because less invasive than surgery.
- **Surgery**: can be successful in those aged 80 years or more in the absence of comorbidity, but with a higher operative mortality. The prognosis without surgery is poor once symptoms have developed.
- **Valve replacement type**: a biological valve is often preferable to a mechanical one because this obviates the need for anticoagulation, and the durability of biological valves usually exceeds the patient's anticipated life expectancy.

Aortic regurgitation

This condition can result from either disease of the aortic valve cusps, infection, trauma or dilatation of the aortic root. The causes are summarized below;

16.88 Causes of aortic regurgitation

Congenital

- Bicuspid valve or disproportionate cusps

Acquired

- Rheumatic disease
- Infective endocarditis
- Trauma
- Causes of aortic dilatation:
  - Marfan's syndrome
  - Aneurysm
  - Aortic dissection
  - Syphilis
  - Ankylosing spondylitis

Clinical features

Until the onset of breathlessness, the only symptom may be an awareness of the heart beat, particularly when lying on the left side, which results from the increased stroke volume. Paroxysmal nocturnal dyspnoea is sometimes the first symptom, and peripheral oedema or angina may occur. The characteristic murmur is best heard to the left of the sternum during held expiration.

Acute severe regurgitation may occur as the result of perforation of an aortic cusp in endocarditis.

16.89 Clinical features of aortic regurgitation

Symptoms

Mild to moderate aortic regurgitation
- Often asymptomatic
- Palpitations

Severe aortic regurgitation
- Breathlessness
- Angina

Signs

Pulses
- Large-volume or 'collapsing' pulse
- Low diastolic and increased pulse pressure
- Bounding peripheral pulses
- Capillary pulsation in nail beds: Quincke's sign
- Femoral bruit ('pistol shot'): Duroziez's sign
- Head nodding with pulse: de Musset's sign

Murmurs
- Early diastolic murmur
- Systolic murmur (increased stroke volume)
- Austin Flint murmur (soft mid-diastolic)

Other signs
- Displaced, heaving apex beat (volume overload)
- Pre-systolic impulse
- Fourth heart sound
- Crepitations (pulmonary venous congestion)

The regurgitant jet causes fluttering of the mitral valve and, if severe, causes partial closure of the anterior mitral leaflet, leading to functional mitral stenosis and a soft mid-diastolic (Austin Flint) murmur.

Investigations

Doppler echocardiography is the investigation of first choice for detecting regurgitation. Box below explain the investigation of aortic regurgitation;

16.90 Investigations in aortic regurgitation

ECG

- Initially normal, later left ventricular hypertrophy and T-wave inversion

Chest X-ray

- Cardiac dilatation, maybe aortic dilatation
- Features of left heart failure

Echo

- Dilated left ventricle
- Hyperdynamic left ventricle
- Doppler detects reflux
- Fluttering anterior mitral leaflet

Cardiac catheterisation*

- Dilated left ventricle
- Aortic regurgitation
- Dilated aortic root

*Not always required.

Management

Treatment may be required for underlying conditions, such as endocarditis or syphilis. Aortic valve replacement is indicated if aortic regurgitation causes symptoms, and this may need to be combined with aortic root replacement and coronary bypass surgery. Those with chronic aortic regurgitation can remain asymptomatic for many years because compensatory ventricular dilatation and hypertrophy occur, but should be advised to report the development of any symptoms of breathlessness or angina.

Lec.7 **GENERAL MEDICINE**
Stage: Fourth
Dr.Anas Hammad

DIABETES MELLITUS

-Etiology
-Clinical Features
-Investigations
-Diagnosis
-Management
-Hypoglycemia

Globally, in 2015, diabetes caused 5 million deaths in those aged 20–79 years. The incidence of diabetes is rising. Globally, it is estimated that 415 million people had diabetes in 2015 (10% of the world adult population), and this figure is expected to reach 642 million by 2040.

Diabetes mellitus is a clinical syndrome characterised by an increase in plasma blood glucose (hyperglycaemia). It has many causes, most commonly type 1 or type 2 diabetes.
Type 2 diabetes is characterised by reduced sensitivity to the action of insulin and an inability to produce sufficient insulin to overcome this 'insulin resistance' whereas Type 1 diabetes is generally considered to result from autoimmune destruction of insulin-producing cells (β cells) in the pancreas, leading to marked insulin deficiency.
Hyperglycaemia causes both acute and long-term problems:

- ✓ Acutely, high glucose and lack of insulin can result in marked symptoms, metabolic decompensation and hospitalisation.
- ✓ Chronic hyperglycaemia is responsible for diabetes-specific 'microvascular' complications affecting the eyes (retinopathy), kidneys (nephropathy) and feet (neuropathy).

The diagnostic criteria for diabetes (a fasting plasma glucose of ≥ 7.0 mmol/L (126 mg/ dL) or glucose 2 hours after an oral glucose challenge of ≥ 11.1 mmol/L (200 mg/dL).

The main types of diabetes are:
Type 1 diabetes: It is due to the body's malfunction to produce insulin in the body, and requires the person to inject insulin. This form was previously referred to as "Insulin-Dependent Diabetes Mellitus" (IDDM) or "Juvenile Diabetes".

Type 2 diabetes: It is due to insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency. This form was previously referred to as non insulin-dependent diabetes mellitus (NIDDM) or "adult-onset diabetes".
Type 2 diabetes can be prevented after following healthy life style such as healthy diet, proper exercise or maintaining healthy weight.

The third main form, Gestational diabetes occurs when pregnant women without a previous diagnosis of diabetes develop a high blood glucose level. It may lead to type 2 DM.

Functional anatomy and physiology
Insulin is the primary regulator of glucose metabolism and storage, and is secreted from pancreatic β cells into the portal circulation. The pancreatic β cell is designed to regulate blood glucose concentrations tightly by coupling glucose and other nutrient stimulus with insulin secretion.

20.1 Metabolic actions of insulin

Increase	Decrease
Carbohydrate metabolism	
Glucose transport (muscle, adipose tissue)	Gluconeogenesis
Glucose phosphorylation	Glycogenolysis
Glycogen synthesis	
Glycolysis	
Pyruvate dehydrogenase activity	
Pentose phosphate shunt	
Lipid metabolism	
Triglyceride synthesis	Lipolysis
Fatty acid synthesis (liver)	Lipoprotein lipase (muscle)
Lipoprotein lipase activity (adipose tissue)	Ketogenesis
	Fatty acid oxidation (liver)
Protein metabolism	
Amino acid transport	Protein degradation
Protein synthesis	

Aetiology and pathogenesis of DM
In both of the common types of diabetes, environmental factors interact with genetic susceptibility to determine which people develop the clinical syndrome, and the timing of its onset.

Type 1 diabetes was previously termed 'insulin-dependent diabetes mellitus' (IDDM) and Type 2 diabetes was previously termed 'non-insulin-dependent diabetes mellitus' (NIDDM); these terms are inappropriate. Because 20% or more of patients with type 2 diabetes will ultimately develop profound insulin deficiency requiring replacement therapy, so that IDDM and NIDDM were misnomers.

Type 1 Diabetes: The immune system of body attacks and destroys the cells that produce insulin. As no insulin is produced, glucose levels further increase, which can seriously damage the body's organs. Type 1 diabetes is often known as insulin-dependent diabetes. It is also sometimes known as juvenile diabetes or early-onset diabetes because it usually develops before the age of 40, often during the teenage years. Type 1 diabetes is less common than type 2 diabetes.

Type 2 Diabetes: Type 2 diabetes is where the body does not produce enough insulin or the body's cells do not respond to insulin. This is known as insulin resistance. Type 2 diabetes, and is far more common than type 1 diabetes.

Risk factors for type 2 diabetes:

- Obesity or being overweight
- Impaired glucose tolerance
- High blood pressure
- Dyslipidemia – Low levels of high-density lipoproteins (HDL) ("good") cholesterol and high levels of triglycerides, high low-density lipoproteins (LDL)
- Gestational diabetes
- Sedentary lifestyle
- Family history
- Age

Gestational Diabetes: Some women tend to experience high levels of blood glucose as during pregnancy due to reduced sensitivity of insulin receptors.

20.9 Aetiological classification of diabetes mellitus

Type 1 diabetes
- Immune-mediated
- Idiopathic

Type 2 diabetes

Other specific types
- Genetic defects of β-cell function (see Box 20.10)
- Genetic defects of insulin action (e.g. leprechaunism, lipodystrophies)
- Pancreatic disease (e.g. pancreatitis, pancreatectomy, neoplastic disease, cystic fibrosis, haemochromatosis, fibrocalculous pancreatopathy)
- Excess endogenous production of hormonal antagonists to insulin, e.g.:
  - Growth hormone – acromegaly
  - Glucocorticoids – Cushing's syndrome
  - Glucagon – glucagonoma
  - Catecholamines – phaeochromocytoma
  - Thyroid hormones – thyrotoxicosis
- Drug-induced (e.g. glucocorticoids, thiazide diuretics, phenytoin)
- Uncommon forms of immune-mediated diabetes (e.g. IPEX syndrome)
- Associated with genetic syndromes (e.g. Down's syndrome, Klinefelter's syndrome, Turner's syndrome, DIDMOAD (Wolfram's syndrome), Friedreich's ataxia, myotonic dystrophy)

Gestational diabetes

(DIDMOAD = diabetes insipidus, diabetes mellitus, optic atrophy, nerve deafness; IPEX = immunodysregulation polyendocrinopathy X)

Investigation

1- **Urine glucose**
2- **Blood glucose**
3- **Interstitial glucose**
4- **Urine and blood ketones**
5- **Glycated haemoglobin**
6- **Islet autoantibodies**
7- **C-peptide**
8- **Urine protein**

Clinical features
The main symptoms of diabetes are:

1) Frequent episodes of thrush
2) Weight loss and loss of muscle bulk
3) Polyphagia: feeling hungry frequently
4) Blurred vision
5) Polydipsia: feeling very thirsty
6) Polyuria: urinating frequently (particularly at night)
7) Weakness
8) Cuts or wounds that heal slowly

Type 1 diabetes can develop quickly, over weeks or even days. Many people have type 2 diabetes for years without realizing because early symptoms tend to be common.

Diagnosis

The traditional way to diagnose diabetes or pre-diabetes has been by using random or fasting plasma glucose and/or an oral glucose tolerance test (OGTT), and in some region the use of glycated haemoglobin (HbA1c) ≥ 48 mmol/mol, to diagnose diabetes..
When a person has symptoms of diabetes, diagnosis can be confirmed with either a fasting glucose of ≥ 7.0 mmol/L (126 mg/dL) or a random glucose of ≥ 11.1 mmol/L (200 mg/dL)..
HbA1c test should not be used to diagnose diabetes in pregnancy, due to the increased red cell turnover that occurs in pregnancy.
When a diagnosis of diabetes is confirmed, other investigations should include;

1- plasma urea,
2- creatinine and
3- electrolytes,
4- lipids,
5- liver function test
6- blood or urine ketones,
7- urine protein and
8- thyroid function test

20.2 Diagnosis of diabetes and pre-diabetes

Diabetes is confirmed by:

- *either* plasma glucose in random sample or 2 hrs after a 75 g glucose load ≥11.1 mmol/L (200 mg/dL) *or*
- fasting plasma glucose ≥7.0 mmol/L (126 mg/dL) *or*
- HbA_{1c} ≥48 mmol/mol

In asymptomatic patients, two diagnostic tests are required to confirm diabetes; the second test should be the same as the first test to avoid confusion

'Pre-diabetes' is classified as:

- impaired fasting glucose = fasting plasma glucose ≥6.1 mmol/L (110 mg/dL) and <7.0 mmol/L (126 mg/dL)
- impaired glucose tolerance = fasting plasma glucose <7.0 mmol/L (126 mg/dL) *and* 2-hr glucose after 75 g oral glucose drink 7.8–11.1 mmol/L (140–200 mg/dL)

HbA_{1c} criteria for pre-diabetes vary. The National Institute for Health and Care Excellence (NICE) guidelines (UK) recommend considering an HbA_{1c} range of 42–47 mmol/mol to be indicative of pre-diabetes; the American Diabetes Association (ADA) guidelines suggest a range of 39–47 mmol/mol. The ADA also suggests a lower fasting plasma glucose limit of ≥ 5.6 mmol/L (100 mg/dL) for impaired fasting glucose.

Glycaemia can be classified into three categories: normal, impaired (pre-diabetes) and diabetes. People categorised as having *pre-diabetes* have blood glucose levels that carry a negligible risk of microvascular complications but are at increased risk of developing diabetes.

A continuous risk of macrovascular disease (atheroma of large conduit blood vessels) with increasing glycaemia in the population, people with
pre-diabetes have an increased risk of cardiovascular disease (myocardial infarction, stroke and peripheral vascular disease).

Management

The aims are to improve symptoms of hyperglycaemia and minimise the risks of long-term microvascular and macrovascular complications. Treatment methods for diabetes include

1- dietary/ lifestyle modification,
2- oral anti-diabetic drugs and
3- injected therapies.

In patients with suspected ***type 1 diabetes***, urgent treatment with insulin is required and prompt referral to a specialist is usually needed. In patients with ***type 2 diabetes***, the first approach to management involves advice about dietary and lifestyle modification. Oral antidiabetic drugs are usually added in those who do not achieve glycaemic targets, or who have symptomatic hyperglycaemia at diagnosis and a high HbA1c.

Diabetes is a complex disorder that ***progresses in severity with time***. In parallel with treatment of hyperglycaemia, other risk factors for complications of diabetes need to be addressed, including treatment of hypertension, and dyslipidaemia, and advice on smoking cessation

20.23 Dietary management of diabetes

Aims of dietary management

- Achieve good glycaemic control
- Reduce hyperglycaemia and avoid hypoglycaemia
- Assist with weight management:
  - Weight maintenance for type 1 diabetes and non-obese type 2 diabetes
  - Weight loss for overweight and obese type 2 diabetes
- Reduce the risk of micro- and macrovascular complications
- Ensure adequate nutritional intake
- Avoid 'atherogenic' diets or those that aggravate complications, e.g. high protein intake in nephropathy

Dietary constituents and recommended % of energy intake

- Carbohydrate: 50%:
  - Sucrose: up to 10%
- Fat (total): <35%:
  - n-6 Polyunsaturated: <10%
  - n-3 Polyunsaturated: eat 1 portion (140 g) oily fish once or twice weekly
  - Monounsaturated: 10–20%
  - Saturated: <10%
- Protein: 10–15% (do not exceed 1 g/kg body weight/day)
- Fruit/vegetables: 5 portions daily

Currently, six classes of oral antidiabetic drugs (OADs) are available: biguanides (e.g., metformin), sulfonylureas (e.g., glimepiride), meglitinides (e.g., repaglinide), thiazolidinediones (e.g., pioglitazone), dipeptidyl peptidase IV inhibitors (e.g., sitagliptin), and α-glucosidase inhibitors (e.g., acarbose).

Medications:

- Insulin: Type 1 diabetes is generally treated with combinations of regular and NPH (neutral protamine Hagedorn) insulin or synthetic insulin analogs. When insulin is used in type 2 diabetes, a long-acting formulation is usually added initially while continuing oral medications.
- Treatment of coexisting medical conditions (high blood pressure, dyslipidemia etc.)

Lifestyle measures

- Regular exercise
- Proper diet
- No smoking
- No alcohol

These goals help in keeping both short-term and long-term blood glucose levels within acceptable limits.

20.34 How to carry out pre-operative assessment of patients with diabetes

- Assess glycaemic control:
  Consider delaying surgery and refer to the diabetes team if HbA_{1c} >75 mmol/mol; this should be weighed against the need for surgery
- Assess cardiovascular status
  Optimise blood pressure
  Perform an ECG for evidence of (possibly silent) ischaemic heart disease and to assess QTc (p. 448)
- Assess foot risk (p. 761)
  Patients with high-risk feet should have suitable pressure relief provided during post-operative nursing
- For minor/moderate operations where only one meal will be omitted, plan for the patient to be first on the list

Presenting problems in diabetes mellitus
Hyperglycaemia
The diagnosis of diabetes is simple: it is based on confirmation of hyperglycaemia using either fasting or random glucose.
Hyperglycaemia causes a wide variety of symptoms. The classical clinical features of type 1 and type 2 diabetes are compared in.

20.12 Classical features of type 1 and type 2 diabetes

	Type 1	Type 2
Typical age at onset	<40 years	>50 years
Duration of symptoms	Weeks	Months to years
Body weight	Normal or low	Obese
Ketonuria	Yes	No
Rapid death without treatment with insulin	Yes	No
Autoantibodies	Positive in 80–90%	Negative
Diabetic complications at diagnosis	No	25%
Family history of diabetes	Uncommon	Common
Other autoimmune disease	Common	Uncommon

Symptoms of polydipsia, polyuria, nocturia and rapid weight loss are prominent in type 1 diabetes but are often absent in patients with type 2 diabetes, many of whom are asymptomatic or have non-specific complaints such as chronic fatigue and malaise.

Uncontrolled diabetes is associated with an increased susceptibility to infection and patients may present with skin sepsis (boils) or genital candidiasis, and complain of pruritus vulvae or balanitis.

20.11 Symptoms of hyperglycaemia

- Thirst, dry mouth
- Polyuria
- Nocturia
- Tiredness, fatigue, lethargy
- Change in weight (usually weight loss)
- Blurring of vision
- Pruritus vulvae, balanitis (genital candidiasis)
- Nausea
- Headache
- Hyperphagia; predilection for sweet foods
- Mood change, irritability, difficulty in concentrating, apathy

Hypoglycaemia

Hypoglycaemia is defined as a blood glucose of less than 3.9 mmol/L (70 mg/dL).

Hypoglycaemia is uncommon in people without diabetes which is called 'spontaneous' hypoglycaemia' but relatively frequent in people with diabetes, mainly due to insulin therapy, and less frequently to use of oral insulin secretagogues such as sulphonylurea drugs, and rarely with other antidiabetic drugs.

If blood glucose falls, three primary physiological defence mechanisms operate:

• endogenous insulin release from pancreatic β cells is suppressed

• release of glucagon from pancreatic α cells is increased

• the autonomic nervous system is activated, with release of catecholamines both systemically and within the tissues.

In addition, stress hormones, such as cortisol and growth hormone, are increased in the blood. These actions reduce whole-body glucose uptake and increase hepatic glucose production, maintaining a glucose supply to the brain.

People with type 1 diabetes cannot regulate insulin once it is injected subcutaneously, and so it continues to act, despite the development of hypoglycaemia. Hypoglycaemia occurs much more frequently in people with type 1 and longer-duration type 2 diabetes.

Clinical assessment

Symptoms of hypoglycaemia comprise two main groups:

- ✓ those related to acute activation of the autonomic nervous system
- ✓ those secondary to glucose deprivation of the brain (neuroglycopenia).

20.18 Most common symptoms of hypoglycaemia

Autonomic	
• Sweating	• Hunger
• Trembling	• Anxiety
• Pounding heart	
Neuroglycopenic	
• Delirium	• Inability to concentrate
• Drowsiness	• Incoordination
• Speech difficulty	• Irritability, anger
Non-specific	
• Nausea	• Headache
• Tiredness	

N.B. Symptoms differ with age; children exhibit behavioural changes (such as naughtiness or irritability), while older people experience more prominent neurological symptoms (such as visual disturbance and ataxia).

Management

Acute treatment of hypoglycaemia

Treatment of hypoglycaemia depends on its severity and on whether the patient is conscious and able to swallow.

Oral carbohydrate usually suffices if hypoglycaemia is recognised early. If parenteral therapy is required, then as soon as the patient is able to swallow, glucose should be given orally.

If the patient fails to regain consciousness after blood glucose is restored to normal, then cerebral oedema and other causes of impaired consciousness – such as alcohol intoxication, a post-ictal state or cerebral haemorrhage – should be considered.

Cerebral oedema has a high mortality and morbidity.

20.20 Emergency treatment of hypoglycaemia

Biochemical or symptomatic hypoglycaemia (self-treated)

In the UK, it is recommended that all glucose levels <4.0 mmol/L (72 mg/dL) are treated ('4 is the floor'). People with diabetes who recognise developing hypoglycaemia are encouraged to treat immediately. Options available include:

- Oral fast-acting carbohydrate (10–15 g) is taken as glucose drink or tablets or confectionery, e.g. 5–7 Dextrosol tablets (or 4–5 Glucotabs), 90–120 mL *original* Lucozade, 150–200 mL pure fruit juice, 3–4 heaped teaspoons of sugar dissolved in water)
- Repeat capillary glucose measurement 1–15 mins later. If still <4.0 mmol/L, repeat above treatment
- If blood glucose remains <4.0 mmol/L after three cycles (30–45 mins), contact a doctor. Consider glucagon 1 mg IM or 150–200 mL 10% glucose over 15 mins IV
- Once blood glucose is >4.0 mmol/L, take additional long-acting carbohydrate of choice
- Do not omit insulin injection if due but review regimen

Severe (external help required)

This means individuals are either unconscious or unable to treat hypoglycaemia themselves. Treatment is usually by a relative or by paramedical or medical staff. Immediate treatment as below is needed.

- If patient is semiconscious or unconscious, parenteral treatment is required:

  IV 75–100 mL 20% dextrose over 15 mins (=15 g; give 0.2 g/kg in children)*

  Or

  IV 150–200 mL 10% dextrose over 15 mins

  Or

  IM glucagon (1 mg; 0.5 mg in children) – may be less effective in patients on sulphonylurea/under the influence of alcohol
- If patient is conscious and able to swallow:

  Give oral refined glucose as drink or sweets (= 25 g) or 1.5–2 tubes of Glucogel/Dextrogel

  Or

  Apply glucose gel or jam or honey to buccal mucosa
- Repeat blood glucose measurement after 10–15 mins and manage as per biochemical hypoglycaemia

*Use of 50% dextrose is no longer recommended.

Adapted from Joint British Diabetes Societies. The hospital management of hypoglycaemia in adults with diabetes mellitus (2013). Available at: abcd.care.

Lec.8 **GENERAL MEDICINE**
Stage: Fourth
Dr.Anas Hammad

Hematemesis and hemoptysis

Hematemesis

Hematemesis or **haematemesis** is the vomiting of blood, is red with clots when bleeding is rapid and profuse, or black ('coffee grounds') when less severe. It is generally from upper gastrointestinal tract (GIT), typically above the suspensory muscles of duodenum, and it is always an important sign.

Causes of Hematemesis; according to affected area:

1- **Bleeding from oesophagus;**
   - **A-** Oesophagitis; it is the most common causes represent 10% of upper gastrointestinal bleeding
   - **B-** Prolonged and vigorous retching that causes tears in the oesophageal mucosa (known as Mallory-Weiss Syndrome)
   - **C-** Oesophageal varices; usually due to liver cirrhosis or portal vein thrombosis
   - **D-** Tumor of oesophagus
   - **E-** Trauma to oesophagus
   - **F-** Arteriovenus mal-formation
2- **Bleeding from stomach**
   - **A-** Gastric erosion; may be due to NSAIDs (non-steroidal anti-inflammatory drugs) or alcohol and its 10-20% of upper gastrointestinal bleeding
   - **B-** Peptic ulceration; represent 35-50% of upper gastrointestinal bleeding, usually associated with H.Pylori infection or due to chronic use of NSAIDs
   - **C-** Tumor of stomach; tumor in oesophagus and stomach represent 2% of upper gastrointestinal bleeding.
   - **D-** Prolonged and vigorous retching that causes tears in the oesophageal mucosa (Mallory-Weiss Syndrome)
   - **E-** Vascular mal-formation; represent 5% of all causes of upper gastrointestinal bleeding

3- **Duodenal bleeding; involve:**
   - **A-** Peptic ulceration also may associated with H. Pylori infection or use of anti-inflammatory drugs
   - **B-** Vascular mal-formation
   - **C-** Aorto-duodenal fistula, rare cause 0.2% of upper gastrointestinal bleeding
4- **Haemorrhagic fever**
5- **Radiation exposure**
6- **Oral surgery that may cause swallowing of some blood**
7- **Some nose-bleeds cause blood to enter the digestive tract**
8- **Coughing hard and excessively**

Symptoms

Symptoms that suggest a person may be bleeding internally include:
Brown or black vomit
Bowel movements that sometimes associated with severe bleeding and hypovolemic shock

Mild Symptoms

Mild symptoms can include;

1- Headache
2- Fatigue
3- Nausea
4- Profuse sweeting
5- Dizziness

Severe Symptoms

Severe symptoms, which must be taken seriously and warrant emergency medical attention, include;

1- Cold or clammy skin
2- Pale skin
3- Rapid, shallow breathing
4- Rapid heart rate
5- Little or no urine output
6- Confusion
7- Weakness
8- Weak pulse
9- Lightheadedness
10- Blue lips and fingernail
11- Loss of consciousness

Management

Minimal blood loss edit;

If this is not the case, the patient is generally administered a proton pump inhibitor (e.g. omeprazole), given blood transfusions (if the level of hemoglobin is extremely low, that is less than 8.0 g/dL or 4.5 - 5.0 mmol/L) and kept NPO which stands for "nil per os" (latin for "nothing by mouth", or no eating or drinking) until endoscopy can be arranged. Adequate venous access (Large-bore cannulas or a central venous catheter) is generally obtained in case the patient suffer a further bleed and become unstable.

Significant blood loss edit;

In a "hemodynamically significant" case of hematemesis, that is hypovolemic shock, resuscitation is an immediate priority to prevent cardiac arrest. Fluids and/or blood administered, preferably by large bore intravenous cannula, and the patient is prepared for emergency endoscopy, which is typically done in theatres.

Surgical opinion is usually sought in case the source of bleeding cannot be identified endoscopically, and laparotomy is necessary. Securing the airway is a top priority in hematemesis patients, especially those with a disturbed conscious level (hepatic encephalopathy in esophageal varices patient). A cuffed endotracheal tube could be a lifesaving choice.

The principles of emergency management of non-variceal bleeding are as following:

1. **Intravenous access**

The first step is to gain intravenous access using at least one large-bore cannula.

2. **Initial clinical assessment**

• ***Define circulatory status.*** Severe bleeding causes tachycardia, hypotension and oliguria. The patient is cold and sweating, and may be agitated.

• ***Seek evidence of liver disease***. Jaundice, cutaneous stigmata, hepatosplenomegaly and ascites may be present in decompensated cirrhosis.

• ***Identify comorbidity.*** The presence of cardiorespiratory, cerebrovascular or renal disease is important, both because these may be worsened by acute bleeding and because they increase the hazards of endoscopy and surgical operations.

3. **Basic investigations**

• ***Full blood count***. Chronic or sub-acute bleeding leads to anaemia but the haemoglobin concentration may be normal after sudden, major bleeding until haemodilution occurs. Thrombocytopenia may be a clue to the presence of hypersplenism in chronic liver disease.

• ***Urea and electrolytes***. This test may show evidence of renal failure. The blood urea rises as the absorbed products of luminal blood are metabolized by the liver; an elevated blood urea with normal creatinine concentration implies severe bleeding.

• ***Liver function tests***. These may show evidence of chronic liver disease.

• ***Prothrombin time.*** Check when there is a clinical suggestion of liver disease or patients are anticoagulated.

• ***Cross-matching.*** At least 2 units of blood should be cross-matched if a significant bleed is suspected.

4. Resuscitation

Intravenous crystalloid fluids should be given to raise the blood pressure, and blood should be transfused when the patient is actively bleeding with low blood pressure and tachycardia.

5. Oxygen

This should be given to all patients in shock.

6. Endoscopy

This should be carried out after adequate resuscitation, ideally within 24 hours, and will yield a diagnosis in 80% of cases.

7. Monitoring

Patients should be closely observed, with hourly measurements of pulse, blood pressure and urine output.

8. Surgery

Surgery is indicated when endoscopic haemostasis fails to stop active bleeding and if rebleeding occurs on one occasion in an elderly or frail patient, or twice in a younger, fitter patient. If available, angiographic embolization is an effective alternative to surgery in frail patients.

9. Eradication

Following treatment for ulcer bleeding, all patients should avoid non-steroidal anti-inflammatory drugs (NSAIDs) and those who test positive for *H. pylori* infection should receive eradication therapy

Heamoptysis

Coughing up blood irrespective of the amount; is an alarming symptom. Care should be taken to establish that it is true haemoptysis and not haematemesis, or gum or nose bleeding. Haemoptysis must always be assumed to have a serious cause until this is excluded. Many episodes of haemoptysis remain unexplained, even after full investigation, and are

likely to be due to simple bronchial infection. A history of repeated small haemoptysis, or blood-streaking of sputum, is highly suggestive of bronchial carcinoma.

Causes of haemoptysis

1- **Bronchial disease**
   - Carcinoma*
   - Bronchiectasis*
   - Acute bronchitis*
   - Bronchial adenoma
   - Foreign body

2- **Parenchymal disease**
   - Tuberculosis*
   - Suppurative pneumonia
   - Parasites (e.g. hydatid disease, flukes)
   - Lung abscess
   - Trauma
   - Actinomycosis
   - Mycetoma

3- **Lung vascular disease**
   - Pulmonary infarction*
   - Goodpasture's syndrome
   - Polyarteritis nodosa
   - Idiopathic pulmonary haemosiderosis

4- **Cardiovascular disease**
   - Acute left ventricular failure (more common causes)
   - Mitral stenosis
   - Aortic aneurysm

5- **Blood disorders**
   - Leukaemia
   - Haemophilia
   - Anticoagulants

Treatment

The treatment of haemoptysis can be specified according to the causes.