Cardiovascular

1. Infective endocarditis
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5. Chest pain
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10. Shock

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Infective Endocarditis (IE)

Definition[1,2,3]
The invasion of the endothelial lining of the heart (endocardium) and cardiovascular structures by microorganisms, most commonly involving the valves, heart wall, and intrathoracic vessels.
Acute: Normal valve, acute HF+/-emboli
Subacute: Abnormal valves, prolonged course, low-grade fever, non-specific sx
- Prosthetic valve endocarditis divided into early (<60 days post-surgery), and late (thereafter)

Presentation[1,2]
- Acute or subacute
- Majority will have systemic constitutional symptoms: fever, chills, rigors, night sweats, fatigue, malaise, anorexia, wt loss
- Symptoms suggesting embolic phenomena to large vessels (brain, viscera), or small vessels (kidney, w/ haematuria or loin pain)

Consider Dx of IE in the following presentations:
- Fever plus new murmur or change in existing murmur
- Embolic event of unknown origin
- Sepsis of unknown origin
- Haematuria, glomerulonephritis and ARF

DDx[1,4,5]
IE is a major differential in PUO
- Libman-Sacks [non-bacterial thrombotic] endocarditis
- Antiphospholipid antibody syndrome
- Endocarditis associated with malignancy, autoimmune disease eg. SLE, heart valve surgery, eosinophilic HD, ruptured mitral chordea, myxomatous degeneration

Mx: Antibiotics-[5]
- Long courses 4-6/52 of high doses IV

Empirical
- Administer 4-hourly
- Benzylpenicillin (cover streptococci) PLUS
- Di/flucloxacillin (cover staphylococci) PLUS
- Gentamicin (cover GN sepsis) 4-6 mg/kg

NB: adjust dose in renal dysfunction

Proven streptococcal MIC up to <4 mg/L, enterococcal IE
- Exclude di/flucloxacillin
- Dosage, frequency and duration depend on MIC and whether complicated* or uncomplicated infection.
- *large vegetation, multiple emboli, symptoms >3m, secondary septic events

Proven streptococcal MIC >4 mg/L, resistant enterococcal IE, prosthetic valve IE
- Vancomycin, slow infusion PLUS
- Gentamicin

Staphylococcal IE (usually s.aureus, rarely s.lugdenesis)
- Di/flucloxacillin

NB: Gentamicin DOES NOT alter outcome

HACEK IE
- Ceftriaxone OR Cefotaxime

-Adjust for culture results, susceptibility
-Gentamicin and vancomycin: monitor blood levels and adjust dose accordingly, clinically monitor for vestibular toxicity, ototoxicity

Ex[1,2,4]
Skin: clubbing, splinter haemorrhages, Oslers nodes on finger pulps (painful, embolic), Janeway lesions on palms, pulps, foot soles (painless, erythematous maculopapular lesions containing bacteria), petechiae
Eyes: Roths spots (boat-shaped retinal haemorrhage due to immune deposition, also in SLE), conjunctival petechiae/haemorrhages
Heart: Regurgitant murmurs (IE cause destruction & perforation of valve leaflets, so valves become floppy), esp new or changing murmur, CHF (from severe regurg), heart block (valve ring abscesses)
Respiratory: dyspnea, tachypnea, pleuritic chest pain (septic PE in right sided IE)
Abdomen: splenomegaly (late sign)
Renal: haematuria
Neurological: embolic signs
Joints: occasionally resembles rheumatic fever pattern

Ix[1,2,4,5,6]
- Confirmation of organism by serial blood cultures: at least 3 sets at different times from different sites at peak fever BEFORE administration of antibiotics

NB: 10% culture negative
Causes of culture negative IE:
- Previous antibiotics, fastidious GP cocci, Legionella sp, Bartonella sp, Coxiella burnetti, or fungi including Candida albicans; use molecular methods for specific Dx

Bloods
- FBC: normochromic, normocytic anaemia, polymorphonuclear leucocytosis, ↑ ESR/CRP (acute IE), U&E (renal dysfunction), LFTs (↑ ALP)

ABG
- If septic PE suspected from right sided IE

Urinalysis
- Haematuria and proteinuria (immune mediated glomerulonephritis)

ECG
- AF or heart block, long PR interval (aortic root abscess)
- New AV block suggestive of abscess formation

Echocardiography
- TOE>TTE for visualising mitral lesions and aortic root abscess
- Vegetations must be >2mm to be seen
- Use to identify valvular dysfunction & mycotic aneurysms
- NB: negative result does not exclude Dx of IE

CXR
- Evidence of HF (cardiomegaly, Kerley B lines, upper lobe blood diversion [erect but not supine film])
- Pulmonary emboli

Prophylaxis[1,5,18]
No RCT to decide the role of antibiotic prophylaxis
Pt with cardiac conditions assoc w/ highest risk of adverse outcomes from IE undergoing specific dental or other procedures
- Prosthetic cardiac valve or recently implanted prosthetic material (eg. pacemaker wire, note excludes coronary stents)
- Previous IE
- Congenital HD: unrepaired cyanotic defects, prosthetic material or devices, residual defects following repair
- Cardiac transplantation with valvular disease

Educate pts of importance of good oral hygiene, regular dental evaluation, sx, when to seek advice, & risk of invasive procedures incl tattooing

Mx: Surgery-[2,7,8]
Make decision about need for cardiac surgery in consultation with cardiologist and cardiothoracic surgeon (and monitor for the development of these indications over course of Rx)
Absolute indications (Level B evidence):

- Development of HF or cardiac decompensation from valve destruction (ie. valve regurgitation)
- Fungal or highly resistant organisms
- IE complicated by heart block, intra-cardiac abscess-annular, aortic; perforation, fistulous tracts, false aneurysms

Consider for pt w/ recurrent emboli, persistent vegetations, persistent bacteriaemia, despite appropriate antibiotic Rx, also to prevent embolisation in presence of large (>1cm) mobile vegetations (Level C evidence)

Epidemiology[1,8]

- Men>women
- Mortality 5-50% treated, 100% untreated

Pathophysiology[1,2,4,5]
A complex interaction between damaged vascular endothelium, local haemodynamic abnormalities, circulating bacteria, and host immune system. Most commonly involves aortic and mitral valves. In IVDU tricuspid valve is most frequently affected.

- Turbulent blood flow traumatizes the endocardium
- Damage to endocardium causes deposition of fibrin and platelets leading to non bacterial thrombotic endocardial lesion (NBTE)
- NBTE colonized by bacteria in the bloodstream
- Vegetations may cause destruction to the valves they colonize, and may lead to regurgitation or obstruction
- Emboli from the vegetation can form in various organs, and may lead to infarction or abscess formation
    - L-sided IE: brain, kidney, spleen, gut
    - R-sided IE: lungs

Complications:

- *Cardiovascular:* heart failure, abscess formation, mycotic aneurysm, pericarditis, aortic valve dissection, fistula formation between aorta and atrium or ventricle
- *Neurological* (25% of episodes): encephalopathy, meningitis, stroke, brain abscess, cerebral haemorrhage from mycotic aneurysms, seizures
- *Renal:* infarction, antibiotic-induced interstitial nephritis, glomerulonephritis, renal abscess
- *Other:* Metastatic abscesses of kidney, spleen, brain, or soft tissues

HACEK[1,6]
Haemophilus aphrophilus, paraphrophilus, and parainfluenzae
Actinobacillus acetinomycetemcomitans
Cardiobacterium hominis
Eikenella corrodens
Kingella kingae

Aetiology[1,2,4,5]

- Caused by wide variety of microorganisms, but GP major cause: 80% Strep & Staph

Native valve, Non-IVDU:

- Staphylococcus aureus, viridans group streptococci, enterococci, coagulase negative staphylococcus, Streptococcus bovis (assoc w/ bowel cancer)

Rarely (native valve):

- GN bacteria HACEK (more insidious course), coxiella burnetii, Chlamydia, fungi including candida, aspergillus, histoplasma

IVDU:

- Staphylococcus aureus

Prosthetic valves:

- Staphylococcus epidermidis, corynebacterium sp, streptococcus sp, enterococci, enteric GN rods, Pseudomonas aeruginosa, Candida albicans, other fungi

Risk Factors

- Structural cardiac defects-
    - Acquired valvular HD with stenosis or regurgitation eg. MVP
    - Valve replacement
    - Structural congenital HD *except* ASD, VSD, PDA, non-endothelialised intracardiac devices
- Hypertrophic cardiomyopathy, previous IE, RHD, IVDU, indwelling pulmonary catheter, bacteremia (overt or covert), dermatitis, renal failure, organ transplantation, DM, post-op wounds, chronic alcoholism, well defined extra-cardiac focus of infection, agglutination antibodies

Duke Criteria for Clinical Diagnosis[1,9]

- 2 major, 1 major + 3 minor, or 5 minor

Major criteria

- +ve blood cultures
    - Typical microorganism consistent w/ IE from 2 separate blood cultures, OR
    - Persistently +ve blood cultures (>2 +ve cultures separated by >12hrs; or 3 or majority of 4+ cultures w/ 1st & last at least 1hr apart)
- Evidence of endocardial involvement
    - +ve echocardiogram
    - Oscillating intracardiac mass on valve/supporting structures, or path of regurgitant jet
    - Abscess
    - New partial dehiscence of prosthetic valve
    - New valvular regurgitation
- Embolic phenomena

Minor criteria

- Predisposition (cardiac lesion, IVDU
- Fever >38 degrees Celsius
- Vascular phenomena (arterial emboli, septic PE, mycotic aneurysm, Janeway lesions, intracranial or conjunctival haemorrhages)
- Immunological phenomena (glomerulonephritos, Oslers nodes, Roth spots, rheumatoid factor)
- +ve blood cultures (not meeting major criteria)
- +ve echocardiogram (not meeting major criteria)

Hypertension

Definition Sustained elevation of systemic arterial blood pressure

Classification[1,10,11]

	sBP	dBP
Grade 1	140-159	90-99
Grade 2	160-179	100-109
Grade 3	≥180	≥110

Malignant HTN=sBP>200, dBP>130mmHg+bilateral retinal haemorrhages and exudates +/- papilloedema. Emergency! May→acute RF, HF, encephalopathy. Untreated 90% die 1yr, treated 70% survive 5yrs. Hallmark is fibrinoid necrosis.

Presentation[1,4,12]

Usually asymptomatic→regular screening crucial

Secondary hypertension:

- *Renal disease:* lethargy, LOA, ankle swelling, SOB
- *RAS:* sudden worsening of HTN, <30yo or >50yo
- *Cushing syndrome:* fatigue, weakness, wt Δ, striae, acne, skin infn, bruising, ↑ thirst & urination, mood Δ
- *Acromegaly:* h/aches, vision Δ, tightness of rings, ↑ shoe size, arthritis, poor sleep, palpitations
- *Thyroid disease:* fatigue, weakness, wt Δ, tachy/bradycardia, palpitations, tremor, dry skin/hair, hair loss, diarrhea/constipation, menstrual irregularities, mood Δ, temp intolerance
- *Phaeochromocytoma:* h/ache, palpitations, sweating, anxiety
- *Sleep apnea:* snoring, pauses in breathing during sleep, fatigue, morning h/aches
- *CoA of aorta:* cold legs, SOBOE, chest pain, syncope

PMH

- DM, CAD, HF, obesity, hyperlipidaemia, renal disease, thyroid disease

Med Hx

- NSAIDs, corticosteroids, OCP, phenylpropanolamines, cyclosporine, tacrolimus, erythropoietin, others

Family Hx

- HTN

Social Hx

- Cocaine, cocaine w/drawal, "herbal ecstasy" (phenylpropanolamine analogs), nicotine, nicotine w/drawal, anabolic steroids, others
- ETOH, sodium, cholesterol, and calorie intake

Symptoms that suggest end organ disease:

- Chest pain
- TIA
- Claudication
- Vision changes
- Left heart failure

Ix[1,4,10]

Quantify absolute CV risk, ID end-organ damage, exclude 2^{o} causes

Bloods: U&E, Ca^{2+}, creatinine, fasting BG, lipid profile

Urinalysis: Proteinuria, haematuria

ECG: LV hypertrophy, past MI

Imaging: Echocardiogram-gold standard for LVH

If the following are suspected:

- *RAS*-renal US/arteriography
- *Cushing syndrome*-urinary free cortisol, dexamethasone suppression test
- *Acromegaly*-IGF-1, GH
- *Parathyroid disease*-serum PTH
- *Thyroid disease*-TSH
- *Phaeochromocytoma*-24-hr urinary metanephrine and normetanephrine
- *Sleep apnea*-sleep study
- *CoA of aorta*-CT angiography
- *Primary aldosteronism*-plasma aldosterone, renin, potassium
- *White coat HTN*-24hr ambulatory BP

Ex[1,4,10,13]

Focus on end organ damage and causes of 2^{o} HTN

Moon face, upper body obesity, striae, buffalo hump (Cushing)

Cardiac:

- Point of maximal intensity displaced laterally (LV hypertrophy)
- LV heave, S4, S3, pulmonary oedema, carotid bruits, valvular murmurs (AS, MR)

Cerebrovascular:

- Neurological deficit

Eye:

- Hypertensive retinopathy, see over

GIT:

- AAA, renal bruits (renovascular HTN), hepatomegaly, palpable kidneys or renal mass (renal disease, polycystic kidneys), striae (Cushing syndrome)

Peripheral vascular:

- ↓, absent &/or delayed femoral pulses or radio-femoral delay (CoA of aorta), or peripheral pulses (PAD), femoral bruits (PAD), peripheral oedema (HF, renal disease)

DDx[10]

- False elevation of BP-improper technique (eg. cuff too small), pseudohypertension (calcified artery)
- Physiologic causes: exercise, anxiety, pain, pregnancy
- Exogenous causes: meds, caffeine, intoxications
- White coat hypertension

Mx[4,10]

Goal: BP<140/90 mmHg or <130/80 mmHg if DM or CKD

Lifestyle Modifications-ALL pts w/ HTN

- Regular physical activity (≥30 min/day mod-intensity, most days)
- Smoking cessation
- Sodium restriction (<4g/day=65mmol/day)-low salt foods, no added salt)
- Wt ↓/maintenance (waist circumference <94cm M, <80cm F; BMI 18.5-24.9)
- Limit ETOH (<20g/day w/ ≥2 ETOH-free days/wk)

Tailor advice, realistic goals, specific written instructions, provide encouragement and review progress regularly

Medications (50-75% pts require 2+)

-Immediately when grade 3 HTN, assoc conditions, end-organ damage, high absolute CV risk (using markers of high risk or NZ CV risk calculator, see below).

-Initial drug choice based on age, presence of assoc clinical conditions or end-organ damage, potential drug interactions, implications for adherence, cost.

NHF recommended 1st line drugs:

- ACE inhibitors (=efficacy to ARB) esp. stroke, CHF
- Dihydropyridine calcium channel blockers, or
- Low-dose thiazide diuretics (if age≥65yo) NB: ↑ risk DM
- Beta-blockers no longer 1st line (unless pregnant or associated CAD) NB: ↑ risk DM
- Start low dose
- If initial not well tolerated then change class. Target BP not reached ≥6 wks, add 2nd agent from different class. Then if BP still above target, ↑ dose of one agent incrementally

Aetiology[1,4,10,12]

>95% Essential HTN (aka primary, no identifiable cause)
5% Secondary Causes:
Suspicion should be in pt <35yo, no family Hx, severe rapid onset, HTN refractory to standard therapy

- Renal (most common)
  - Any cause of CKD eg, GN, PAN, systemic sclerosis, chronic pyelonephritis, polycystic kidneys
  - Renovascular disease eg. Atheromatous, fibromuscular dysplasia
- Endocrine
  - Cushing syndrome
  - Primary hyperaldosteronism eg. Conn's syndrome
  - Acromegaly
  - Hyperthyroidism
  - Hyperparathyroidism
- Neurogenic
  - Brain tumour
  - Bulbar poliomyelitis
  - Intracranial hypertension
- Drugs-NSAIDs, OCP, MAOI, steroids, cyclosporine, tacrolimus, erythropoietin, adrenergic meds, ephedrine, ETOH, cocaine, amphetamines
- Pregnancy-nb Pre-eclampsia/eclampsia is a special high-risk hypertensive condition
- Other
  - Phaeochromocytoma
  - OSA
  - CoA

Hypertensive Retinopathy

I: silver or copper wiring
II: A-V nipping
II: Flame haemorrhages, cotton wool spots
IV: Papilloedema

Hypertensive Emergencies

- HT encephalopathy (cerebral oedema)
- Aortic dissection
- Rapid lowering of BP required (urgent hospitalization)

Epidemiology[1,4,10]

- >50% 60-69yo
- 75% ≥70yo
- Associated with ↑ all-cause mortality

High CV Risk Groups[10]

Following groups can be assumed to have high CV risk w/out using risk calculator:

1. Pts ≥75yo
   a. >15% in next 5yrs
2. Pts w/ existing CV disease
   a. Symptomatic CV disease eg. Angina, MI, CHF, stroke, TIA, PAD
   b. LV hypertrophy Dx w/ECG or echo
   c. >20% in next 5yrs
3. Pts w/ assoc clinical conditions and end-organ disease
   a. >15% in next 5 yrs
   b. Requires antihypertensive drug Rx

For all pts estimate absolute risk using modified NZ CV risk calculator

Causes: APE ERECTIONS

- **A**nxiety
- **P**regnancy (esp pre eclampsia)
- **E**xertion
- **E**ssential
- **R**enal (GN, chronic pyelonephritis, PCKD, RAS, obstructive uropathy)
- **E**ndocrine (DM, thyrotoxicosis, Cushings, Conns, ovarian tumor, phaeochromocytoma)
- **C**oarctation of aorta
- **T**oxaemia
- **I**atrogenic
- **O**CP(and other meds: steroids, analgesics, NSAIDs, anti depressants)
- **N**eurogenic (raised ICP, bulbar disease/polio, head injury, hypothalamic lesion)
- **S**leep apnoea

Pathophysiology[11]

Normal BP

- Function of CO and PVR, influenced by multiple genetic, environmental, and demographic factors
  - CO is highly dependent on BV, which is greatly influenced by sodium intake
  - PVR determined mainly at level of arterioles and affected by neural and hormonal factors. Reflects balance b/w vasoconstrictors (angiotensin II, catecholamines, endothelin) and vasodilators (kinins, PGs, NO). Autoregulation of vessels, whereby ↑BF→vasoconstriction, also plays a role.
- Local factors (eg. pH, hypoxia, alpha- and beta-adrenergic systems) also influence HR, cardiac contraction, & vascular tone

Role of Kidneys-Renin-angiotensin system:

- Juxtaglomerular cells secrete renin when ↓ BP→converts angiotensinogen to angiotensin I, then converted to angiotensin II by ACE→↑PVR (via vascular SM cells) and ↑BV (via aldosterone)

Vasodilator substances (eg. PGs, NO)

- ↓BV→↓GFR→↑sodium reabsorption→↑BV

Essential HTN

A complex, multifactorial disorder, likely influences by interactions of mutations or polymorphisms at several loci, and variety of environmental factors.

- Accelerates atherogenesis:
  - Hyaline arteriolosclerosis-plasma ptn leakage, ↑SM cell matrix synthesis
  - Hyperplastic arteriolosclerosis-in malignant HTN, "onion-skin lesions", concentric laminated thickening of walls and luminal narrowing, SM cells w/ thickened reduplicated BM, fibrinoid deposits, vessel call necrosis, esp in kidney

Uncontrolled or poorly controlled HTN leads to complications in a number of systems:

- Cardiac (CAD, MI, HF, RAD, aortic regurgitation, atrial flutter)
- Cerebrovascular (TIA, intracerebral haemorrhage)
- Peripheral vascular (limb)
- Renal (A/CRF)
- Ophthalmologic (retinal haemorrhage, blindness)

Arrhythmias Disturbance in normal heart rate and/or rhythm

- Important to elicit whether benign or haemodynamically severe or indication of underlying heart disease
- Can arise from cardiac abnormalities, most commonly MI, CAD, valvular disease, cardiomyopathy, pericarditis, or myocarditis
- Other non-cardiac causes: Drugs (nicotine, ETOH, caffeine), meds (beta2-agonists, dixogin, +++), and metabolic imbalances (K^+, Ca^{2+}, Mg^{2+}, $\uparrow O_2$, $\uparrow CO_2$, thyroid disease)
- May be asymptomatic

Hx[4,12]

- PC: palpitations, CP, dizziness, syncope, dyspnea, fatigue, confusion, anxiety
- Hx HD, arrhythmias, angina, MI, HTN, ↑ chol, DM
- Drugs (see DDx)
- ETOH, smoking. recreational drug use
- Family hx HD

Ex[1,3]

- Vital signs-temp, HR, BP, RR, O_2sats
- Palpation-
  - Pulse: weak, thready (tachycardia), irregularly irregular (AF)
- Cardiac auscultation
- Signs and symptoms of cardiac disease (see 'Heart Failure')

Vasovagal manoeuvres[1]

- holding breath
- carotid sinus massage
- valsalva
- coughing

→ ↑ AV block

Ix[1,4,12,14,16]

- *Blood tests:* FBC, U&E, inorganic chemicals (Ca, Mg, phosphate), glucose, TFT, cardiac enzymes (troponin I, BNP, ?CKMB)
- *ECG*
  - *Atrial tachycardia:* abnormal shaped P wave, +/- # P waves > # QRS
  - *Multifocal atrial tachycardia:* 3+ P wave morphologies, irregular QRS
  - *Atrial flutter:* 250-350 bpm, negative directed saw-tooth deflections in leads II, III, aVF, positive directed saw-tooth deflections in lead V1, +/- usually 2:1 or higher grade AV block
  - *AF:* fibrillary waves >300/min, irregular narrow QRS, usually fast rate
  - *WPW syndrome:* short PR interval, wide QRS w/ delta wave (slurred upstroke), ST-T changes
  - *Junctional tachycardia:* 150-250bpm, P wave within QRS or after QRS
  - *VT:* regular wide QRS complex tachycardia, either complete AV dissociation or 1:1 retrograde atrial capture
  - *Hypokalaemia:* U waves
- *Echocardiogram*
  - Structural heart disease
- *Provocation tests*
  - Cardiac stress test (exercise ECG)
- *Holter monitor*-ambulatory ECG worn around neck for 24hr
- *Invasive investigations* can include electrophysiological testing and cardiac catheterization

CHADS2 score[1,14,15]

For predicting risk of thromboembolic stroke in pts w/ AF

- *C*ongestive heart failure
- *H*ypertension
- *A*ge ≥75yo
- *D*iabetes mellitus
- *S*troke or TIA

1 point for each of the above risk factors except for stroke (2 points). Max score out of 6. Pts w/ score ≥2/6 are recommended to be put on oral anticoagulation eg. warfarin (target INR 2-3):

Score 0-aspirin or nothing; score 1-warfarin or aspirin

- AF is the most common arrhythmia, and is common particularly in the elderly
- May be asymptomatic, or pts may experience palpitations, dizziness, LOC
- Contraindications to anticoagulants are bleeding diathesis, thrombocytopenia ($<50x10^3$/microL), non-adherence to treatment and monitoring, previous intracranial, retinal or GIT bleeding, and pregnancy (teratogenic).

Sick sinus syndrome[1,14]

- Sinus bradycardia, sinus pauses, or alternating tachy- and bradycardia syndrome. Requires pacing if symptomatic
- Usually idiopathic, rarely caused by conduction defects (eg. amyloidosis, Chagas disease), meds (eg. digoxin)

Torsades de pointes[14]

- VT with varying axis, due to ↑ QT interval
- "Twisting of the peaks" morphology on ECG
- May → VF
- Drug-induced, including-
  - Procainamide, quinidine, sotalol, amiodarone, arsenic, methadone
  - Antibiotics (eg. clarithromycin, erythromycin)
  - Antiemetics (eg. domperidone, metoclopramide)
  - Antipsychotics (chlorpromazine, haloperidol)

Long QT[14]

- Characterised by prolonged QT on ECG
- Assoc w/ ventricular tachyarrhythmias and resulting sudden cardiac death
- Can be genetic or acquired (eg. drugs, electrolyte imbalance, starvation)

Bradycardia Resting heart rate <60bpm

DDx[14]

May be due to rhythm disturbances resulting from sinus node dysfunction, AV conduction disturbance or heart block

- *Physiological* eg. athlete
- *Drugs*-beta blocker, antiarrhythmics eg. flecainide, digoxin, TCA, lithium, cholinesterase inhibitors eg. neostigmine, heroin (and many more...)
- *Poisoning*-many, including opiate overdose toxidrome, insecticide/organophostphate
- *CVS*-Heart block, HD, MI, arrhythmia, cardiomyopathy, neurogenic shock, hypothermia
- *Infection*-bacterial overwhelming sepsis
- *Metabolic*-Electrolyte disturbances (eg. hyperkalemia), diabetic autonomic neuropathy syndrome, malnutrition, starvation
- *Endocrine*-hypothyroidism, adrenocorticoid deficiency
- *Allergies*-anaphylaxis
- *Trauma*-brain injury, traumatic brain haemorrhage
- *Psych*-anorexia nervosa

Mx of bradycardia[1]

- Address underlying cause & stop any associated drugs
- Asymptomatic, HR >40bpm→no specific treatment required
- Symptomatic, or HR<40bpm→treat
  - Atropine 0.6-1.2 mg IV (≤3mg)
  - If no response, insert temporary pacing wire
  - May require isoprenaline infusion or use external cardiac pacing

Side-effects of amiodarone[12,14]

- Corneal deposits
- Photosensitivity
- Hepatitis
- Arrhythmias
- Pulmonary fibrosis, pneumonitis
- Hyper-/hypothyroidism
- Increased INR
- Nightmares

Must monitor LFT and TFT!

Tachycardia Resting heart rate >100bpm

Classification[1,4,12]

Narrow complex (rate>100bpm, QRS width <120ms)-electrical signal passes through AV node

- Sinus tachycardia
- SVT [Rx: vagotonic maneouvres, IV adenosine or verapamil, DC shock if compromised]
  - Atrial tachycardia
  - Multifocal atrial tachycardia-most commonly in COPD; ≥3 morphologically distinct P waves, irregular P-P intervals
  - Atrial flutter (macro-reentrant atrial tachycardia; 2:1 AV block common)
  - AF
    - Paroxysmal: recurrent, terminates spontaneously <7d
    - Persistent: >7d or <7d but requires cardioversion
    - Longstanding: >1yr
    - Holiday Heart Syndrome-binge drinking in pt with normal heart→AF (DDx: marijuana use). [Rx: ETOH abstinence, verapamil, beta-blocker, amiodarone, digoxin (nb 2nd-line unless AF w/ HF]
  - Junctional tachycardia
    1. AV nodal re-entry tachycardia (ANNRT)
    2. AV re-entry tachycardia (AVRT)
    3. His bundle tachycardia
  - WPW syndrome-congenital accessory conduction pathway b/w atria and ventricles arrhythmias esp. AVRT, AF, atrial flutter

Broad complex (rate>100bpm, QRS width >120ms)-AV node or conduction system dysfunction. Supraventricular or ventricular in origin.

- VT (>3 ventricular ectopics, HR>100bpm, QRS duration >120ms) [Rx: IV amiodarone or lidocaine, no response then DC shock]
  - Torsades de pointe
- SVT- abnormal conduction or ventricular pre-excitation can→ any SVT to produce a broad complex tachycardia

DDx[14]

- *Physiological* eg. Exercise, fear, stress, pregnancy
- *Drugs*-amphetamines, ecstasy, cocaine, ETOH, caffeine ++
- *CVS*-Heart block, heart disease, MI, arrhythmia, cardiogenic or hypovolemic shock
- cardiomyopathy
- *Electrolyte disturbances*-hypokalemia
- *Poisoning*-botulism, carbon monoxide
- *Infection*-pericarditis, acute infective illness, overwhelming sepsis
- *Metabolic*-hypokalemia, acidosis, hypoxia, dehydration
- *Endocrine*-hyperthyroidism, adrenocorticoid excess (eg. Cushing syndrome), hypoglycaemia
- *Vascular*-Anaemia
- *Neoplastic*-phaemochromocytoma
- Malignant hyperthermia
- *Psych*-anxiety, mania, hyperactive delirium
- NMS syndrome

Mx of tachyarrhythmias[1]

- Address underlying cause
- If compromised use DC conversion
- For AVRT, vasovagal maneouvres, if unsuccessful then try IV adenosine (CI in asthma, 2nd/3rd degree AV block, sinoatrial disease), failing that then IV verapamil
- Amiodarone loading dose (200mg/8h po 7d, then 200mg/12h 7d), followed by maintenance Rx (200mg od)
- In regular broad complex tachy-assume VT until proven otherwise, give O2, obtain IV access and draw bloods (U&E, cardiac enzymes, Ca2+, Mg2+), obtain 12-lead ECG, do ABG
  - VT: amiodarone or lidocaine, failing that or if compromised, use DC shock
  - VF: use asynchronised DC shock

Valvular Heart Disease

Definition Congenital or acquired valvular defects leads to restriction to blood flow (stenotic) or incompetency of the valves and backward flow (regurgitation/insufficiency)

Presentation[1,4,13]

- AS: exertional angina or weakness, SOBOE, effort-related syncope, CHF
- AR: SOBOE, CHF, palpitations
- MS: SOBOE, exertional weakness, palpitations, orthopnea, PND, AF, haemoptysis, CHF
- MR: SOBOE, orthopnea, PND, cough, palpitations, haemoptysis
- All assoc w/ fatigue
- Elicit hx of rheumatic heart disease in pt
- Known or presumed CAD may accentuate or mask symptoms
- (*CHF-for S&S see CHF document)

DDx[4]

Systolic murmur-

- AS, HOCM, PS, VSD, MR, TR; innocent flow murmur- hyperdynamic state (eg. thyrotoxicosis, anaemia, infection, pregnancy, after exercise)

Diastolic murmur-

- AR, PR, MS, TS

Ex[1,4,6,12,13]

	AS	*AR*	*MS*	*MR*
Age	Childhood/adolescence-middle age-bicuspid aortic valve >65yo-calcific (degenerative), aortic stenosis	Younger person-RHD, Marfan's, ankylosing spondylitis Older age--degenerative AV, dilated aortic root/aortic aneurysm from HTN, cystic medical necrosis or atheroma	10-50-depends on prevalent rates of rheumatic fever. Severe MS can occur at young age if recurrent bouts of RF	Depends on aetiology eg. RHD, Marfan's, myxomatous mitral valve, mitral valve prolapse, functional MR due to MI, cardiomyopathy or HF
Ex	Sustained forceful apical impulse Weak/delayed carotid pulse Carotid upstroke (delayed) Single S2 (valve static) LV heave	Increased pulse pressure (water-hammer pulse) Corrigan's pulse, Hill's sign, pistol-shot femoral pulses, Duroziez's sign, de Musset's sign, Quincke's pulse	Loud S1, opening snap, AF, RV heave, hepatomegaly (pulsatile), pulmonary oedema, malar flush	Soft S1, AF, brisk carotid upstroke w/ ↓ volume, S3 gallop, hyperdynamic apex, RV heave
Murmur	Crescendo-decrescendo systolic ejection, radiate to neck w/ assoc thrill, ↓ intensity w/ valsalva	Early decrescendo diastolic murmur	Non-radiating apical diastolic rumble	Pansystolic, radiating from apex to axilla Mid to late systolic if MVP
ECG	LV hypertrophy, left anterior hemiblock	Increased LV mass	LA enlargement (broad notched P waves), RV hypertrophy, R axis deviation, AF	Increased LV mass, AF
CXR	Poststenotic aortic dilatation, boot shaped heart	Cardiomegaly, left HF	LA enlargement, RA enlargement, Kerley B lines, prominent pulmonary arteries	Cardiomegaly, left HF

- Echocardiogram for Dx and assessment of severity
- Cardiac catheterization to confirm DX, estimate severity, measure pressure gradient and intrachamber pressures, and if valve replacement surgery is to be undertaken

Mx[1,4,5]

- Symptomatic severe AS managed purely medically has worst prognosis (50% 1 yr)
- In remainder, medical (echocardiography monitoring) is initial approach, with surgery reserved for progression of symptoms
- If lesion arises acutely, surgery is necessary earlier in the course

To relieve symptoms:

- Digoxin (esp if AF)
- Diuretics
- Vasodilators for AR or MR (contra-indicated in AS)
- Anticoagulation esp in AF, and also in MS

Valve repair or replacement

- Bioprosthesis {tissue valves-10-15 yr lifespan; used in elderly)}
- Mechanical prosthesis (exceed human life span; used in young pt)
- Decision based on the need for anticoagulation with its risks when mechanical valves are used and on the durability-before symptoms, or for ventricular decompensation

Percutaneous balloon valvuloplasty (stenotic cases)

Antibiotic prophylaxis no longer routinely recommended against IE for dental and surgical procedures unless high risk features

Aetiology[4,11]

- In adult population due to acquired defects (congenital in paeds), most commonly affecting AV and MV.
- ARF: scarring of the valve apparatus and fusion of the valve cusps→ more prone to mechanical degeneration and failure (stiffening and thickening of the valve leaflets as well as the resultant turbulent flow) and more prone to become involved in IE causing further valvular damage
- Several valvular entities have particular specific aetiologic associations
    - AS: congenital bicuspid valve, calcific (senile) degeneration
    - AR: congenital bicuspid valve, IE, rheumatic fibrosis, syphilitic aortitis, RA, Marfan syndrome, cystic medial necrosis
    - MS: RHD (mitral annular calcification), rarely endomyocardial fibroelastosis, malignant carcinoid syndrome, SLE
    - MR: MV prolapse, abnormal leaflets and commissures postinflam (RHD, IE), papillary muscle dysfunct (MI), LV enlargement (myocaditis, hypertrophic cardiomyopathy), idiopathic myxomatous degeneration

Epidemiology[1]

- Most 7th decade (MS usually 3-5th decades)
- Rheumatic fever was initially most common aetiology, but now RF ↓ in incidence
- Wear and tear degeneration assoc w/ ageing is now the more common cause

Pathophysiology[11,13]

- Leads to restriction to blood flow (stenotic) or incompetency of the valves and backward flow (regurgitation/insufficiency).
    - Stenotic lesions: pressure overload on the upstream cardiac and vascular structures→concentric LV hypertrophy is AS
    - Regurgitant lesions: volume overload→LV dilatation & eccentric hypertrophy→ ↑ contractility (Starlings' Law)

The following pathogenic responses result:

- AS
    - Concentric LV hypertrophy (initial)
    - LA hypertrophy (secondary to ↑ role of atrial contraction in diastolic filling of the hypertrophied LV)
    - ↓ LV ejection fraction (late)

  Complications: LV hypertrophy (concentric), exacerbation of CAD, arrhythmia, syncope, IE
- AR
    - LV dilation (early)
    - LV hypertrophy (secondary)
    - ↓ LV contractility (late) causing HF
- MS
    - Fusion of commissures, leaflet thickening, shortening of chordae tendinae
    - Cusps fuse→↑ LA pressure→ LA enlargement (early) with subsequent development of AF
    - Pulmonary venous congestion (early)
    - ↑ pulmonary vascular resistance and pulmonary HT N(late)
    - RV hypertrophy and RHF (late)

  Complications: AF, IE, atrial flutter, pulmonary HTN, emboli from LA thrombus, RVH, RVF, CHF, pressure from enlarged LA on local structures may cause hoarseness, dysphagia, bronchial obstruction
- MR
    - ↑ LA pressure→LA enlargement (early) causes AF
    - Pulmonary congestion (late)
    - Pulmonary HTN (late)
    - LV failure (late, as LV no longer able to compensate for regurgitant flow by ↑ systolic emptying)

  Complications: LVH, LA dilation, hyperdynamic cardiomegaly, LHF, RHF, atrial flutter, AF

- These changes will only occur if the valvular lesions develop slowly over time (eg RHD). Initially compensatory, but usually at the eventual cost of chamber failure
- If rapid valvular lesion (in acute AR or MR from IE or acute MR in setting of AMI) abrupt congestive failure results
- Abnormal valve surfaces are thrombogenic (esp when associated with AF): emboli (stroke)

Chest Pain (CP)

Funny feeling in chest!

Questions to ask on Hx[1,4,12]

- Determine the severity, location, duration, and-

Character:

- Central, crushing -MI
- Constricting -angina, oesophageal spasm, anxiety
- Sudden, tearing -aortic dissection
- Sharp, pleuritic -pneumonia, PE, pericarditis

Radiation:

- Arms, neck/jaw -MI
- Shoulder -MI, cholecystitis, GORD, PUD
- Interscapular -aortic dissection
- Back -pancreatitis, GORD, PUD

Exacerbating and relieving factors:

Cardiac (also psychogenic)-

- ↑ by exercise, emotion
- ↓ by rest, nitrates

Pleuritic-

- ↑ by deep breathing

Oesophageal disease-

- ↑ by food, lying down, hot drinks, ETOH
- ↓ by antacids

Musculo-

- ↑ by movement or local pressure

Note-Pericarditis, pancreatitis, oesophageal disease may be relieved by sitting forwards

Associated sx:

- Dyspnea -LVF, PE, pneumothorax, pneumonia, anxiety
- N&V -MI, oesophageal rupture, acute cholecystitis, pancreatitis
- Palpitations -arrhythmias, thyrotoxicosis, anxiety
- Syncope -cardiac events, vasovagal 'faints'
- Prodrome viral illness -viral pleuritis or pericarditis

PMHx

- Specific cardiac risk factors-known cardiac disease, ↑ chol, HTN, smoking, family Hx
- Risk factors for DVT-prolonged immobilization, recent surgery, hospitalization, travel, smoking, OCP

Med Hx

- NSAID use may suggest gastric aetiology

Social Hx

- Cocaine use (cardiac ischaemia)

DDx[1,4,12]

- Common aetiologies in 1^{o} care setting are musculoskeletal (36%), GIT (19%), stable angina (10.5%), unstable angina or MI (1.5%)

Life threatening causes must <u>always</u> be excluded:

- *Acute coronary syndrome* (AMI, unstable angina)-severe central chest pain radiating to jaw or upper extremities, assoc w/ nausea, vomiting; may have life-threatening arrhythmias, cardiogenic shock, pulmonary oedema
- *Aortic dissection*-sudden, severe pain, "tearing" sensation radiating to mid-back
- *Tension pneumothorax*-acute, sharp, pleuritic pain assoc w/ dyspnea, tachycardia, tachypnea, hypoxia; mediastinal shift with compression of great vessels causes ↓ BF to heart→shock
- *PE*-acute SOB, pleuritic pain, syncope, imminent cardiopulmonary arrest
- *Cardiac tamponade*-suddenly as result of trauma or aortic dissection, or gradual, with muffled heart sounds, distended neck veins, pulsus paradoxus
- *Oesophageal rupture*-localised abrupt onset lower thoracic pain ↑ w/ swallowing, neck flexion, preceded by vomiting

Cardiac:

- Angina, MI, pericarditis, myocarditis, pericardial effusion, aortic dissection

Respiratory:

- PE, pneumothorax, pneumonia, pleuritis, pleurodynia

GIT:

- Oesophagitis, hiatus hernia, oesophageal spasm, PUD, acute cholecystitis, pancreatitis, splenic infarction, hepatitis

Chest wall:

- Ribs-fracture, costrochondritis
- Nerves-herpes zoster, trauma
- Muscles-rheumatic

Psychogenic:

- Anxiety, panic attack

Pleuritic pain-↑ w/ inspiration or cough, aggravated by movement or position (pulmonary aetiologies, pericarditis, musculoskeletal)

Visceral pain-dull ache, tightness, burning pain, poorly localized (MI, oesophageal disease)

Ex[1,4,12,13]

Vitals

- Dyspnea, tachypnea (pneumothorax, PE)
- BP-unequal b/w arms (aortic dissection)

Inspection

- ↑ JVP (cardiac tamponade)
- Rash in region of dermatological burning pain (herpes zoster)

Palpation

- Reproduction of CP by palpation (musculoskeletal eg. costochondritis)
- Examine legs for DVT-LL oedema, erythema, with tender firm calf

Auscultation

- Cardiac auscultation for ↓heart sounds (cardiac tamponade), MR murmur (ACS, heart failure)
- Respiratory auscultation-
  - ↓ breath sounds (pneumothorax, collapsed lobe)
  - Crepitations in lung bases (pneumonia, HF)
  - Pleural rub (pulmonary infarct, pneumonia)
  - Hyperresonance, tracheal deviation to opposite side (pneumothorax)

Acute Mx[1,4,12]

- Continuous monitoring of vitals (temp, PR, BP [both arms initially], RR, O_2 sat)
  - O_2 saturation <90% →high-flow O_2
- Take bloods (see 'Ix') and insert IVC
- Administer analgesia, antiemetics as required
- See 'Ix' for more info on imaging etc

Pharmacological

- Analgesia-
  - NSAIDs in suspected musculoskeletal aetiologies or pericarditis
  - Severe pain→morphine IV
- *AMI*-antiplatelet (ASA, clopidogrel, and/or GPIIb/IIIa inhibitor) and antithrombotic Rx (heparin/LMWH). Consider B-blocker & IV GTN
  - *STEMI*→acute reperfusion therapy with primary angioplasty (<6hrs) or thrombolytics, if primary PCI unavailable
  - *NSTEMI*-stabilize with B-blocker, nitrates. Angiography+PCI within 24 hours
- *Aortic dissection*→IV beta-blockade for HR and BP control
- *PE*→systemic anticoagulation with heparin or LMWH
- *GORD*→PPI

Non-Pharmacological

- *Tension pneumo*→needle decompression followed by tube thorarostomy to prevent acute decompensation
- *CAD*→Coronary angioplasty

Ix[1,4,12]

- Continuous monitoring of vitals (temp, PR, BP [both arms initially], RR, O_2 sat)

Bloods

- FBC (anaemia, infection), U&E (renal profile), cardiac biomarkers (CK, CK-MB, troponin I & T), BNP, D-dimer (exclude PE), & LFT, serum lipase, ABG if acute cholecystitis or pancreatitis suspected
  - CK peaks @ 48hrs
  - Troponin T or I peaks @ 12-24hrs, more sensitive and specific for cardiac damage. Nb Consider non-AMI causes for +ve troponin eg. HF arrhythmia, myocarditis, PE renal failure, septic shock

ECG

CXR

- Look for signs of heart failure
  - ↑ cardiac silhouette, dilated upper lobe vessels, alveolar and perihilar shadowing, Kerley B lines, pleural effusions
- Widened mediastinum→dissecting aorta
- Large globular heart→cardiac tamponade

Echocardiography

- TTE for Dx cardiac tamponade, and pts w/ high suspicion for PE→RV hypokinesis and paradoxical septal motion indication of acute RVF
- CT chest w/ IV contrast or TOE to confirm Dx aortic dissection

V/Q scan

- In presence of pleuritic pain and clinical suspicion of PE

Abdo Imaging

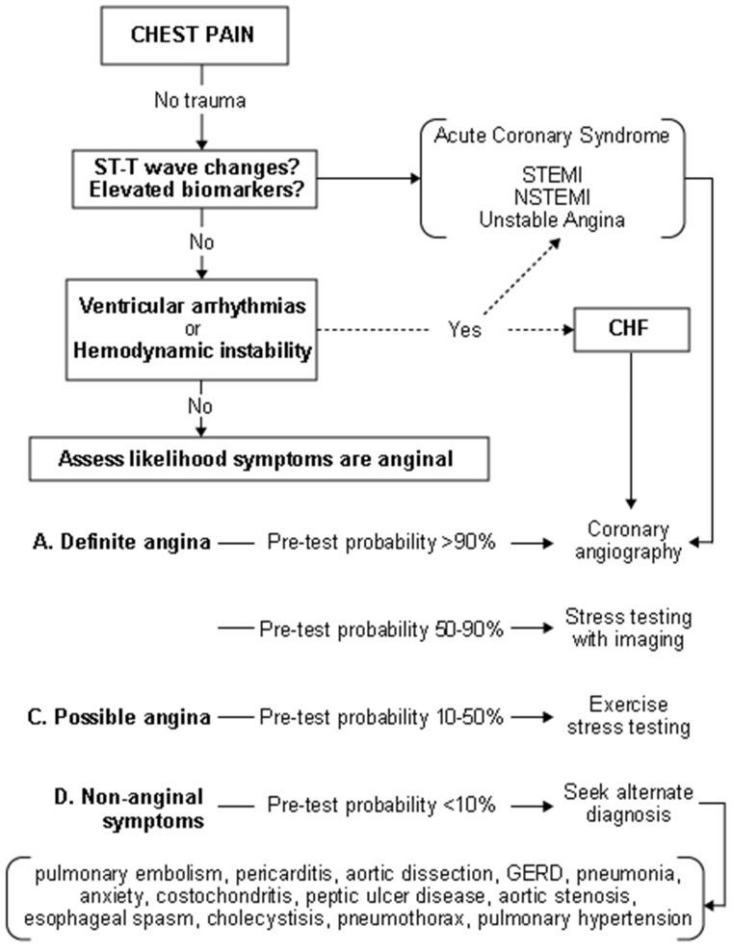
- US or CT in suspected acute cholecystitis or pancreatitis

Exercise treadmill test or stress test with imaging

- In probable angina

Barium swallow

- Oesophageal spasm,→corkscrew or rosary bead appearance



BMJ Editorial Team. Chest pain [Internet]. BMJ Evidence Centre: BMJ Publishing Group Limited; 2011 [cited 2011 Apr-Jun]. Available from: BestPractice

Myocardial Infarction

Definition Death of myocardium from coronary ischaemia

Classification [1,4]

1. ST-segment elevation (or new onset LBBB)
2. NSTEMI incl non-Q wave, subendocardial MI-ECG may show ST depression, T wave inversion, non-specific changes, or may be normal

Acute coronary syndrome includes unstable angina, STEMI, NSTEMI

Presentation[4,12]

- Acute retrosternal chest pain:
  - reaches max over several minutes, lasts >20 mins
  - prolonged or recurrent
  - may radiate to back, neck, arms or jaw
  - nitrates may provide relief, but generally not resolution
- No pain ('silent' infarct) in elderly (dementia), diabetics, post op (analgaesics)-may have pulmonary oedema, epigastric pain, post-op hypotension or oligouria, acute confusional state, stroke, diabetic hyperglycaemic states
- Palpitations, diaphoresis, anxiety
- Dyspnea, numbness
- Nausea, vomiting
- Light-headedness, syncope
- Fatigue
- PMH of new-onset angina or angina w/ increasing severity, duration, or frequency; Hx MI, IHD, HTN, hyperlipidaemia, DM, hypothyroidism

Ix[4,16]

Bloods

- FBC, U&E, glucose, lipid profile, troponin T or I, CK-MB, myoglobulin, prothrombin time with INR

Cardiac biomarkers

- Troponin T and I-
  - ↑ 3-12hr, peak 24-48hr, ↓ to baseline 5-14days. Nb Can detect elevated levels even earlier with the new high sensitive troponin assays
- CK (CK-MM {skel muscle}, CK-BB {brain}. CK-MB {heart})-
  - ↑ 3-12hr, peak ≤24hr, ↓ to baseline 48-72hr
  - Sensitivity 95%, high specificity (CK-MB only)
  - Note low sensitivity very early MI (<6hr after Sx onset), or later (>36hrs after Sx onset)
- Myoglobulin-
  - Rise w/in 1-4h, highly sensitive but not specific

ECG – check early and recheck frequently (see over page)-acute Mx algorithm based on presence (STEMI) or absence of ST-segment elevation (NSTEMI)

CXR

- Signs of HF, heart size usually normal unless previous MIs/HF
- Other causes of chest pain: pneumonia, PE, aortic dissection

Cardiac echocardiography (transthoracic and transoesophageal)

- Regional wall motion abnormalities indicative of ischaemia or infarct
- Structural complications such as aneurysms, pericardial effusions, valvular incompetence, mural thrombi
- Assess LV function and segmental wall motion

Coronary angiography – usually performed in setting of AMI with goal of mechanical revascularisation

- Identify precise location of a thrombus
- Detect other atherosclerotic lesions

Ex[4,13]

- Can be entirely normal
- Anxious, restless, uncomfortable
- Ashen, diaphoretic, cool, cyanosis
- Tachycardia, bradycardia (inferior wall MI)
- Irregular pulse
- BP usually ≥110mmHg, often hypertensive (anxiety) or hypotensive (shock)
- 4th sound (↓ compliance of ischaemic myocardium)

Complications suggested by:

- ↑ JVP, 3rd HS, basal crepitations (signs of HF)
- Pansystolic murmur (papillary muscle dysfunction, VSD)
- Pericardial friction rub

DDx[4,12]

- Angina, pericarditis, myocarditis, aortic dissection
- PE, tension pneumothorax

Oesophageal spasm, reflux or rupture, cholecystitis, pancreatitis)

Mx[1]

Medical emergency: prompt therapy to limit infarct size + preserve ventricular function post infarct

Pre-hospital:

- Aspirin 300mg po, GTN sublingual, analgesia IV

At hospital:

- Rapid clinical assessment w/ 12-lead ECG and CXR
- Administer O_2 (↑ myocardial oxygen delivery result in ↓ pain)
- Analgesia w/ morphine IV
  - Pain relief→↓ adrenergic tone→↓ oxygen demand
  - Opiates (morphine): pain and anxiolysis; also ↓ HR ↓ BP thus improve haemodynamics
- Administer antiplatelet and antithrombotic therapy for coronary thrombosis

Goals of acute care

- Relief of pain, ↓ myocardial oxygen demand, improve/restore myocardial perfusion. recognition & treatment of complications

Therapies

Monitor for complications, institute secondary prevention, assess/treat residual atherosclerotic disease, physical rehabilitation

- STEMI: primary angioplasty or thrombolysis
- NSTEMI: stabilize with aim of angiography plus/minus PCI with 1-2 days
- Proven evidence-based therapies for secondary prevention after MI include,
  1. Beta-blockers (esp if HF, ventricular arrhythmia)
  2. ACE-inhibitors (esp if HF)
  3. High-dose statins
  4. Anti-platelet therapy-note need dual antiplatelet therapy for 12m if received stent
- After discharge pt gradually ↑ activity over 8/52
- Educate! Cardiac rehab program, identify & modify risk factors

Aetiology and Pathophysiology[1,4,12]

- Plaque rupture, thrombosis, inflammation, irreversible myocyte death and necrosis
- Most often occurs by occlusion of a coronary artery by a thrombus that forms as a result of the spontaneous rupture of a pre existing atherosclerotic plaque
- Spontaneous fissuring and rupturing or a coronary atherosclerotic plaque exposes a highly thrombogenic surface leads to platelet aggregation and fibrin formation, thus thrombus
- Large thrombus completely occlude lumen→STEMI; coronary thrombus w/ subtotal occlusion→NSTEMI
    - Transmural or Q wave infarct involves entire thickness of myocardium
    - Subendocardial or non Q wave infarct from subtotal or transient occlusion (thrombus), followed by spontaneous lysis before occurrence of full thickness infarct; also in setting of vessel occlusion with extensive distal collateralisation
- Coronary artery dissection (often in setting of dissecting aortic aneurysm)
- Coronary vasospasm (either idiopathic or drug induced, e.g., cocaine)
- In situ thrombus formation (hypercoagulable state)
- Other: coronary embolism, vasculitis (Kawasakis disease), CO poisoning

Complications[1,12]

Early death:1/12-

- Arrhythmias (VFs/V tachy, complete heart block)
- HF (cardiogenic shock)
- Ventricular rupture (peak 3-5 days)
- Other mechanical complications (VSD, mitral papillary rupture)

Death after 1/12-

- Reinfarction
- Progressive HF
- Sudden arrhythmias

Epidemiology[1,4]

- 50% die w/in 2hr onset sx
- Worse prognosis if elderly, LV failure, ST changes

Risk Factors

Non-modifiable:

- Age>40yo, male, family hx IHD

Modifiable:

- Smoking, HTN, DM, hyperlipidaemia, obesity, sedentary lifestyle

ECG and MI[1,16]

Horizontal plane:

- V1, V2: RV
- V3, V4: IVS & anterior wall LV
- V5, V6: anterior & lateral walls LV

Vertical plane:

- Left lateral heart: I, VL
- Inferior heart: II, III, VF
- Right atrium: VR

Infarct patterns:

- Antero septal: V1 to V4 (LAD)
- Anterolateral: V5-V6, I, aVL (LCX)
- Inferior: II, III, aVF (RCA)
- Posterior V1-V2 {tall R, not Q}(RCA)

Anteroseptal/Anterior infarct

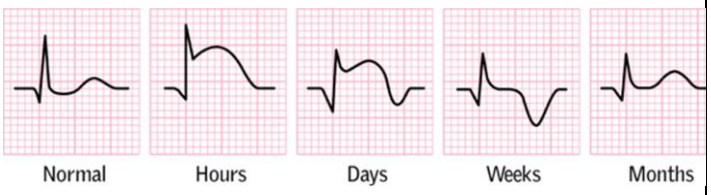
- Artery: LAD and branches
- Leads: V1-V4
- Possible abnormalities: ST elevation, Q waves, T wave inversion in leads V1-V4

Anterolateral infarct

- Artery: LCX
- Leads: V5-V6, I, aVL
- Possible abnormalities: ST elevation, Q waves, T inversion in leads I, aVL, V5-6

Inferior infarct

- Artery: RCA
- Leads: II, II, VF
- Possible abnormalities: ST elevation, Q waves, T inversion in leads II, III and VF



Longmore M, Wilkindon IB, Davidson EH, Foulkes A, Mafi AR. Oxford Handbook of Clinical Medicine. 8th ed. Oxford: Oxford Univeristy Press; 2010. Fig 1, Sequential ECG changes following acute MI; p. 113

Blood Supply of the Myocardium[1,2,11]

- **LCA** –between LA and pulmonary trunk to reach AV groove, dividing into
    - **LAD**: in anterior IV groove toward cardiac apex
        - **Septal br** supply ant 2/3 IVS, apical part of ant papillary muscle
        - **Diagonal br** supply ant LV
    - **LCX**: continues in L AV groove, passes around L border of heart to posterior surface
        - Large **obtuse marginal br** supply lateral and posterior wall of LV (and variable parts of posterior heart)
- **RCA** – in R AV groove, passing posteriorly between RA and RV
    - **Acute marginal br** supply RV
    - **posterior descending artery** (85% from RCA; 8% from LCX)
        - Travels from inferioposterior aspect to the apex
        - Supplies inferior and posterior walls of RV and variable portions of LV
    - **AV nodal artery** given off usually prior to posterior descending branch
    - **SA nodal artery** (70% from RCA, 25% from LCX)

Coronary Artery Disease

Definition Thickening and hardening with focal narrowing (aka. atherosclerosis) of large and medium epicardial coronary arteries

Presentation[4]

- Chest pain or discomfort-stable or unstable angina
  - Stable=by exertion or emotion; pain ↑ over mins and ↓ by rest over mins
  - Unstable=pain at rest, or significant change in pattern of existing chronic angina
  - Atypical=atypical pain characteristics or dyspnea only (esp underlying diabetes)
- Substernal or central pressure, heaviness, squeezing, or choking
- Rarely described as sharp localized pain or of sudden onset
- Radiation to jaw, shoulder, back or arms
- Sx of co-existing peripheral artery disease such as intermittent claudication
- Meds: OCP
- PMH: ↑LDL, ↓HDL, HTN, DM
- FHx: HD, HTN, DM
- Social Hx: Smoking, type A personality

DDx[4]

- MI, aortic dissection
- PE, pneumothorax (tension)
- GIT: oesophageal spasms, cholecystitis, pancreatitis
- Nonatherosclerotic CAD: collagen vascular disease (eg. Kawasaki disease, Takayasu arteritis), ID (septic emboli)

Ix[1,4,12]

For RFs and assoc conditions:

- Lipid profile, glucose, creatinine, urine microalbumin

Resting ECG

- Normal in 50%
- Old infarct: Q waves, inverted T waves
- Ischaemia: ST depression > 1mm depression in 2 leads
- Evidence of LV hypertrophy

Stress ECG testing-diagnostic, risk assessment, best utility in patients w/ intermediate pre-test likelihood of CAD (Bayes theorem)

- Exercise (preferred)-treadmill, bicycle ergometer with standardized increasing workload
- Discontinue if chest pain, dizziness, severe dyspneoa, > 2mm ST depression, ↓ sBP > 15mm Hg, ventricular tachys
- Diagnostic ST depression positive test
- Nb Exercise or pharm stress echo or perfusion imaging more sens and spec than EST but also more $

Coronary arteriography – diagnostic, 1st line high risk pt

- Determine if mechanical revascularisation (bypass or angioplasty) possible and to guide this therapy (depends on number of vessels, coexisting illness, age, functional status, severity and nature of sx)

Perfusion imaging (SPECT)

- If resting ECG has pre-excitation or >1mm ST

Complications[4]

- Angina pectoris
- ACS including MI
- Sudden cardiac death (VF/asystole)
- HF
- Arrhythmias particularly VT/VF
- Kidney function decline
- Depression

Ex[1,3]

NB: May have a normal Ex, esp if asymptomatic at time of exam

- Obesity

Vitals:

- HTN

Auscultation:

- S3, S4 (HTN), MR

Findings due to predisposing conditions or atherosclerosis outside of coronary arteries:

- Retinal vascular damage (see "Hypertension")
- Arterial bruits (peripheral atherosclerosis) eg. carotid, renal
- Absent or diminished peripheral pulses (peripheral atherosclerosis)
- Xanthelasmata, tendon xanthomas (familial hyperlipidaemia)

Mx[1,17]

Goals: Control symptoms, stop or limit progression, and avoid MI, improve prognosis

Pt Education

- Recognizing sx of MI, action plan

Risk Factor Mx

- Smoking cessation
- Treat hyperlipidaemia (↓ intake sat'd fats; statin)
- Treat HTN
- Control diabetes
- Weight management (BMI 18.5-24.9)
- ↑ physical activity
- Moderate ETOH
- Reduce emotional and physical stress

Meds-goals are control sx and secondary prevention

- Aspirin 75-162 mg/day
- ACE inhibitors-↓ mortality, MI, hospital admission for HF
- Beta blockers-if hx angina, MI, ACS, or LV dysfunction
- Statins-↓ mortality, MI
- Nitrates (nitroglycerin, isosorbide dinitrate);
  - Systemic venodilation→↓ ventricular wall tension→relieving cardiac workload
  - Coronary artery dilatation→↑ myocardial blood flow
  - Sublingual (acute ischaemia); patches, slow release oral (long acting to limit frequency and severity of attacks); IV nitroglycerin for severe acute.
  - SE: hypotension, lightheadedness, headache
  - Other antianginal agents are calcium channel blockers and nicorandil

Coronary Revascularization

- PCI/stent or CABG-depends on coronary anatomy and LV dysfunction

Epidemiology[1,4]

- Majority of infarcts occur in vessels <50% stenosed; 40% infarcts lead to sudden death
- >50% stenosed vessels lead to exertional angina (early warning)

Aetiology and Pathophysiology[11]

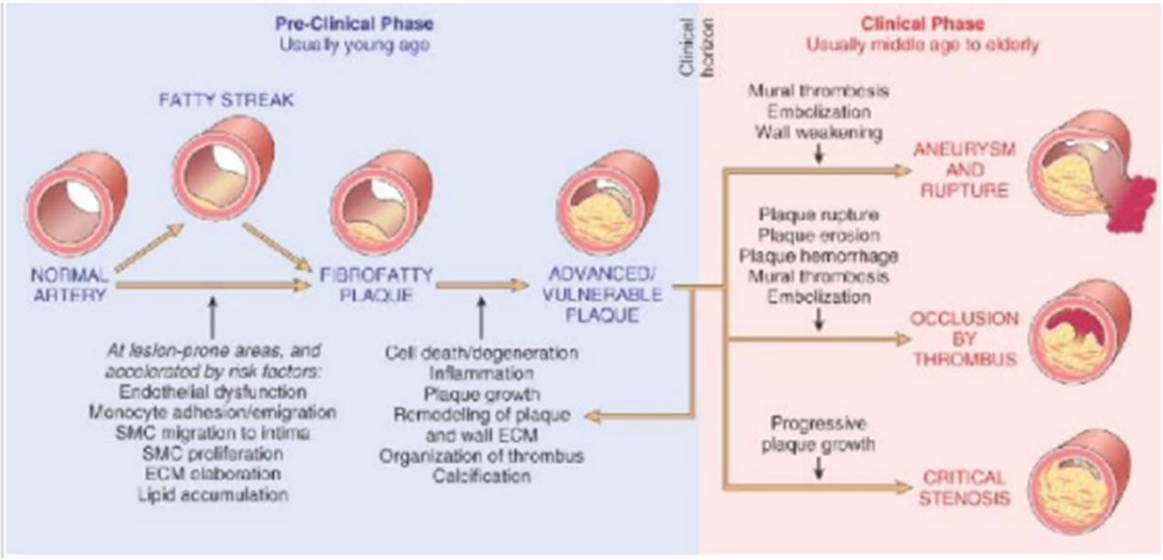
Fatty streak

- Longitudinal accumulation of lipid-filled foamy macrophages
- Multiple minute flat yellow spots→coalesce into elongated streaks ≥1cm
- Earliest lesions in atherosclerosis
- Can happen early in life <1yo, seen in virtually all children >10yo, regardless
- Same anatomic sites that later tend to develop into plaques
- Not all destined to become advanced lesions
-

Atheroma (atherosclerotic plaque)

- Fibrofatty plaque within intima→impinge on lumen of artery
- Raised lesion w/ soft, yellow necrotic core of lipid (cell debris, cholesterol, cholesterol esters, calcium) covered w/ fibrous cap (smooth muscle, collagen, lipid, foam cells)
- Response-to-injury hypothesis
  - Chronic inflammatory and healing response of arterial wall to endothelial injury
  - Interaction of modified lipoproteins, macrophages, T lymphocytes, with normal cellular constituents of arterial wall

1. Endothelial injury/dysfunction (hyperlipidaemia, HTN, smoking, toxins, haemodynamic factors, immune reactions, viruses)→↑ vascular permeability, leukocyte adhesion, thrombosis
2. Accumulation of lipoproteins (mainly LDL)→oxidised
3. Monocyte adhesion to endothelium→emigration to intima→transformation to macrophages→ingest oxidized LDL→foam cells
4. Platelet adhesion
5. Factor release from activated platelets, macrophages, vascular wall cells→smooth muscle cell recruitment, other inflam cells
6. Smooth muscle cell proliferation and ECM production
7. Lipid accumulation
8. Areas of cell necrosis and calcification within the plaque occur
9. Formation of fibrous cap results in narrowing of lumen of coronary artery
10. Blood flow reduced to the distal myocardium; oxygen supply becomes limited
11. Under increased demand, ischaemia occurs in myocardium (CSA <30% of normal)
12. Progressive luminal compromise



Kumar V, Abbas Abul, Fausto N, Ater J. Robbins and Cotran Pathologic basis of disease. 8th ed. Saunders Elsevier US; 2010.
Fig 11-5, Natural hx, morphologic features, main pathogenic events, and clinical complications of atherosclerosis; p. 505

Risk Factors for CAD

- A – age, activity, A-type personality
- B – blood pressure, bloke
- C – cigarette or cigar smoking, cocaine
- D – diabetes, dyslipidaemia (↑TG, ↑ total chol, ↑LDL, ↓HDL)
- E – early menopause
- F – family hx, fatty boomba
- G – *silent G*
- H – hyperhomocysteinaemia, hyperuricaemia

Risk Factors for Mortality[1,4,11]

- Extent of coronary disease-# vessels affected
- Extent of LV damage-result of previous MIs
- Renal impairment (GFR<60mL/min/1.73m^2) and proteinuria (≥1+ dipstick)
- Depression
- Low functional support
- Limited social support

Heart Failure

Definition The inability of the heart to pump blood at a rate that meets metabolic demands.

Classification[1,4]
Classified according to
- The predominance of the ventricle affected (RHF vs LHF)
  - Cor pulmonale=RHF 2^{o} lung disease
  - Together as congestive cardiac failure (CCF)
- The predominant form of myocardial dysfunction
  - Systolic-inability of ventricle to contract normally→↓CO, EF<40%
  - Diastolic-inability of ventricle to relax and fill normally→↑ filling pressures, EF>50%
  - Usually co-exist
- Time course
  - Acute-new onset, or decompensation of chronic; characterized by pulmonary and/or peripheral oedema +/- signs of peripheral hypoperfusion
  - Chronic-progresses slowly; venous congestion common, arterial press well maintained until late

Hx[1,3,4]
LHF
- Dyspnea (initially exertional, then at rest), orthopneoa, PND, nocturnal cough, wheeze (cardiac 'asthma')
- Poor exercise tolerance, fatigue
- Nocturia
- Cold peripheries
- Weight loss, muscle wasting

RHF
- Peripheral oedema (up to thighs, sacrum, abdominal wall)
- Nausea, anorexia, abdominal pain (liver distension)
- Facial engorgement (HF in children), venous pulsation ("v" wave) in neck (tricuspid regurgitation)

Ex[4,13]
Pts w/ compensated chronic HF may be normal on examination
LHF
- Tachypnea (↑ pul pressures), central cyanosis (pul oedema), Cheyne-Stokes breathing, peripheral cyanosis (low CO), hypotension (low CO), cardiac cachexia
- Sinus tachycardia (↑ sympathetic tone), low pulse pressure (low CO), pulsus alternans
- Laterally displaced and/or dyskinetic apex beat (esp w/ systolic dysfunction)
- 3rd heart sound (systolic dysfunction)
- Functional mitral regurgitation (2^{o} to valve ring dilatation)
- Dullness at lung bases, basal inspiratory crackles and wheezes (↑ preload, pleural effusions)

Signs of underlying or precipitating cause:
- IHD, cardiomyopathy, aortic or mitral regurgitation, systolic HTN, anaemia, thyrotoxicosis, rapid arrhythmia

RHF
- Pitting ankle and/or sacral oedema, ascites (Na+ & water retention, ↑ venous press)
- Cool peripheries, peripheral cyanosis (low CO)
- Low volume arterial pulse (low CO)
- Raised JVP (↑venous pressures, ↑ R heart preload), Kussmaul's sign (↑JVP on inspiration), large V waves (function TR 2^{o} to valve ring dilatation)
- RV heave (pulmonary HTN)
- RV S3, pansystolic murmur (TR)
- Tender hepatomegaly (↑ venous press), pulsatile liver (TR)

Signs of underlying or precipitating cause:
- COPD, LHF, TR, right MI, cardiomyopathy

DDx[1]
If known CVD, Dx generally made clinically
Rule out common causes for dyspnea:
- COPD, asthma, pneumonia, arrhythmia, IS LD, anaemia, PE

Rule out other causes for peripheral oedema:
- ARF, CKD, hepatic disease, venous insufficiency, endocrine disease, drugs

Ix[4,6]
Bloods
- FBC, U&E, Ca^{2+}, Mg^{2+}, BNP, lipid profile, LFTs, TSH

ECG
- Ischaemia, arrhythmia, MI, hypertrophy

CXR
- Enlarged cardiac silhouette (cardiothoracic ratio >50%), dilated prominent upper lobe vessels, diffuse IS or alveolar shadowing, perihilar 'bat's wing' shadowing (alveolar oedema), Kerley B lines (IS oedema), pleural effusions

Echocardiography
- Valve function and overall ventricular function
- Systolic dysfunction: ↓ ejection fraction, cardiomegaly
- Diastolic dysfunction: ejection fraction normal and ventricular wall thickening without dilatation may be present

Mx[1,17]
Lifestyle Modifications
- Regular physical activity tailored to pts capacity (10-30 min/day, 5-7/7)
- Nutrition-
  - Limit saturated fat intake
  - High-fibre diet (constipation common due to relative GIT hypoperfusion)
  - Sodium restriction (Class II≤3g/day, III/IV≤2g/day)
- Fluid Mx
  - Daily weights (morning, before breakfast)
  - ↑/↓ ≥2kg over 2 days→contact GP or specialist w/out delay
  - Fluid restriction (<1.2-2.0L/day)
  - ETOH restricted to 10-20g/day
  - Limit to 1-2 cups caffeinated beverages a day
- Smoking cessation
- Flu vaccination
- Depression and social isolation are important associated factors and shown to have direct causal relationship. Turn that frown upside down!
- Pts are at increased risk of DVT-long flights may predispose to accidental omission of meds, lower limb oedema, dehydration, and DCT, therefore pt should be counseled prior to travel and DVT prophylaxis considered

Pharmacological
ACE-I*
- LV systolic dysfunction
- If cough, use ARB
- Up-titrate to doses shown to be benefit in major trials

Beta-blockers*
- NOT initiated during a phase of acute decompensation, only after pt has stabilized

Aldosterone antagonists (spironolactone, epleronone)*
Diuretics
- To achieve euvolaemia in fluid-overloaded pts
- Loop SE: ↓K^{+}, renal impairment
- Thiazide-consider in refractory oedema

*improves LV function and long-term prognosis

Mx Cont…
Second-Line Agents:
Digoxin

- LV systolic dysfunction, signs and symptoms w/ standard therapy
- For symptom relief and to reduce HF hospitalization
- Especially beneficial in CHF pts w/ AF

Pt Education is essential

- Educate about underlying condition, beneficial lifestyle changes, function of medication, possible SE of therapy, signs of deterioration of their condition, importance of adherence to therapy
- Exercise rehab reduces sx and improves effort tolerance

Epidemiology[1,4]

- 1-3% general population, 10% >70yrs
- 5yr mortality 25-50%

Aetiology[1,4,11,13]
Systolic HF

- IHD, MI, systemic HTN, valvular HD (incl AS, MR), myocarditis, arrhythmia, IE, dilated cardiomyopathy (genetic, viral, ETOH, chemotherapy), hypertrophic cardiomyopathy,

Diastolic HF

- Systemic HTN, constrictive pericarditis, tamponade, restrictive cardiomyopathy (sarcoidosis, haemochromotosis, amyloidosis)

RHF

- LHF (commonest causes)
  - Severe chronic LHF→↑ pulmonary pressures→2^{o} RHF
- COPD, pulmonary embolism→pulmonary HTN
- Volume overload-
  - ASD, primary TR
- Other causes of pressure overload-
  - Mitral stenosis, pulmonary stenosis, idiopathic pulmonary HTN
- Myocardial disease-
  - RV MI, cardiomyopathy

LVF: Pulmonary in nature due to ↑ LVEDP→pulmonary venous congestion

- Myocardial disease-
  - IHD, cardiomyopathy
- Volume overload-
  - Aortic or mitral regurgitation, PDA
- Pressure overload-
  - Systolic HTN, aortic stenosis

Precipitating factors: noncompliance w/ meds, excess fluid intake, high output states w/ increased metabolic demands (fever, infection, hypothyroidism, anaemia, AV fistula, pregnancy, cocaine)

New York Classification of HF[1,2,4]

I HD present, no sx
II Comfortable at rest, but fatigue, palpitation, dyspnea on ordinary physical activities
III Fatigue, palpitations, dyspnea provoked by less then ordinary activity, which is limiting
IV Sx of cardiac insufficiency at rest, all activity causes discomfort

Pathophysiology[11]
CO determined by

1.Preload (LVEDP): pressure required to distend the ventricle to a given end diastolic volume
2.Contractility: the stroke work (CO) the heart generates at a given preload – describes functional state of myocardium; ↑ preload→↑ stroke work
3.Afterload (sBP): the dynamic resistance against which the heart contracts

Systolic Dysfunction=abnormality in force generation (contractility)

- ↓ contractility or lowered inotropic state (due to loss of viable myocardium or dysfunction of myofibrils
- For a given preload, get ↓ inotropic state, ↓ ventricular function, ↓ ejection fraction
- ↓ ejection fraction→↑ end diastolic volume, thus ↑ end diastolic pressure (preload) and restorating ventricular function
- A limit exists to which preload can ↑ to compensate for ↓ inotropy or ↑ afterload
- Once the preload> pulmonary capillary oncotic pressure, fluid passes into the alveolar space leading to pulmonary congestion
- Activation of RAA and SNS: systemic vasoconstriction and ↑ afterload further impairing systolic function
- Accumulation of salt and water (expansion of intravascular volume) further impairs systolic function, also causes peripheral oedema

Diastolic Dysfunction=decreased ventricular compliance, contractile function usually normal

- Due to abnormalities in active relaxation during diastole or abnormalities of elastic properties of the heart itself (surrounding tissues)
- ↓ compliance→↑ LVEDP for a given end diastolic volume, and pressure transmitted across pulmonary capillaries
- If place ↑ demand on heart, need still higher pressures required to produce the greater ventricular filling to meet the increased output demand
- Once filling pressure> oncotic pressure of pulmonary capillaries, fluid moves into alveolar space causing pulmonary congestion
- Avid salt and water retention and vasoconstriction are not commonly seen in pure diastolic dysfunction

Complications:

- Cardiac arrhythmias, salt and water retention, end-organ damage (hypoxic liver injury, worsened renal function, sleep disorder, depression

Vasculitis

Definition Heterogeneous group of disorders characterized by inflammation of blood vessels

Classification[4,12,14]

Classified by the size of the blood vessels involved:

Large-vessel

- *Takayasu's arteritis* ("pulseless disease"): aorta and major branches
- *Temporal (Giant cell) arteritis* (GCA): carotid, temporal, vertebral, ophthalmic, aortic arch

Medium-vessel

- *Polyarteritis nodosa* (necrotizing vasculitis) (PAN): small and med muscular incl renal and visceral NOT pulmonary or splenic
- *Kawasaki's disease* (acute febrile mucocutaneous LN syndrome): coronary, other extraparenchymal muscular incl celiac, femoral, mesenteric, renal, iliac, axillary

Small vessel (venules and arterioles)

- *Churg-Strauss disease* (allergic granulomatosis angiitis) (CS): pulmonary +/- any organ system esp skin, NS, heart, kidneys, abdominal viscera
- *Wegener's granulomatosis* (WG): renal, pulmonary
- *Behcet syndrome*: multisystem-oral, genital, eye, CNS, GIT, synovium, veins, arteries, meninges, brain
- *Hypersensitivity angiitis*
  - Cutaneous vasculitis aka. palpable purpura
  - Disseminated lesions: Henoch-Schonlein Purpura (HSP), cryoglobulinaemic vasculitis, serum sickness

Presentation[4,12,14]

- Generally sub-acute
- Differ in clinical severity and organ involvement
- Constitutional sx: Fever, wt loss, malaise, myalgia, arthralgia +/- accompanying organ specific symptoms

Takayasu's

- Cool peripheries, claudication of upper arm(s), headache, visual Δs, dizziness, stroke, angina pectoris, hemiparesis

GCA

- New onset headache, scalp tenderness, pain when eat, blurring vision, assoc w/ polymyalgia rheumatica

PAN

- Episodic painful red skin nodules, headache, abdo pain, N&V, peripheral neuropathy

Kawasaki

- Erythematous polymorphous rash, erythema, dryness of oral cavity and extremities, abdo pain, vomiting, diarrhea, cervical LN swelling less common

CS

- Recurrent asthma attacks, allergic rhinitis, sinus polyposis, peripheral neuropathy

WG

Triad of-

1. acute necrotizing granulomas of RT→sinus pain, bloody nasal discharge, nasal septal perforation and 'saddle deformity', hearing loss
2. necrotizing or granulomastous vasculitis of small to med vessels esp. lungs &URTI→dyspneoa, cough, haemoptysis
3. Progressive focal necrotizing and cresentic GN→proteinuria, haematuria, RF

Behcet

- Intermittent arthritis, recurrent oral and genital ulcers

Hypersensitivity angiitis

- Sx depend on organ involvement, incl palpable purpura, petechiae, urticaria, ulcers. May be hx of offending toxin

Associated disease: SLE, RA, chronic Hep C +/-arthropathy, IgA nephritis and abdo pain (intususseption)

Ex[4,12,14]

Takayasu

- HTN (from RAS), ↑ BP in legs, painful skin nodules, retinal haemorrhages, carotid, subclavian or abdominal aorta bruits, AR (aortic root dilation), ↓ peripheral pulses

GCA - Medical emergency!

- H/ache, scalp tenderness, amaurosis fugax (painless vision loss), ↓ BP in 1 or both arms, carotid, axillary or brachial bruits

PAN

- HTN, uremia, splenomegaly, RF, foot/wrist drop (infarction of radial or peroneal nerve, respectively), large cutaneous ulcers esp. over lower extremities

Kawasaki

- Irritability, extensive erythematous rash <5d following fever onset, bilat conjunctival injection, red, dry and peeling oral cavity, gallop rhythm, tachycardia, diffuse erythema and oedema of hands and feet

CS

- Erythrematous maculopapular rash, palpable purpura* esp. lower extremities and buttocks (hydrostatic press greatest), livedo reticularis, , nasal polyps, bloody nasal discharge, wheeze, haematuria, peripheral neuropathy

WG

- Otorrhoea, ear pain, sinus pain, nasal discharge, epistaxis, nasal ulcers, nasal septal perforation, saddle nose deformity, haemoptysis (pulmonary haemorrhage)

Behcet syndrome

- Cutaneous lesions, erythema nodosum, ulcers

Hypersensitivity angiitis

- Palpable purpura, petechiae, urticaria, ulcers

Palpable purpura: red-purple, raised, do not blanch, lower extremities

Small-med vascilitides assoc w/ livedo reticularis: lace-like bluish discolouration of skin esp lower limbs, aggravated by cold

DDx[4]

- Embolic disease-endocarditis, atrial myoma, chol embolisation
- Vessel stenosis or spasm-atherosclerosis, fibromuscular dysplasia, drug-induced spasm
- Venous thrombosis-DIC, TTP, Coumadin-associated necrosis, antiphospholipid antibody syndrome
- Small to med vessel-Inflammatory rheumatic diseases, hep B, hep C, HIV
- Palpable Purpura-Disseminated meningococcal, gonococcal infection

DDx for specific vasculitides

- *Takayasu:* carotid artery dissection, syphilis, Ehlers-Danlos
- *GCA:* RA, inflammatory arthritidies, amyloidosis
- *PAN:* subacute bacterial endocarditis, SLE
- *Kawasaki:* viral infections (incl enterovirus, EBV, measles), bacterial infections (scarlet fever, leptospirosis), SJS
- *CS:* allergic bronchopulmonary aspergillosis, sarcoidosis, hypereosinophilic syndrome), other causes of eosinophilia (eg. drug, parasite)
- *WG:* septic arthritis, lymphomatoid granulomatosis
- *Hypersensitivity angiitis:* cryoglobulinaemia, malignancy (1% vasculitis assoc w/ lymphoproliferative diseases)

Ix[4,12]

Bloods

- ↑ ESR, ↑ CRP, U&E (N/↑), HBsAg, LFT (↑ ALP in GCA), ANCA (WG→c-ANCA, PAN→p-ANCA), IgE (↑ in CS)
- Normochromic, normocytic anaemia, leukocytosis, thrombocytosis, eosinophilia (CS)
- Hep C antibody (in mixed cryoglobulinaemia), Hep B surface antigen (30% PAN)

Urinalysis

- Haematuria, proteinuria, RBC casts

ECG

- Ischaemic pattern (Takasayu), tachy, arrhythmia, ↑ PR, ↓ QRS (Kawasaki)

CXR

- Pulmonary infiltrates (WG, CS); widened aorta (Takayasu)

Biopsy

- Definitive test to show inflammation and destruction of vessels with direct immunofluorescence; vasculitis is focal/segmental, therefore easy for biopsy to miss affected area (≥3cm)
  - GCA: biopsy of temporal artery, see focal granulomatous inflammation w/ mural lymphocytes, macrophages, and giant cells which engulf and disrupt elastic lamina

Conventional angiography

- For medium- and large-vessel vasculitis esp Takayasu's, GCA, PAN
  - Takayasu: see stenosis & dilatation in aorta & subclavian
  - PAN: see beaded appearance of aneurysms and segmental stenosis of the mesenteric arteries

MRA

- For large-vessel vasculitis

Echocardiography

- In pts w/ suspected Kawasaki: coronary aneurysms esp LAD, RCA, LMCA, ↓ LV contractility, pericardial effusion, mild MV (less commonly aortic) regurgitation

Pathophysiology[4,12]

- Pathophysiology not clear cut
- Majority due to immune mechanisms
- Immune complex deposition in vessel wall→activation of complement cascade & circulating antibodies (cell-mediated T-cell response to antigen)→directly attack vessel walls→
  - Fibrinoid necrosis of BV wall
  - Karyorrhexis
  - RBC extravasation
- Systemic symptoms due to circulating cytokines
- Organ specific symptoms due in part to ↓ luminal diameter→tissue ischaemia
- May also be thrombus formation in inflamed vessel and aneurysms between inflamed segments

ANCA

- PAN, WG & microscopic polyangiitis, typically assoc w/ anti-nØ cytoplasmic auto-antibodies (ANCA)
- ANCA → directly activate nØ→degranulate → release of O_2-free radicals and proteolytic enzymes → endothelial cell-nØ interactions → endothelial cell damage
  - c-ANCA w/ WG
  - p-ANCA w/ PAN

Vasculitis	*Pathology*
Takayasu's	Usu not biopsied!
GCA	granulomas
PAN	Mononuclear, PMNs, fibrinoid necrosis
Kawasaki	Mononuclear, CD8+ T cells, IgA plasma cells
CS	Granulomas with eosinophils
WG	Necrotizing and granulomatous
Hyperensitivity	Leukocytoclastic, IgA in H-Sch

Mx[12]

- Withdraw offending drug if serum sickness
- HSP-supportive care, often remits on its own

Pharmacological

- Corticosteroids PLUS
- Bone protective agents (eg. Ca^{2+}/vit D, biphosphonates) PLUS
- Immunosuppressant if life-threatening disease or risk to vital organs (eg. Cyclophosphamide 3-6/12 [SE cystitis, bladder cancer, myelodysplasia, infertility])

OR

- Anti-metabolite (eg. Methotrexate)-1st line in pts in the absence of life-threatening disease or risk to vital organs, and after 3-6/12 for remission maintenance

Aetiology[4]

- Systemic autoimmune disorders of unknown aetiology
- May be associated with immune complex deposition (Type III hypersensitivity); others have a more prominent granulomatous involvement, suggesting a cell-mediated pathology
- Kawasaki has a likely infectious aetiology which triggers an abnormal inflammatory response (significant cytokine cascade stimulation, endothelial cell activation) in genetically predisposed
- Hypersensitivity angiitis assoc w/ exogenous antigens incl drugs (esp sulfa), certain foods, viruses; also assoc w/ CT disease and cancer
- HLA-DR is associated with Takayasu, GCA, and Behcet syndrome

Epidemiology[4]

Depends on type of vasculitis, and pt specific factors including age, gender, and ethnicitiy

- Takayasu: 86% F, 15-45yo, Asian
- GCA: 80% F, 90% >60yo, Northern European
- PAN: young adults esp. M
- Kawasaki: young children, 85% <5yo leading cause of acquired HD in young children, esp Japanese
- CS: 30-40yo, slight M>F
- WG:: age 50-60yo, M>F
- Behcet: young adults esp F, Eastern European

More handy info[4,12]

- Granulomatous arteritis includes CS, WG, temporal, and Takayasu
- Pts w/ systemic inflammatory disorders often have family hx of identical or related disorders including RA, SLE, AI thyroid disease, MS or myasthenia gravis
- In consideration of rheumatic syndrome, be sure to enquire about sicca symptoms, uveitis, pleurisy, CP, oral or genital ulcers, urethral or vaginal discharge, skin rash, hair loss, diarrhea, dysphagia, Raynaud's phenomenon
- Vasa nervorum are small arteries which supply blood to peripheral nerves. ↓ blood supply through vasa nervorum→mononeuritis multiplex or polyneuropathy

Shock

Decreased end-organ oxygenation caused by an imbalance between tissue O_2 delivery & demand→ O_2 debt. [12]

Classification[1,4,12]
- Hypovolaemic
- Cardiogenic
- Obstructive
- Distributive-includes anaphylactic, septic, neurogenic, adrenal crisis

Presentation[1,4,12]
- May have chest or abdo pain
- Haematemesis, melena, haematochezia
- Prolonged vomiting, diarrhea
- ↓ or no UO (renal dysfunction)
- Worsening mental status (may make Hx tricky!)

Med Hx-
- Hx CHD, ACS, HTN, ↑ chol, DM (cardiogenic)
- Blood transfusion (anaphylaxis)

Meds and allergies-
- Recent use of corticosteroids (adrenal crisis)
- NSAIDs, anticoagulants
- Allergies & recent exposure eg. bee stings

Social Hx-
- Exposure to new foods or drugs

Ex[1,4,12]
- Usually ↓ BP **BUT** normal BP does not necessarily mean normal perfusion, as adequate pressure≠adequate CO

Vitals
- Fever (septic shock)
- Hypoxia (tension pneumothorax)

Inspection
- Dehydration-dry skin & mucosa, ↓ skin turgor, ↓ UO
- Facial oedema, tongue swelling (anaphylaxis)
- Assess JVP (volume status)
- Following trauma look for signs of external bleeding, open fracture, unstable pelvis is fractured
- Look for evidence of bites and stings, rash (anaphylaxis)
- Look for source of infection eg. wound site (septic shock)

Palpation
- Epigastric tenderness (upper GI haem, trauma, pancreatitis)
- Calf tenderness (PE)

Auscultation

Cardiac→muffled heart sounds (cardiac tamponade)

Respiratory→
- Absent unilateral breath sounds, hyperresonance to percussion on affected side, tracheal deviation to opposite side (tension pneumothorax)
- ↓ breath sounds & dullness to percussion may indicate haemothorax following trauma)
- Rales (cardiogenic shock)
- Wheezing (anaphylaxis)
- Pulsus paradoxus (cardiac tamponade)

Rectal Ex (if suspect GI haemorrhage)
- Upper haem: melaena (consider doing FOBT)
- Lower haem: fresh blood +/- clots

Beck's Triad (cardiac tamponade)
1. Muffled heart sounds
2. ↑ JVP
3. ↓ HR

Ix[1,4,12]
- Arterial line-to monitor vitals (see Mx)

Urine Output
- <0.5mL/kg/hr indicates ↓ organ perfusion; record hrly

Bloods
- FBC: ↑ WCC (septic shock)
- U&E: ↓ Na^+, ↑K^+, ↓ glucose, ↑ Ca^{2+}, eosinophilia (adrenal insufficiency), ↑ urea/Cr, ↑ ammonia (GI haemorrhage)
- Amylase, LFTs, CRP if suspect pancreatitis
- Cardiac markers eg. troponin, creatine kinase
- Lactate-indicator of regional perfusion
  - >4mmol/L assoc w/ ↑ mortality
  - Measure from an arterial gas sample 2-3x per day, to monitor response to Rx
- Blood cultures

ECG
- AMI: ST changes, **Q waves** may suggest previous AMI, predisposition to cardiogenic shock
- PE: ↑ HR, RBBB (RVF)

CXR
- Bilateral infiltrates (pul oedema)
- Enlarged cardiac silhouette (tamponade, cardiomyopathy)
- Mediastinal shift (tension pneumo)

Echocardiogram
- MI: Regional wall and valvular abnormalities
- Pericardial tamponade: moderate to large pericardial effusion, diastolic collapse of RA/V
- PE: RHF

Mx-Time is tissue! [1,4,12]

Goal: Restore O_2 delivery to tissues and restore O_2 debt

Monitor vitals-
- Hamodynamic monitoring (eg. MAP, sBP, & dBP, w/ arterial line & confirm w/ hrly noninvasive BP monitoring
  - MAP= 2/3(dBP) + 1/3(sBP)
- ↑ HR, ↑ RR
  - Failure to ↑ HR in presence of ↓ BP suggests conduction disturbance
- Pulsus paradoxus (↓ sBP >10mmHg w/ inspiration) (cardiac tamponade)
- Hourly urine output-best indicator of cardiac output

Hypovolaemia→
- Control source of bleeding (to quote Naughty Morty "turn water off from tap, don't' ring Mundaring Weir")!
  - Local haemostatic measures, tourniquets
  - Coagulation support and monitoring in setting of major trauma
- Volume resus w/ IV fluids
  - Coagulopathies may result from high-volume blood transfusion (deficient in clotting factors) or consumption of factors if continued bleeding→use FFP & platelets

Cardiogenic→
- Immediate Mx MI (revascularization, anticoagulation by 1^O angioplasty or thrombolysis)
- Acute HF may require resp support (noninvasive or invasive mech vent, urgent diuresis)

Obstructive→
- *Tension pneumo:* immediate needle thoracostomy drainage followed by formal chest drain
- *Cardiac tamponade:* urgent echo evaluation, pericardiocentesis
- *PE:* anticoagulation or thrombolysis

Mx Cont…[1,4,12]

Distributive →

- *Anaphylaxis:* subcut epinephrine immediately, stop all potentially offending agents
- *Septic shock:* volume resuscitation, immediate empirical Abs AFTER collection of appropriate cultures, consider inotropes (eg. norepinephrine, dobutamine) after adequate resus if pt remains hypotensive; low-dose IV hydrocortisone in pts who develop corticosteroid insufficiency (Dx by ACTH stimulation test or based on high vasopressor requirement)
- *Neurogenic:* immediate imaging, possible intervention to reverse permanent deficits
- *Adrenal crisis:* hydrocortisone IV

Aetiology and DDx[1,4,12]

Hypovolaemic

↓ preload→↓ CO with diversion of blood from splanchnic circulation to vital organs and ↑ SVR

- Haemorrhage-
  - GI bleeding or trauma, AA rupture, retroperitoneal bleeding, long-bone fractures
- Fluid depletion-
  - GIT losses (eg. diarrhea, vomiting)
  - Insensible losses (eg. full-thickness burns)
  - 3rd space losses (eg. major surgery, pancreatitis, intestinal obstruction)

Cardiogenic

Heart pump dysfunction→↓ CO in setting of ↑ preload; compensatory surges in catecholamines→↑ SVR

- MI→ventricular dysfunction &/or structural complications (rupture of papillary muscle(s), ventricular septum, myocardium)
- Cardiomyopathies-viral, ETOHic
- CHF (eg. RHF 2^{O} to PE)
- Cardiac valvular lesions

Obstructive

- Outflow restriction: PE, severe pul HTN, AS or MS
- Filling restriction: cardiac tamponade, tension pneumo

Distributive

Significant vasodilation in setting of relative hypovolaemia & ↓ SVR

- Anaphylaxis
- Septic shock (low SVR)
- Neurogenic shock-spinal anaesthesia, spinal cord injury, fainting (vasovagal reaction)
- Adrenal insufficiency
- Also thiamine deficiency, AV fistula

Measure	Hypovolemic	Cardiogenic	Obstructive	Distributive
Preload (central venous pressure/Pulmonary artery occlusion pressure)	Decreased	Increased	Either	Decreased
Afterload (Systemic vascular resistance)	Increased	Increased	Increased	Decreased
Contractility (cardiac index/stroke volume index)	Decreased	Decreased	Decreased	Increased
Oxygen delivery	Decreased	Decreased	Decreased	Increased
Systemic oxygen consumption (venous oxygen saturation	Increased	Decreased	Decreased	Decreased
Oxygen balance (venous oxygen saturation/capillary oxygen saturation)	Decreased	Decreased	Decreased	Increased

BMJ Editorial Team. Shock [Internet]. BMJ Evidence Centre: BMJ Publishing Group Limited; 2011 [cited 2011 Apr-Jun]. Available from: BestPractice

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Pathophysiology [1,4,12]

- Imbalance between O_2 delivery and cellular metabolic demand→ O_2 debt
- Oxygen delivery determined by CO and O_2 content of blood
  - CO=HRxSV
    - SV affected by preload (filling), LV contractility (pump function), afterload (SVR)
  - O_2 content a compositve of Hb and arterial O_2 saturation
- ↓ CO or ↓ TPR→↓ BP→↓ perfusion and O_2 delivery
- Initially compensated shock-
  - Early reversible stage where homeostatic mechanisms compensate for ↓ perfusion by ↑ HR
- Evolves to overt shock (loss of 20-30% plasma volume)-
  - Manifested by ↓ BP, ↓ UO, ↑ RR, altered mental status
- Lack of tissue oxygenation→accumulation of products of anaerobic metabolism eg. lactate→systemic pro-inflammatory state with excess cytokine release and other inflammatory mediators
- Can evolve to irreversible cell death and organ damage

Cardiogenic →

- ↓ CO, ↑ PCWP*, ↑ SVR, ↑ CVP
- Compensatory mechanisms include-
  - Release of ADH, RAA system activation, endogenous catecholamines

Hypovolaemic →

- ↓ circulating volume→↓ preload, ↓ SV, ↓ CO, ↓ PCWP*
- Compensatory mechanisms include-
  - Vasoconstruction (↑ output from SNS)
  - Fluid shift into IV space (↓ capillary hydrostatic press)
  - Renal Na^{+} & H_2O retention (↑ secretion ADH & activation RAA system)

Septic →

- Bacterial products stimulate host defense cells→systemic inflammation (from eg. activation serum ptroeins, cytokines, leukocyte extravasation) & activation pro-inflam mediators (eg.TNF-alpha, IFN-alpha & –gamma, bradykinin) →tissue damage)

Neurogenic →

- Lack of neuronal control→hypotension
- ↓/normal/↑ CO, ↓ PCWP, ↓ SVR
- Normal circulatory volume

*PCWP=pulmonary capillary wedge pressure

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