CLINICAL FEATURES

- ***Symptoms***

1. cardiac ***failure***
   i. fatigue
   ii. syncope
   iii. dyspnoea, cough, haemoptysis
   iv. cyanosis
   v. peripheral oedema
   vi. abdominal distension & pain, nausea & vomiting
2. cardiac ***ischaemia***
   i. pain
   ii. anxiety
3. arrhythmias
   i. palpitations
   ii. syncope

- ***Causes of Chest Pain***

1. cardiac
   - ischaemia | infarction
   - pericarditis
2. oesophageal
   - spasm, motility disorders
   - functional or anatomical obstruction
   - rupture / tear - Mallory-Weiss
   - reflux, hiatal hernia
3. aortic
   - dissection, aneurysmal stretching
4. thoracic wall
   - pneumonia, pleurisy
   - muscle tear / strain, chostochondritis, fractured ribs, tumour
5. vertebral
   - spinal nerve entrapment / trauma, tumour
   - Hepres zoster
6. abdominal disease
   - acute cholecystitis
7. psychogenic

Causes of Syncope

1. ***autonomic***
   - vasovagal - micturition, defecation
     - tussive, deglutition
     - Valsalva
   - carotid sinus syncope
   - ANS dysfunction / neuropathy
2. ***cardiac***
   - AMI
   - arrhythmia - prolonged QT syndrome
     - AV block
     - sick sinus syndrome
     - pacemaker related
   - AS, HOCM
   - atrial myxoma
   - pulmonary - embolism
     - pulmonary stenosis
     - primary pulmonary hypertension
3. ***cerebral***
   - CVA, TIA
   - subclavian steal syndrome
   - epilepsy
4. metabolic
   - hypocarbia, hypoglycaemia
5. psychiatric

Clubbing

- described in four stages,

1. increased glossiness, cyanosis and prominence of the skin at the root of the nail
2. obliteration of the normal 15° angle at the base of the nail
3. increased concavity in both directions - "watch-glass" contour
4. hypertrophy of the soft tissue of the nail pulp, allowing the nail to float freely

NB: may result from cellular hyperplasia 2° to ***platelet derived growth factor***
usually takes 1-2 months to develop

- ***Causes of Clubbing***

1. ***pulmonary***
   - i. malignancy — * bronchogenic carcinoma
     - pleural tumours
     - lymphoma, thymoma
     - very rarely with secondary lung tumours
   - ii. vascular — - AV malformations, hepatopulmonary syndrome
   - iii. pyogenic — - bronchiectasis, lung abscess, empyema
2. ***cardiac***
   - i. bacterial endocarditis
   - ii. cyanotic congenital heart disease
   - iii. thoracic aortic aneurysm
3. ***gastrointestinal***
   - i. hepatic — - cirrhosis
   - ii. colonic
     - malignancy — - adenocarcinoma
     - inflammatory — - ulcerative colitis, granulomatous colitis
       - polyposis coli
4. miscellaneous
   - familial
   - hyperthyroidism (acropachy), hyperparathyroidism
   - syringomyelia
5. unilateral
   - aneurysm of aorta, innominate or subclavian arteries
   - apical lung carcinoma
   - chronic shoulder dislocation
6. lower limb
   - coarctation of the aorta

- ***Split Second HS***

1. fixed — - ASD
2. persistent with normal inspiratory widening
   - RBBB
   - ↑ RV afterload — - PS, pulmonary embolism
3. paradoxical spilt → delayed LV ejection
   - LBBB, RV pacemaker
   - ↑ LV afterload — - AS, hypertension
   - ↓ LV contractility — - ischaemia, infarction

NYHA Classification of Angina		
Class	Symptoms	Maximal VO_2
Class O	• asymptomatic[1]	
Class I	• ordinary physical activity, such as walking or climbing stairs, does not cause angina • angina with ***strenuous*** or ***rapid prolonged*** exertion at work or recreation or with ***sexual relations***	> 20 ml/kg/min
Class II	• slight limitation of ordinary activity • walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, or in cold, or in wind, or under emotional stress, or only during a few hours after awakening • walking more than ***2 blocks*** on the level, or more than ***1 flight of stairs*** at a normal pace and in normal conditions	16-20 ml/kg/min
Class III	• marked limitation of ordinary physical activity • walking 1 or 2 blocks on the level and 1 flight of stairs at a normal pace and in normal conditions • "comfortable at rest"	10-15 ml/kg/min
Class IV	• inability to carry on any physical activity without discomfort • anginal syndrome may be present ***at rest***	< 10 ml/kg/min

[1] asymptomatic, but known presence of heart disease

- ***Causes of Autonomic Dysfunction***

1. diabetes
2. alcoholism
3. chronic renal failure
4. drug induced - anticholinergics, α/β-blockers
5. familial dysautonomia - Riley-Day
6. Parkinsonism
7. rare causes
   - tetanus
   - porphyria, syringomyelia, amyloidosis
   - hypokalaemia

ACUTE MYOCARDIAL INFARCTION

- ***Incidence***

a. males ~ **3.5 : 1000**

b. females ~ 1.0 : 1000 (age 20-65 yrs)

NB: ↑ risk ~ 5 fold with 2 major risk factors
↑ risk ~ 8 fold with 3 factors (risk ~ 2^x, x = factors)

- ***Aetiology***

a. atherosclerosis ~ 99%
   - ***thrombotic occlusion*** > 95% of ***transmural*** AMI
     ~ 20-40% of subendocardial MI

b. embolism
   - thrombus, septic thrombus
   - air, amniotic fluid

c. coronary arteritis
   - polyarteritis nodosa, SLE, RA, etc.
   - Kawasaki's disease, Takayasu's disease

d. coronary dissection - PTCA related

e. aortic dissection 2° - aortitis, syphilis, Marfan's, trauma

f. congenital coronary anomalies - LCA from PA, TGA

g. myocardial hypertrophy & aortic stenosis

h. severe trauma, electrocution

i. severe hyperthermic syndromes

j. prolonged cardiopulmonary bypass

k. prolonged hypotension / hypovolaemia

l. severe coronary artery spasm
   i. variant angina
   ii. nitrate workers
   iii. thyroid hormone excess
   iv. cocaine / amphetamine abusers

- ***Predisposing Factors***

a.	***smoking***$^{++}$	- ↑ [COHb] - vasoconstriction - accelerated atherosclerosis - ↑ lipids and platelet adhesiveness - ↑ incidence of sudden death and MI
b.	***hypertension***$^{++}$	
c.	***hyperlipidaemia***$^{++}$	- high cholesterol:HDL ratio
d.	family history	* type 2 hypercholesterolaemia
e.	diabetes mellitus	
f.	obesity	
g.	gender	- males > females
h.	age	
i.	lifestyle factors	

- ***Aggravating Factors***

a. anaemia
b. hypoxaemia
c. tachycardia / hypertension
d. surgery, trauma
e. thyroid disease
f. pulmonary embolism
g. chronic lung disease

- ***Clinical Presentation***

a.	silent AMI	**~ 25%** in Framingham study
b.	chest pain	
c.	atypical pain	
d.	syncope / arrhythmias	
e.	LV failure / acute pulmonary oedema	
f.	hypotension / cardiogenic shock	
g.	peripheral emboli from mural thrombus	
h.	sudden death	**~ 25%** of sudden deaths at PM due to acute MI - AMI or sudden death → 1st presentation of CAD in ≥ 50% - vast majority 2° to **VF**

- ***Clinical Signs***

  a. fever - commences in 1st 24 hours, lasting up to 1 week
  ≤ 38°C

  b. CCF

  c. tachycardia ~ 25% of anterior MI

  d. bradycardia ~ 50% of inferior MI

  e. pericardial friction rub ~ 10-15%
  - ***not*** a C/I to anticoagulation

  f. signs of cardiogenic shock if present

- ***Time Course of Infarction***

  NB: irreversible myocardial necrosis occurs ***~ 60 minutes*** after "no flow"
  coronary thrombosis is demonstrated in ≥ 90% of acute MI

  a. EM changes ~ 15 min

  b. light microscope changes ~ 6 hrs

  c. macroscopic changes ~ 24 hrs

  d. commencement of healing ~ 2 wks

  e. fibrotic scar ~ 6 wks → period of greatest irritability

- ***Anatomical Relationships***

  a. RCA - inferior
  - posterior
  - SA & AV nodes (85-90%)

  b. LCA - anterior
  - septum

  c. circumflex - anterolateral

Diagnosis

a. ***history*** and ***examination*** - most important

b. ECG → ***sensitivity*** **~ 73 %** (LBBB see below)
specificity **~ 95%**

- ***ST elevation*** ³ **1 mm** → ≥ 2 adjacent ***limb*** leads
³ **2 mm** → ≥ 2 adjacent ***precordial*** leads
- LIGW states ≥ 1 mm → ≥ 2 limb leads, ***or*** $\mathbf{V_{4\text{-}5\text{-}6}}$
≥ 2 mm → ≥ 2 $V_{1\text{-}2\text{-}3}$
- ± T wave inversion
- pathological Q waves - usually > 3 hrs, maximal by 12 hrs
- appear earlier with ***thrombolysis***
- new LBBB

c. cardiac enzymes

i. **CK (MB)** - - **8-24** / ↓ 48-72 hrs
> 15% CK-MB → highly specific

- myocardium contains ~ 20% MB / 80% MM bands
- ***acute myocarditis*** may produce elevation
- angina & pericarditis ***do not*** result in elevation
- plasma CK-MB **> 4%** & > 10 IU/l → sensitivity **~ 98%**
specificity **~ 95%**
- absolute elevation gives crude estimate of infarct size & prognosis
- earlier peak and clearance with thrombolysis
- may remain elevated with large MI's or delayed excretion

ii. LDH (LDH_1) - ↑ 24-48 hrs / ↓ 7-14 days
- LD_1:LD_2 ratio reversal → "LD flip"
~ 75% sensitivity
~ 97% specificity

iii. cardiac troponin T - ↑ 3-4 hrs / ↓ **6 days**
- sensitivity / specificity cf. CK-MB

d. radioisotope scans

i. Tc^{99m} → hot spots at 1-10 days

ii. Th^{201} → cold spots

e. gated blood pool scan
- regional wall motion abnormalities
- papillary muscle dysfunction
- ejection fraction

f. coronary angiography - usually in assessment for CABG

g. echocardiography
- regional wall motion abnormalities
- papillary muscle dysfunction
- ejection fraction
- pericardial effusions
- valvular, papillary muscle function

h. CXR — * ***best*** indicator of degree of ***LVF***
- not helpful in early diagnosis

i. nonspecific changes
   i. ↑ ESR — - at 48 hrs, maximal at 5 days
   ii. ↑ BSL
   iii. ↑ WCC — < 15-20,000 / µl
   - may persist for 7-10 days
   iv. ↑ urea & myoglobin

▪ ***AMI & LBBB***

• data from the GUSTO I trial
• factors independently predictive of AMI with LBBB,

1.	ST elevation concordant with QRS	> 1 mm	5 pts	(OR ~ 25:1)
2.	ST depression in V_{1-2-3}	> 1 mm	3 pts	(OR ~ 6:1)
3.	ST elevation discordant with QRS	> 5 mm	2 pts	(OR ~ 4:1)

• Sgarbossa *et al* NEJM 1996 used point score ≥ 3 pts for treatment →

a. sensitivity ~ 40%
b. specificity ~ 96%

▪ ***CPK Asymptomatic Elevation***

a. factitious — - haemolysis
- laboratory error

b. physiological — - newborn
- post-partum
- post-exercise

c. cardiac origin — - traumatic contusion
- silent AMI

d. skeletal muscle — - trauma, surgery
- alcoholic myopathy
- Duchene's muscular dystrophy (female carrier)
- hypothyroidism

e. MH susceptible patients,
   i. family history of MH
   ii. inherited and congenital myopathies
   iii. Duchene's muscular dystrophy
   iv. King-Denborough syndrome
   v. skeletal deformities
   vi. ? myotonia

Treatment - Aims

1. relief of ***symptoms***
2. limitation of ***infarct size***
3. prevention of ***reinfarction***
4. detection and treatment of ***complications***
   - i. ***arrhythmias*** - responsible for ~ 40% of post-MI deaths
   - ii. CCF - acute pulmonary oedema, hypoxaemia
     - acidaemia, hypoperfusion
   - iii. CVA
   - iv. cardiac rupture or septal perforation
   - v. acute valvular dysfunction
   - vi. ventricular aneurysm
   - vii. Dressler's syndrome - pericarditis, friction rub, fever ± pneumonitis
     - rare, occuring at weeks to months
5. ***rehabilitation***

- ***Options: Contemporary Management AJM 1995***

1. initial stabilization
2. acute reperfusion measures
3. anti-platelet and antithrombin agents
4. other pharmacotherapy
5. elective coronary revasulcarization

Treatment - General

a. education, explanation and reassurance

b. bed rest

c. analgesia

d. supplemental O_2
   - only of benefit with AGA evidence of hypoxaemia

e. continuous ECG monitoring in CCU for ≥ 48/24
   - not actually shown to alter outcome prior to use of thrombolysis

f. ***arrhythmia prophylaxis***
   - was recommended by the AHA but ***not proven*** to decrease the incidence of VF
   - some studies have actually shown decreased survival in lignocaine group
   - now no longer recommended by AHA
   - *Civetta* recommends - post-VF / VT requiring defibrillation
     - multifocal or frequent VEB's > 6/min

g. ***anticoagulants***

   i. ***low dose heparin*** in all patients
      - ↑ survival in unstable angina ~ 50% decrease death & non-fatal MI

   ii. prevention of systemic emboli - large anterior infarcts
     - CKMB ≥ 160
     - CPK ≥ 8 x normal
     - presence of AF or ventricular aneurysm

   iii. following ***thrombolytic therapy***

▪ ***Antithrombin Therapy***

- Rogers, AJM 1995, "evidence to confirm that antithrombin therapy reduces mortality in AMI ***is not*** as solid as that for antiplatelet therapy"
- heparin is required to maintain vessel patency following tPA, however,

   a. ***is not*** required following anistreplase, and

   b. ***may not*** be required following streptokinase

   NB: the longer acting, non-fibrin-specific agents provide hrs → days of auto-anticoagulation, so that IV heparin may not be required

- Serneri, Lancet 1995, IV / sc heparin versus aspirin for unstable angina,

   a. aspirin ***did not*** significantly affect incidence of ischaemia

   b. both sc & IV heparin → ↓ ***frequency*** of angina (91%) & silent ischaemia (86%)
     ↓ ***duration*** of ischaemia

   NB: sc heparin is effective in control of ischaemia in patients with ***unstable angina***

Myocardial Salvage

- ***Aims***

1. prevention of CAD
2. limitation of infarct size
3. prevention of reinfarction

- ***Prevention of CAD***

1. education
2. treatment / elimination of risk factors
   - risk modification is of benefit ***after*** the development of CAD
   - Helsinki heart study 1988, 4081 asymptomatic ***dyslipaemic*** patients,
     10% reduction in ***cholesterol*** → 34% ↓ in CAD over 5 years
   - JAMA 1984: 1% ↓ serum cholesterol → 2% ↓ risk of cardiac event
   - control of ***hypertension*** decreases overall mortality (↓ CVA),
     but ***does not*** alter the incidence of CAD ? except with β-blockers
   - cessation of ***smoking*** * greater benefit than β-blockers

- ***Limitation of Infarct Size***

a. ***thrombolytic*** therapy ~ **70%** patency & reperfusion
   ~ **20%** reduction in early ***mortality***
   - this equates to 3-6 lives per 100 infarcts
   - 9 trials, 58600 patients ~ 18% lower 35d mortality (9.6 vs 11.5%, $p < 0.00001$)

b. immediate ***coronary angioplasty***
   i. ***routine***, following thrombolysis
      - 3 studies → ↑ bleeding, acute re-occlusion, emergency CABG, mortality

   ii. ***selective***, patients failing recanalization
      - ***rescue*** angioplasty → ↑ survival, especially anterior MI within 8 hrs
      - problems of patient identification & logistics of procedure

   iii. routine, patients ineligible for thrombolysis

c. IV heparin - post-tPA & unstable angina only absolute indications

d. early IV b-***blockers*** - small benefit in large AMI*

e. early ACE inhibitors ~ **7%** reduction in early mortality
   - this equates to 0.5 lives per 100 infarcts

f. GTN
   - ISIS-4 & GISSI-3: total 73,719 patients → ***no effect*** on outcome
   - still used in > 50% of patients for angina, hypertension, pulmonary congestion

- ***Prevention of Reinfarction***

a. ***antiplatelet agents*** - ***ISIS II*** Lancet 1988: STK / aspirin / both
- aspirin 100-150 mg/d → ↓ mortality at 1 month

• thrombolysis actually → ↑ risk of re-thrombosis,
∝ stimulating thrombin generation, which in turn activates platelets

b. b-***blockers***

i. ***ISIS I*** Lancet 1986*
- 16,000 patient R_X atenolol within 5 hrs of MI
- early IV → ~ 15% ↓ mortality with IV β-blockers in ***addition*** to oral
- reduction in ***early deaths*** (24-48 hrs) ? due to ↓ incidence of cardiac rupture
- ***no decrease*** in mortality from day 2 onwards, cf. thrombolytics alone
- may have additive benefit with STK, as early deaths with thrombolysis often ∝ rupture
- current opinion (AHA), "slight improvement in mortality, not warranted"

ii. pooled results from multiple studies (Civetta), long-term oral R_X
- orally → **~ 25%** reduction in reinfarction & late mortality
- considered for a period of 1-2 years for patients at risk of recurrent events
- C/I in presence of CCF, conduction blockade, bradycardia, CAL/asthma

iii. Rogers AJM 1995
- estimated 40% of post-MI patients could safely use oral β-blockers
→ ↓ reinfarction, sudden death, overall mortality

c. ***warfarin*** ~ 25% ↓ re-thrombosis following thrombolysis/angioplasty

d. ***ACE inhibitors***

i. Pfeffer *et al.* NEJM 1992 - 2231 patients, °CCF / **LVEF < 40%**
- captopril improved survival → ↓ risk ~ 19% ($p < 0.019$)
- benefits also seen post-thrombolytics and with asprin & β-blockers

ii. ***ISIS 4*** Lancet 1995
- 58,050 patients suspected MI → captorpil, mononitrate, $MgSO_4$
- captopril ~ 7% reduction in 5/52 mortality
~ **5** fewer deaths / 1000 patients at 5/52 and at 12/12
- benefits appeared greater in high risk groups - previous MI, CCF
- mononitrate & magnesium showed ***no*** overall benefit

e. coronary ***angioplasty*** - delay for 1 week post-MI, not effective early
~ 90-95% success in "appropriately selected" patients
~ 33% recurrence in first 3-6 months

f. ***CABG*** * LAD ***or*** triple vessel disease & depressed LV function

g. Ca^{++}-entry blockers - ***no*** proven benefit
? oral diltiazem in non-Q-wave infarction

ISIS II 1988

• 17,187 patients with suspected MI, within 24 hours of onset of symptoms
• randomised into 4 groups,

1. oral aspirin ~ 20% ↓ mortality
2. streptokinase[§] ~ 23% ↓ mortality
3. streptokinase + aspirin **~ 42%** ↓ mortality
4. neither

NB: [§]there was an increase in incidence of reinfarction with ***streptokinase alone***, due to streptokinase enhancement of ***platelet activation*** with release of TXA_2

• ***morbidity*** is also reduced,

1. improved LV function
2. improved exercise tolerance
3. decreased incidence of CCF

CASS Study 1983

• surgically treated patients subjectively better
• ***no*** improved survival with,

a. mild angina
b. 2 or 3 vessel disease with normal LV function

• patients with severe angina (CHA III or IV) and 2 vessel disease with depressed LV function "probably" benefit in terms of improved prognosis
• improved long-term patency has been demonstrated with ***internal mammary arterial conduits*** cf. saphenous vein bypass grafts

NB: improved survival has ***only*** been demonstrated with surgery for,

1. ***left main disease***, or
2. ***triple vessel disease*** with depressed LV function (LVEF < 40%)

Thrombolytic Therapy

a. ***types***
   i. streptokinase
   ii. recombinant tPA
   iii. ASPAC (anisoylated streptokinase-plasminogen activator complex)
   iv. urokinase

b. ***indications***
   i. clinical & ECG evidence of MI
      • δST segment elevation > 0.1 mV
        ≥ 2 contiguous leads
   ii. IV access | supplemental O_2 | continuous ECG monitoring
   iii. onset within 4-6 hrs * time frame now extended up to **12 hrs**

c. ***absolute contraindications***
   i. risk of ***bleeding***
      • active internal bleeding
      • suspected aortic dissection
      • active peptic ulceration *task force → relative risk
      • prolonged or traumatic CPR
      • recent head trauma or known intracranial neoplasm
      • haemorrhagic ophthalmic condition
      • pregnancy or post-partum
      • history of CVA known to be haemorrhagic
      • trauma or major surgery < 2 weeks
      • uncontrolled ***hypertension*** > 200/120 mmHg
   ii. ***allergy*** to streptokinase or anistreplase ? recent streptococcal infection

d. ***relative contraindications***
   i. risk of bleeding
      • trauma or recent surgery > 2 weeks
      • history of chronic severe hypertension
      • history of peptic ulceration
      • history of CVA, recurrent TIA's
      • known bleeding diathesis or use of anticoagulants
      • recent central venous or arterial puncture
      • short duration of CPR
      • significant hepatic dysfunction
   ii. potential allergy / Ab's - streptokinase within 1 year
   iii. risk of systemic emboli - MS, AF, aneurysm

NB: modified from ACC/AHA task force guidelines

- ***Complications of Streptokinase***

1. hypotension, vasodilatation
2. reperfusion arrhythmias
3. febrile reaction
4. allergy / anaphylaxis
5. ***haemorrhage*** ~ 5-15%
   - major haemorrhage much less common
   - ICH ≤ 0.5% → ↑ risk with,
   i. age > 75 yrs
   ii. uncontrolled hypertension
   iii. diabetes

- ***Indications for TPA***

1. used to be indication for streptokinase + ***allergy***
2. following results of ***GUSTO*** (*see over)* →
   i. early presentation < 4 hours
   ii. anterior infarct
   iii. age < 75 years

NB: ie. increased cost justified in subgroups where benefit maximal

- ***Monitoring***

1. clinical examination
2. HR / BP
3. continuous ECG
4. FBE
5. plasma ***fibrinogen*** - if profound decrease then delay anticoagulation
6. APTT - prior to & during heparinisation

Comparison of Streptokinase and tPA			
Factor	Streptokinase	rTPA	ASPAC
Artery patency at 2 hours	55%	70%	
Incidence of re-occlusion	15%	20%	
Reduction in ***mortality***	23%	26%	
+ ***aspirin*** (ISIS II)	**42%**		
Hypotension	20%		
Anaphylaxis	0.1%		
Fibrin specific	No	**Yes**	No
Fall in Fibrinogen	80%	30%	
Cerebral Haemorrhage	0.4%	0.5%	
Major Haemorrhage	0.6%	**4%**	
Plasma Half Life $t_{½\beta}$	23 min	5 min	90 min
Concomitant medications	Aspirin ± Heparin[1]	Aspirin IV Heparin	Aspirin
Cost (USA pharmacy)	$285	$2,200	$1,650

Administration	
Streptokinase	• 1.5×10^6 Units over 45-60 minutes
rTPA ***standard***	• 10 mg IV bolus + 50 mg over 1 hr + 40 mg over 2 hrs
accelerated	• 15 mg bolus + 50 mg over 30 mins + 35 mg over 1 hr
ASPAC	• single bolus injection • 30 IU over 2-5 minutes
Heparin	• full anticoagulation for 24-48 hrs
Aspirin	• 100-300 mg/day from day 3 • continued for at least 12 months

[1] addition of heparin to STK is now controversial & may ***not*** be required

- ***GUSTO Trial NEJM 1993***

NB: **G**lobal **U**tilisation of **S**treptokinase and **T**PA for **O**ccluded arteries
15 countries, 1081 hospitals → ***41021 patients***,
4 study arms assessing → ***30 day mortality***

• started in 1991 following results of ISIS-3 and GISSI-2 failed to show any improvement in mortality with rTPA cf. STK, even though ***early patency*** rates were known to be higher
• claimed reasons for failure of former studies due to,

1. traditional rate of administration of TPA → 100 mg / 3 hrs
2. use of subcutaneous heparin, too late → higher re-occlusion rates

R_X Group	Mortality	ICH	CVA	TIMI 3[1]
• STK + s.c. heparin	7.2%	0.49	1.22	29.5 %
• STK + IV heparin[2]	7.4%	0.54	1.4	32.6 %
• Acc-tPA + IV heparin	**6.3%**[3]	**0.72**	1.55[4]	**53.6 %**
• STK + tPA + IV heparin	7.0%	0.94	1.64	37.4 %

[1] 2431 were randomised into angiography sub-trial measuring vessel patency, TIMI-3 = "completely open artery", results at 90 min

[2] no apparent advantage to IV heparin following STK

[3] represents a **14% reduction** in mortality cf STK ($p < 0.001$)
effectively save 1 patient per 100 treated

[4] combined end-point of death + disabling stroke also less (6.9 vs 7.8%, $p < 0.006$)

- ***Accelerated Dose TPA***

1. bolus - **15** mg
2. rate 1 ~ 0.75 mg/kg / 30 min (≤ **50** mg)
3. rate 2 ~ 0.5 mg/kg / 60 min (≤ **35** mg)

- ***Criticisms***

1. more patients in the tPA arm underwent subsequent ***CABG surgery***
2. almost half patients in the STK(sc) group received IV heparin
   - ∴statements re efficacy of heparin with STK difficult
3. 78% of all patients were treated within ***4 hours***
   - ∴main benefit of tPA is seen in early administration
4. early ***angioplasty*** provides better early patency rates → ~ 80% at 90 min

■ ***Rawles et al BMJ 1996***

- multivariate analysis of a randomised double blind trial
- 29 rural practices in Aberdeen, 311 patients with suspected AMI within 4 hrs of symptoms

  → anistreplase 30 units IV

- main outcome measure → death within ***30 months*** of entry into trial
- death positively related to,

1. ***age*** ($p < 0.0001$)
2. ***delay*** between start of symptoms and thrombolytic treatment ($p = 0.0004$)
3. earlier presentation
   - probability of death within 30 months was negatively related to the logarithm of the time of randomisation ($p = 0.0163$)
   - ?? "sicker" patients seek medical attention earlier
4. patients presenting 2 hours after start of symptoms, each hour's delay in receiving thrombolysis led to the loss of,
   i. ***21 lives*** per 1,000 @ 30 days (CI 1 to 94, $p = 0.03$)
   ii. 69 lives per 1000 @ 30 months (CI 16 to 141, $p = 0.0004$)

NB: "the magnitude of the benefit from earlier thrombolysis is such that giving thrombolytic treatment to patients with acute myocardial infarction should be accorded the same degree of urgency as the treatment of cardiac arrest"

MI Complications

1. ***arrhythmias***
   - i. VEB's ~ 80%
   - ii. multifocal VEB's ~ 15-25%
   - iii. VT ~ 15-20%
   - iv. VF ~ 3-5%
   - v. AF ~ 15%
   - vi. CHB ~ 5-7%
2. warning arrhythmias - 'R on T', multifocal, runs, RBBB pattern
   - observed in ~ 60% of patients ***not*** developing VF, absent in ~ 40% of patients developing VF → ***not*** specific/sensitive
   - events associated with a higher incidence of VF include non-sustained VT (3^+ beats) and sustained VT occurring,
     - i. within first 2 hrs of chest pain
     - ii. in association with large MI or with CCF
     - iii. with autonomic dysfunction
   - ***prophylactic lignocaine*** is associated with a higher mortality (MacMahon, JAMA 1988)
   - long-term class IC agents are also associated with increased mortality
   - ***amiodarone*** results in ~ 50% reduction in arrhythmogenic complications
3. CCF
   - has both therapeutic and prognostic significance
     - i. PAOP < **18** mmHg | CI > **2.2** l/min ~ 1% mortality
     - ii. PAOP > 18 mmHg | CI > 2.2 l/min ~ 10% mortality
     - iii. PAOP < 18 mmHg | CI < 2.2 l/min ~ 20% mortality
     - iv. PAOP > 18 mmHg | CI < 2.2 l/min ~ 60% mortality
4. cardiogenic shock **~ 5%**
5. cardiac rupture **~ 1.5%**
   - i. VSD ~ 50% mortality in first week
     ~ 82% mortality at 2 months
     - pan-systolic murmur plus step-up in SO_2 from RA to RV
     - survival ∝ LV function, if cardiogenic shock then surgery is of ***no benefit***
   - ii. free wall with tamponade
   - iii. papillary muscle with acute valvular dysfunction
6. thromboembolism
   - i. mural thrombi ~ 30% of anterior MI
     ~ 3% of inferior MI
     - CVA occurs in **~ 15%** of patients with LV thrombus over 2 years post-MI
     - this is reduced ~ 50% by heparin
     - repeat echo at 1/52 and if thrombus present then anticoagulate for 3/12
   - ii. DVT & PTE

7. reinfarction **~ 10%**
8. aneurysm formation ? reduced by ACE inhibitors
9. persistent angina - reduced by sc heparin
10. pericarditis
11. Dressler's syndrome
    - similar syndrome may be seen post-percardiotomy & with cardiac trauma
    - common factors of myocardial injury and blood in the pericardial cavity
    - produces - fever
      - ↑ ESR, ↑ WCC
      - arthralgias
      - pericardial chest pain
      ± ECG changes
    - managed with NSAIDs ± corticosteroids for recurrent bouts
12. psychological problems

Mortality

a. prior to hospital ~ **25%**

b. within 1 month ~ 10-15%
   - this figure was prior to thrombolytic era
   - 30 d mortality from GUSTO trial ~ **6-7%**

c. within 1 year ~ 10%

d. each subsequent year ~ 5%

NB: not proven to be altered by CCU/ICU's,
prior to the introduction of ***thrombolytic therapy***

~ 40% of those who die do so within 2 hours,
with ~ a half of these dying before reaching hospital,
∴ therapy can only influence mortality in **~ 20%**

LV function is the most powerful predictor of survival

Right Venticular Infarction

- occurs in **~ 25%** of patients with posterior LV infarction
  - → ~ 93% of whom have > 75% luminal narrowing of the RCA
- clinical features,
  1. ↑ CVP
  2. clear lung fields
  3. hypotension
  4. ECG findings → ST elevation
     - i. V_3R and V_4R
     - ii. sR' V_1 in a patient with inferior MI ~ 80% sensitivity, ~ 40% specificity
  5. ↑ incidence
     - AV block
     - RV thrombus
     - R→L shunt through foramen ovale
     - tricuspid regurgitation
- haemodynamically significant RV infarction requires,
  1. ↑ CVP > 10 mmHg
  2. CVP:PAOP ratio > 0.8
  3. Kussmaul's sign → ↑ CVP in inspiration
- usually associated with posterior LV involvement, ***∴abnormal LV function***
- this may be exacerbated by RV dilatation & ventricular interdependence
- differential diagnosis,
  1. constrictive pericarditis
  2. cardiac tamponade * ***no*** Kussmaul's sign
  3. restrictive cardiomyopathy
  4. PTE with tricuspid incompetence

PERIOPERATIVE MYOCARDIAL REINFARCTION

NB: incidence in the absence of previous infarction **~ 0.1-0.4%**

Goldman (1977)

→ 1001 patients over 40 yrs
surgery was LA, endoscopies (TURPs excluded)
multivariate discriminant analysis

- ***Independent Variables***

1. history
   i. age > 70 yrs
   ii. AMI in last 6 months
   iii. poor general medical condition
2. examination
   i. S_3 gallop or ↑ JVP
   ii. VEB's > 5/min or rhythm other than sinus
   iii. aortic stenosis
3. procedure
   i. abdominal or thoracic procedure
   ii. emergency operation

- ***Insignificant Variables***

a. smoking
b. hyperlipidaemia
c. diabetes
d. hypertension
e. PVD
f. stable angina, ST/T wave changes
g. old MI > 6 months
h. RBBB
i. cardiomegally
j. mitral valve disease
k. controlled CCF

Tarhan (1972)

→ 32,877 patients over 30 yrs at the Mayo Clinic
422 with previous MI

- ***Reinfarction Rate***

a. < 3 months ~ 37%

b. 3-6 months ~ 16%

c. > 6 months ~ 4-5%

NB: most occurred on the 3rd day post-op. → ***mortality* ~ 54%**

Mahar, Steen & Tinker (1978)

→ **148** patients
226 non-cardiac surgical procedures
99 with previous CABG

a. none of the CABG group had an MI

b. 5% of 49 without prior CABG had an AMI

c. all in AMI group had ***triple vessel disease***

Steen, Tinker & Tarhan (1978 - also at the Mayo Clinic)

→ **587** operations 1974-75, all patients with previous AMI
overall ~ **6.1%** reinfarction rate → ~ **69%** ***mortality***

a. < 3 months ~ 27%

b. 3-6 months ~ 11%

c. > 6 months ~ 4-5%

- ***Other Risk Factors***

a. preoperative hypertension

b. intraoperative hypotension

c. thoracic and upper abdominal operations > 3 hrs duration

NB: striking correlation between ***duration*** of anaesthesia and reinfarction in all groups

- ***Factors Unrelated to Reinfarction***

  a. postoperative ICU care
  b. diabetes
  c. angina
  d. age or sex
  e. site of the previous MI

Rao, El Etr (1983)

Reinfarction Rate		
Interval	Control Group[1] (n=364 / 1973-76)	**Prospective Group** (n=733 / 1977-82)
< 3 months	36%	**5.8%**
3-6 months	26%	**2.3%**
> 6 months	~ 5% p.a.	**~ 1.5-1.7% p.a.**[2]

[1] NB: ***retrospective control group***

[2] intensive therapy long ceased after 6 months, therefore reinfarction rate should have returned to control rates ~ 4-5% p.a.

• other factors associated with a higher reinfarction rate in both groups,

  1. CCF
  2. intraoperative hypertension and tachycardia
  3. intraoperative hypotension

NB: "results ***suggest*** that preoperative optimisation of the patient's status, aggressive invasive monitoring of the haemodynamic status, and prompt treatment of any haemodynamic aberration may be associated with ***decreased*** perioperative morbidity and mortality in patients with previous myocardial infarction"

• however, Slogoff states, (ASA Lectures 1992)

  1. the original abstract was not peer reviewed, and these claims were subsequently withdrawn in their own peer reviewed article
  2. no other group using intensive postoperative management have been able to approach these figures (including the late figures, making the initial claim suspect)
  3. still quoted by various groups to "support their own opinion", ie. regarding use of PA catheters

Hertzer *et al.* (1984)

→ 1001 patients scheduled to undergo ***elective vascular surgery***

1. coronary ***angiography*** revealed significant CAD in **~ 60%**
2. of those suspected of IHD → 78% had significant vessel narrowing
3. of 500 with ***normal ECGs*** → **37%** ≥ 70% narrowing ≥ 1 coronary artery
   - up to 15% of patients with ***triple vessel disease*** have a normal resting ECG
4. the presence of a ***carotid bruit*** is highly suggestive
   → perioperative mortality being 15-17%, cf. 2.1% in a control group
5. ***CABG*** thought indicated in 251,
   i. 216 underwent CABG
      - 12 (5.5%) operative deaths during CABG
      - ? 200 peripheral arterial surgery ~ 1.5% early cardiac deaths
        ~ 12% late cardiac deaths

   ii. 35 without CABG
      - 16 peripheral arterial surgery ~ 12% early cardiac deaths

NB: ***does not*** answer question of whether CABG should occur before PVD surgery

Slogoff, Keats (1985)

→ **1023** elective CABG patients

a. ECG ischaemia in 37%, half of these ***pre-induction***

b. post-operative AMI in,
   i. 6.9% ***with*** perioperative ischaemia (**3x** -)
   ii. 2.5% ***without*** perioperative ischaemia
   - ***but*** was independent of when the ischaemia occurred

c. ischaemia related to ***tachycardia*** * ***not*** hypo/hypertension

d. ischaemia occurred frequently in the ***absence*** of haemodynamic changes,
   ? probably due to fluctuations in coronary vascular tone

- ***Other Associated Factors***

a. "anaesthetist No.7"

b. poor quality anastomosis

c. prolonged ischaemic time

NB: ***unrelated*** to patient type, LAD lesion, or LVEF
therefore, the frequency will relate primarily to ***perioperative management***, rather than patient selection

Foster (1986)

• Coronary Artery Surgery Study (CASS) registry data of 1600 patients undergoing major ***noncardiac*** operations between 1978-81
• showed an ***perioperative mortality*** of,

a. controls ~ 0.5%
b. CAD + CABG ~ 0.9%
c. CAD ~ 2.4% ($p < 0.009$)

NB: however, ***no difference*** between the groups for AMI

• supports the use of CABG in patients with significant CAD ***prior*** to undergoing major noncardiac surgery, especially with the following risk factors,

1. high LV "score"
2. diabetes
3. LVH
4. use of nitrates
5. males
6. exertional dyspnoea

Knight, Hollenburg & London *et al.* (1988)

• incidence of haemodynamically unrelated intraoperative ischaemia is identical to that experienced by the patient in the 2 days preoperatively

NB: the risk of intraoperative ischaemia, and therefore postoperative MI, is determined primarily by the patients ***native disease severity***, not by perioperative anaesthetic management

Fleischer & Barash (CJA, 1992)

• in a review of the literature, suggest that the established data is ***inaccurate*** for the following reasons,

1. patients have been stratified according to ***time*** from infarction & ***operation type***
2. none of the patient groups were homogenous with regard to the ***extent of CAD*** and the risk for subsequent infarction
3. no distinction was made between "Q-wave" and "non-Q-wave" infarction*
   i. recent data suggests that survivors of a "non-Q-wave" MI, are at ***greater*** risk of a subsequent MI
   ii. although "Q-wave" infarcts are at a lower risk of MI, they are still prone to arrhythmias
4. most of the published data is prior to the widespread use of ***thrombolytic therapy***

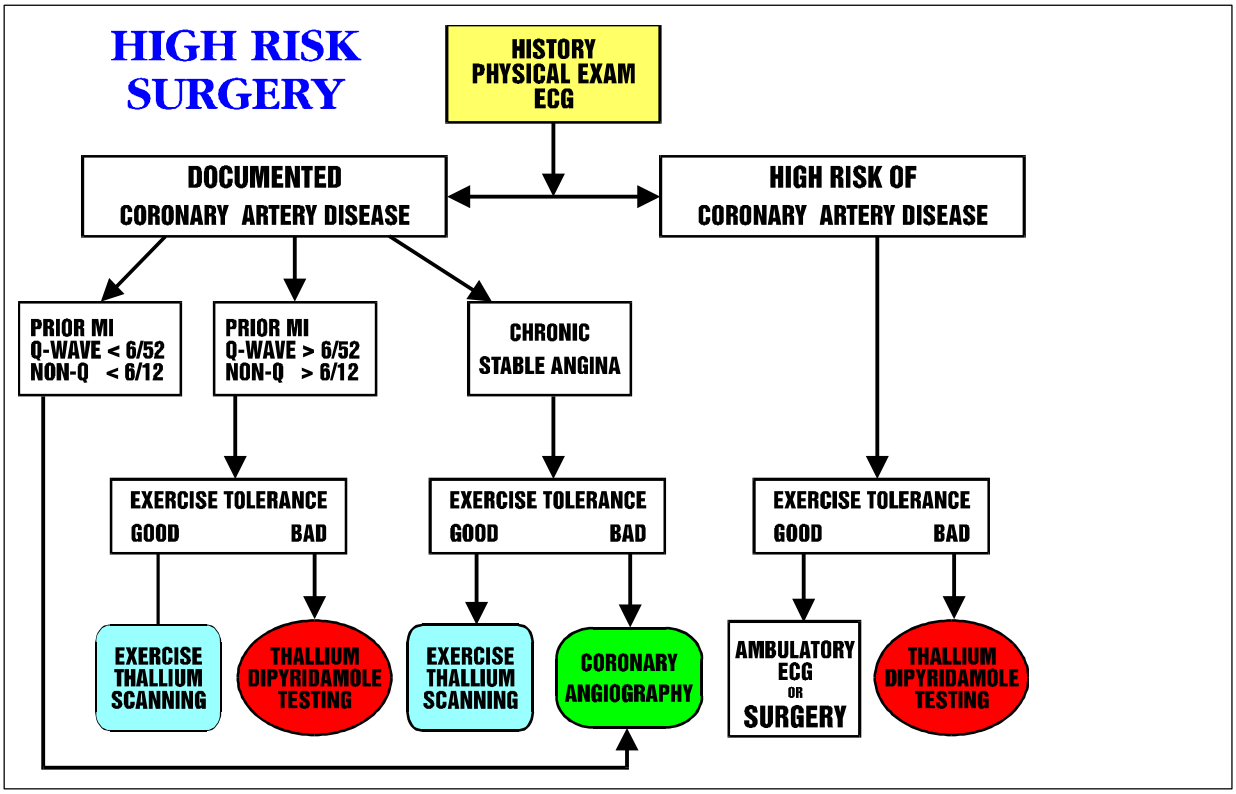
• although distinction between "Q-wave" and "non-Q-wave" infarction* may be relevant, it is important to remember that,

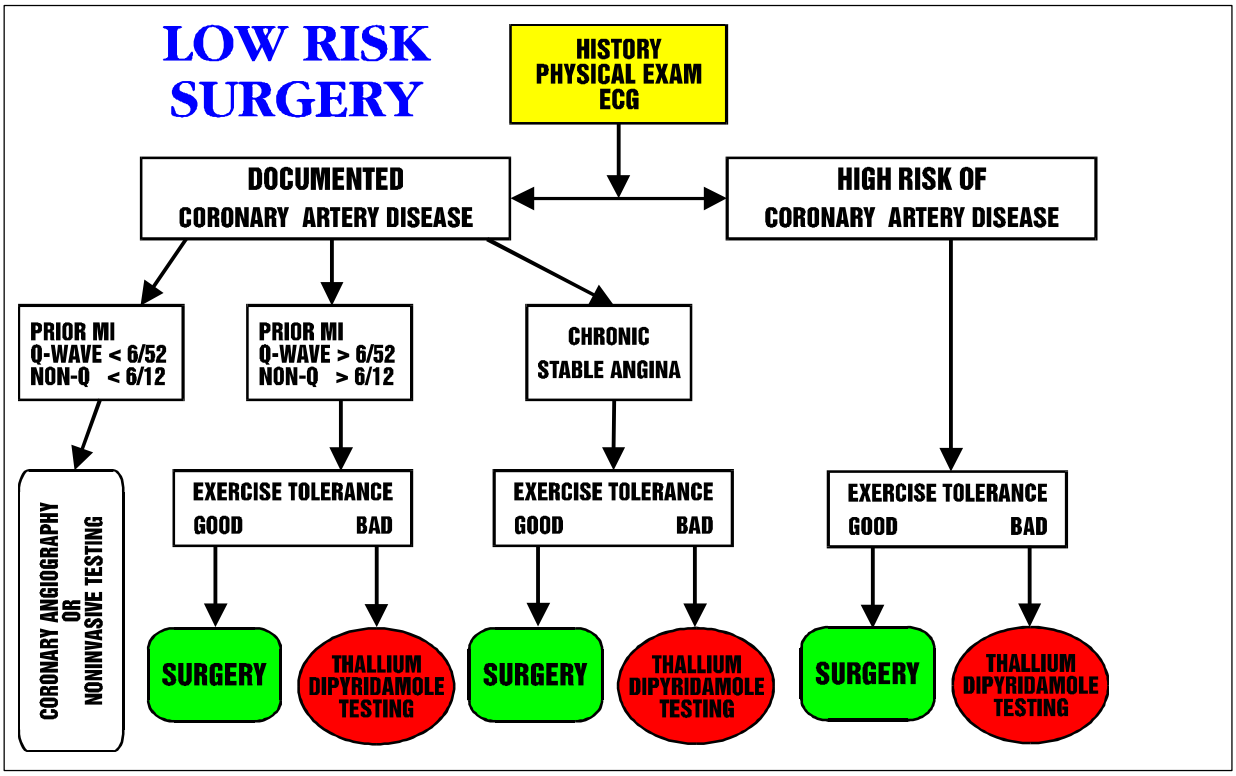
a. ECG classification as such ***does not*** necessarily correlate with transmural and subendocardial infarction
b. there is significant overlap between these groups, especially with the use of thrombolytic therapy

• they suggest a more appropriate approach is ***symptom limited exercise testing***, based upon whether the person is about to undergo high, or low risk non-cardiac surgery
• this, or cardiac catheterisation, is recommended by the AHA for virtually all patients within 6-8 weeks following a MI

NB: irrespective of infarct type, within the first ***6 weeks*** there will be remodelling and fibrosis, and the myocardium is sensitive to any additional stresses

• their approach is therefore limited to "recent infarction", ie. 6 weeks to 6 months
• the choice of which test is performed initially depending upon the nature of the patients disease and the extent of the planned surgery


HIGH RISK SURGERY
HISTORY PHYSICAL EXAM ECG
DOCUMENTED CORONARY ARTERY DISEASE
HIGH RISK OF CORONARY ARTERY DISEASE
PRIOR MI Q-WAVE < 6/52 NON-Q < 6/12
PRIOR MI Q-WAVE > 6/52 NON-Q > 6/12
CHRONIC STABLE ANGINA
EXERCISE TOLERANCE GOOD BAD
EXERCISE TOLERANCE GOOD BAD
EXERCISE TOLERANCE GOOD BAD
EXERCISE THALLIUM SCANNING
THALLIUM DIPYRIDAMOLE TESTING
EXERCISE THALLIUM SCANNING
CORONARY ANGIOGRAPHY
AMBULATORY ECG OR SURGERY
THALLIUM DIPYRIDAMOLE TESTING


LOW RISK SURGERY
HISTORY PHYSICAL EXAM ECG
DOCUMENTED CORONARY ARTERY DISEASE
HIGH RISK OF CORONARY ARTERY DISEASE
PRIOR MI Q-WAVE < 6/52 NON-Q < 6/12
PRIOR MI Q-WAVE > 6/52 NON-Q > 6/12
CHRONIC STABLE ANGINA
CORONARY ANGIOGRAPHY OR NONINVASIVE TESTING
EXERCISE TOLERANCE GOOD BAD
EXERCISE TOLERANCE GOOD BAD
EXERCISE TOLERANCE GOOD BAD
SURGERY
THALLIUM DIPYRIDAMOLE TESTING
SURGERY
THALLIUM DIPYRIDAMOLE TESTING
SURGERY
THALLIUM DIPYRIDAMOLE TESTING

Assessment of Myocardial Reserve

- ***Exercise Electrocardiography***

  a. patients able to achieve an exercise ***heart rate*** up to **85%** of predicted maximum

  b. ***upsloping*** ST-segment depression > 2mm at 0.08s from the J-point

  c. ***horizontal*** ST-segment depression > 1mm at 0.06s from the J-point

  d. ***downsloping*** ST-segment depression > 1mm at 0.06s from the J-point

     i. increased mortality cf. upsloping or horizontal changes

     ii. associated with an increased number of diseased vessels

     iii. > 1mm represents severe transmural ischaemia

  e. ***elevated*** ST-segment > 1mm at 0.06s from the J-point

     - in the absence of haemodynamic or rhythm disturbance suggests coronary artery spasm (Prinzmetal's angina)

- a positive result represents a high risk, however, may be misleading as,

  1. ischaemia may not occur at the same BP & HR as it would in normal daily life
  2. exercise produces ***tachycardia*** with little δBP, whereas anaesthesia may associated with both a rate and pressure load
  3. most ischaemia occurring perioperatively ***is not*** associated with alteration of haemodynamic variables
  4. ambulatory ECG data shows that individuals suffer ischaemia at different (lower) HR/BP levels to those occurring during exercise
  5. the ***critical HR*** for the development of ischaemia displays ***circadian variation***, being lowest in the early morning

- ***Ambulatory Electrocardiography***

- ***silent ischaemia*** accounts for at least **75%** of all ischaemic episodes (? higher in diabetics)
- this correlates with a worse prognosis, both in terms of ***cardiac events*** and ***mortality*** in,

  1. non-cardiac surgical patients with CAD
  2. patients post-AMI
  3. following CABG surgery

  NB: ∴the absence of angina ***is not*** a reliable indicator of the stability of a patient's CAD

  further, angina is not a reliable indicator of myocardial ischaemia

Exercise Thallium Imaging

• **^{201}Th** is an analogue of ***potassium*** and is actively taken up into the myocardium
• better able to determine the ***extent*** and ***location*** of the myocardium at risk cf. exercise ECG
• discrimination of fixed versus reversible thallium defects distinguishes between scarred and ischaemic myocardium
• ***dipyridamole-thallium scanning*** is highly sensitive in predicting perioperative myocardial ischaemia in patients unable to exercise,

a. dipyridamole vasodilatation of normal vessels preferentially distributes flow away from an ischaemic area, which appears as a "cold spot"

b. as the vasodilatory effects subside, flow redistributes with reappearance of the ischaemic area

c. "fixed" defects were traditionally thought to represent scar tissue

d. more recent work has shown that ***fixed defects*** on standard delayed imaging may occur in the presence of viable myocardium and critical stenosis, being termed ***hibernating myocardium***

e. several authors have demonstrated that the presence of a redistribution defect is predictive of a postoperative cardiac event, in patients undergoing peripheral vascular surgery

f. the overall sensitivity of DPT scanning is comparable to exercise-thallium scanning

NB: in rare circumstances the DPT scan may appear "normal" in patients with severe 3 vessel disease, as there are no "normal" areas to provide contrast in ^{201}Th uptake

• other scanning methods presently being evaluated include,

a. stress simulation thallium scanning using ***adenosine*** instead of dipyridamole

b. newer ^{99}Tc isotopes in conjunction with PET

Predictive Value of Adverse Cardiac Outcome[1]

Test	Sensitivity	Specificity	Positive Predictive Value	***Negative*** Predictive Value
Exercise ECG	30.6	83.2	30.6	**83.2**
Ambulatory ECG	43.4	86.3	35	**89.9**
Dipyridamole ^{201}Th	**83.5**	68	37.9	**94.7**[2]
DPT - Cunningham	85-93%	64-80%		

[1] Mazer-CD: The diagnosis and perioperative management of myocardial ischaemia. Can J Anaes. 1992: 39 (5); R90-R95

[2] ie. DPT scanning does not effectively predict, but ***excludes*** likelihood of adverse event

- Eagle *et al*. demonstrated that in patients with ≥ 3 clinical risk factors,
    1. angina
    2. age > 70 years
    3. diabetes
    4. Q-waves on ECG
    5. ventricular ectopy requiring treatment

    NB: undergoing peripheral vascular surgery
    had a **50%** chance of a perioperative ***adverse cardiac outcome***,
    irrespective of the above test results →

        i. cardiac death
        ii. AMI
        iii. unstable angina
        iv. acute pulmonary oedema

    NB: ∴ they recommended ***cardiac catheterisation*** as the initial test in these patients

Congestive Heart Failure

- clinical CCF was shown to be predictive of an adverse outcome by Goldman 1977
- the predictive value obtained by ***objective*** measurement of LVEF is less certain
- studies using radionuclide imaging LVEF measurements have been both predictive and non-predictive
- baseline resting LVEF is probably only useful in patients with poor or questionable exercise tolerance, or documented CAD
- more important is the ***functional response*** to stress, using either
    a. exercise echocardiography
    b. dipyridamole echocardiography
    c. exercise radionuclide ventriculography
    d. diastolic BP during standard exercise ECG (extremely sensitive marker)

    NB: these have been shown in various studies to be ***predictive*** of,

        i. cardiac death
        ii. AMI
        iii. unstable angina
        iv. acute pulmonary oedema (Tischler 1991)

Angina

▪ ***Stable Angina***

• in the original work by Goldman, chronic stable angina was ***not*** predictive of perioperative cardiac morbidity
• however, NYHA class IV angina was excluded from the study due to the small number
• Shah *et al.* (1990) found that chronic stable angina ***was*** a predictive factor, and this is now generally accepted
• patients with either,

1. frequent anginal symptoms, or
2. poor exercise tolerance

→ almost a ***100% positive*** result to stress ECG testing,
∴ this offers little information, and a negative result is usually false

• angiography may provide useful information,

1. the ***extent*** and area of myocardium at risk
2. whether the patient is likely to benefit from ***revascularisation***
3. baseline LVEF
4. the coronary anatomy

• however, if neither percutaneous balloon angioplasty nor CABG are options, and the non-cardiac surgery is required, then this information is superfluous

NB: preoperative testing of patients with chronic stable angina should only be performed if the results are likely to alter the perioperative care

• however, even in patients with chronic stable angina, **~ 75%** of all ischaemic episodes, as defined by ECG, echocardiography, or nuclear imaging occur in the ***absence*** of symptoms

▪ ***Unstable Angina***

1. ***new onset*** < 2 months, of severe angina
2. angina at rest or with ***minimal activity*** = NYHA & CCS Class IV
3. recent increase in the frequency, or duration of chronic angina
4. recurrent angina within several days of an AMI, without enzyme changes

NB: Shah *et al.* (1990) **~ 28%** of those undergoing non-cardiac surgery suffer a perioperative MI or cardiac death, ie. same as recent infarct (< 3/12)
clearly this is a prohibitive risk for anything but emergency surgery

- management,

a. IV nitroglycerine

b. ***heparin*** infusion ~ 1.5-2.0x baseline APTT
- reduces the frequency of angina and subsequent MI
- after 3-5 days, therapy should be continued with aspirin ± warfarin
- Serneri *et al*., Lancet 1995, RCT of 108 patients with ***refractory*** angina

i. heparin sc or IV equally effective in control of unstable angina

ii. aspirin had no significant effect

c. ***aspirin***
- irreversibly acetylates ***cyclo-oxygenase***, inhibiting synthesis of TXA_2 & PGI_2
- low dose aspirin may inhibit TXA_2 and spare PGI_2 synthesis, as,

i. endothelial cyclo-oxygenase is less sensitive cf. the platelet enzyme

ii. endothelial cells are capable of re-synthesizing the enzyme, cf. platelets
- at high doses (900-1200 mg/day) ASA results in dose-dependent enhancement of the fibrinolytic system and reduced activity of factors II, VII, XI & X
- clinical studies have shown that doses ~ 100-325 mg/day reduce,

i. AMI

ii. occlussive stroke & TIA's

iii. early graft thrombosis & late phase occlusion in aorto-coronary bypass grafts
- primary prevention studies have shown a reduction in AMI, however, no reduction in ***overall mortality***, ∴not recommended for prevention
- Serneri's study above would suggest ***not effective*** in unstable angina

d. CABG
- improved survival in patients with left main disease, or three vessel disease with impaired LV function (LVEF < 40%)
- no improvement in patients with one/two-vessel disease
- questionable improvement in 3-vessel disease with normal LV function

e. PTCA percutaneous transluminal coronary angioplasty
- success rates for proximal stenosis ~ 90-95%
- acute coronary occlusion / AMI rates ~ 5%
- emergency operation rates ~ 5-7%
- restenosis rates ~ 30% at 5 months
- restenosis is not altered by - aspirin, dipyridamole, PGI_2, CEBs, warfarin ? hirudin
- for 1 vessel disease,

i. survival rates ~ 98.7% at 12 months

ii. repeat angioplasty ~ 20%

iii. CABG ~ 5%
- these figures are comparable to those for medical treatment alone, ∴exact role of PTCA needs to be established

Studies of Perioperative Ischaemia Research Group (SPIRG, JAMA 1992)

NB: series of 7 articles from D. Mangano's group
almost ***all data*** from Veteran's Affairs hospital, therefore older men

▪ ***Predictors of Postoperative MI in Noncardiac Surgery***

• 474 men scheduled to undergo major noncardiac surgery, entry criteria,

a. definite CAD
- previous MI
- typical angina
- atypical angina + positive exercise ECG or DPT scan

b. high risk of CAD

i. vascular surgery, past or present

ii. any 2 of
- age > 65
- hypertension
- smoker
- NIDDM / IDDM
- high cholesterol

• 5 major independent preoperative ***predictors*** of ***postoperative ischaemia***,

1. definite CAD
2. LVH by ECG
3. history of hypertension
4. diabetes mellitus
5. use of digoxin

NB:
0 factors → 22%
1 factor → 31%
2 factors → 46%
3 factors → 70%
4 factors → 77%

• other factors associated with a high incidence were,

1. ***preoperative ischaemia*** as detected by holter monitor, and
2. ***intraoperative ischaemia*** as detected by 12 lead ECG or holter monitor

■ ***Monitoring for Myocardial Ischaemia in Noncardiac Surgery***

• comparison of TEE or 12-lead ECG, versus 2-lead ECG (CC_5 & CM_5) plus preoperative predictors of ischaemic outcome*
• 332 patients, in whom 285 had technically adequate studies by all 3 techniques

1. predictors + 2 lead ECG* (26%) identified more patients with ischaemia than,
   i. TEE ~ 15%
   ii. 12 lead ECG ~ 14%
2. 111 (**~ 39%**) had intraoperative ischaemia →
   i. ~ 2-3x ↑ in perioperative adverse cardiac outcome
   ii. 63 (19%) had adverse cardiac outcomes, with 11 ischaemic outcomes
3. using only ***ischaemic*** cardiac outcome ***none*** of the 3 methods was predictive

NB: concluded that, "in comparison with preoperative clinical data and intraoperative monitoring with two-lead ECG,

TEE and 12-lead ECG have little if any incremental value"

• this contrasts Smith *et al.* (Circul^{n}.1985) who assessed TEE during ***CABG surgery***,

a. TEE ~ 48% versus ECG 12%
b. ***all*** ST changes were in patients with RWMA's

NB: generally accepted that TEE is a ***more sensitive*** monitor for CABG patients

■ ***Ventricular Arrhythmias in Patients Undergoing Noncardiac Surgery***

• ventricular arrhythmias occurred in 44% of the study group
• more common in,

1. smokers
2. history of CCF
3. ECG evidence of myocardial ischaemia

NB: adverse cardiac outcome ***was not*** related to the occurrence of arrhythmias

• therefore, when these occur ***without*** concomitant signs or symptoms of ***myocardial ischaemia***, they ***do not*** require additional monitoring or treatment in the perioperative period

■ ***Intraoperative & Postoperative Myocardial Ischaemia in Peripheral Vascular Surgery***

• 115 patients (M&F) undergoing elective vascular surgery at the Brigham & Womens hospital
• screened at "***low risk***" for adverse cardiac outcome,

1. 35 patients with postoperative ischaemia
2. 14 of these developed an adverse cardiac outcome
3. all of these 14 also had ***preoperative*** myocardial ischaemia
4. none of the 15 patients with postoperative ischaemic changes, without preoperative changes, developed an adverse outcome

NB: ***preoperative ischaemia*** was the single most important predictor of adverse outcome,

sensitivity **~ 88%**
specificity **~ 91%**

intraoperative ischaemia in this group was relatively uncommon **~ 18%** and was a significant, but much weaker, predictor of adverse outcome, especially in patients at low risk of CAD

■ ***Long-Term Cardiac Prognosis Following Noncardiac Surgery***

• 444 consecutive patients at ***high risk*** for CAD, followed for ~ 2 years after elective surgery
• 47 (**11%**) had major CVS complications during the follow-up period,

1. cardiac death
2. MI
3. unstable angina, or new angina requiring hospitalisation
4. progressive angina requiring CABG or angioplasty

• 5 independent ***predictors*** for long-term outcome were identified,

1. definite CAD
2. postoperative MI or unstable angina
3. postoperative ischaemia
4. history of CCF
5. history of vascular disease

NB: those surviving a postoperative, in-hospital MI had a,

i. 28x increase in adverse outcome within 6 months, and
ii. 15x increase in adverse outcome at 1 year

• the development of CCF or VT without ischaemia, ***were not*** associated with adverse long-term outcome

Summary of Preoperative & Intraoperative Factors

NB: According to Roizen, in Miller 3rd Ed.

- ***Preoperative Findings Correctable***

1.	recent MI	< 6 months
2.	uncompensated CCF	- S_3, ↑ JVP, pulmonary crepitations
3.	severe angina	- NYHA Class IV
4.	significant aortic stenosis	
5.	heart rhythm other than sinus	
6.	VEB's	> 5/min
7.	BUN	> 18 mmol/l
8.	serum [K^+]	< 3.0 mmol/l

- ***Preoperative Findings Uncorrectable***

1.	old age	> 70 years
2.	emergency operation	
3.	cardiomegaly	
4.	history of CCF	
5.	stable angina	
6.	ECG evidence of ischaemia	- ST, T-wave changes - abnormal QRS complex
7.	significant MR murmur	

- ***Intraoperative Findings Correctable***

1.	use of vasopressors	
2.	hypotension	
3.	high rate-pressure product	- HR x BP_{SYS} > 11,000
4.	long operations	

- ***Intraoperative Findings Uncorrectable***

1.	emergency surgery	
2.	major abdominal or thoracic procedures	

CORONARY ARTERY BYPASS GRAFTING

- ***Right Coronary Artery***

  a. originates from the ***anterior*** aortic sinus

  b. runs forward between the PA and right atrial appendage
  → the right atrioventricular groove

  c. branches include the,
  i. acute marginal branch - inferior border of the heart (RV)
  ii. branch to the ***SA node***
  iii. ***posterior interventricular artery***, or PDA

  d. anastomoses with,
  i. the circumflex artery - in the AV groove
  ii. the LAD via the PDA branch - in the interventricular septum

  e. dominant in **85-90%** → supplies the ***AV node***, plus
  - posterior septum
  - posterior wall of the LV

- ***Left Coronary Artery***

  a. arises from the ***left posterior*** aortic sinus and is larger than the right

  b. passes first behind, then left of the PA, between this and the LA appendage in the AV groove

  c. runs for ~ 2 cm then branches into the,
  - ***anterior descending artery***

  i. passes down the anterior interventricular groove
  ii. supplies the LV, anterior septum, & some RV
  iii. also branches to form the,
  - septal perforators
  - diagonal branches - variable number
    - supply the LV apex

  - ***circumflex artery***

  i. passes around the left AV groove
  ii. anastomoses with a branch of the RCA
  iii. does not reach the PDA in > 80%
  iv. branches to form the,
  - obtuse marginal - supplies the posterior LV wall

Preoperative Management

- essentially the management of severe preoperative myocardial ischaemia
- indications for ***elective CABG***,
    1. significant CAD
        i. LAD stenosis
        ii. triple vessel disease with LVEF < 40%
    2. good LV function
    3. graftable coronary vessels

- indications for ***emergency CABG***,
    1. unstable angina
    2. myocardial salvage post-AMI, eg. after thrombolytics
    3. CAD + acute systemic disease resulting in ischaemia

- patients at ***high risk*** during CABG,
    1. tight LAD stenosis > 90%
    2. low EF ≤ 35%
    3. low CI ≤ 2.2 l/min/m^2
    4. extreme myocardial irritability
    5. uncontrolled CCF
    6. diabetes

- ***Preparation Stage 1***

a. ABC / resuscitation, O_2
b. complete history & physical examination
c. baseline investigations
   i. FBE, U,C&E's, AGA's
   ii. ECG
   iii. CXR
d. morphine IV - vasodilation, analgesia, anxiolysis
e. antianginal therapy
   i. GTN infusion - 25-250 µg/min
      - 20 mg/500 ml @ 8 ml/hr ~ 5 µg/min (HPIM starts at 5 µg/min)
      - NAC if used > 24 hrs
   ii. diltiazem, isordil, perhexiline
f. antiarrhythmics
   i. digoxin / amiodarone for AF
   ii. β blockers for sinus tachycardia
g. R_X complications
   i. anaemia
   ii. infection
   iii. fluid overload
h. reduce reinfarction rate - aspirin, anticoagulation, β blockers
i. reduce afterload - vasodilators, ACEI
j. exclude exacerbating pathology

- ***Preparation Stage 2***

a. cardiology consultation
b. echocardiogram
c. radionucleotide studies
d. cardiac catheterization

- ***Preparation Stage 3***

a. mechanical ventilation to reduce VO_2
b. balloon counterpulsation
c. ventricular assist devices

Post-operative Management

- ***Principles***

1. maintain optimal
   i. oxygenation
   ii. blood volume
   iii. CO and organ perfusion
2. adequate analgesia
3. treat arrhythmias
4. R_X biochemical disorders - especially K^+, Mg^{++}
5. support ventilation until
   i. circulation stable
   ii. normothermia
   iii. weaning criteria satisfied

- ***Monitoring***

1.	cardiovascular	- HR, rhythm, BP - CVP ± PAOP, derived haemodynamic data - CXR, echocardiography
2.	respiratory	- physical examination - ventilator settings, spirometry - CXR, AGA's
3.	renal	- urine output, C&U
4.	biochemistry	- Na^+, K^+, HCO_3^-, AGA's
5.	haematology	- Hb, platelets, coagulation profile
6.	temperature	- core & peripheral

- ***Failure to Successfully Defibrillate***

1. hypothermia < 32°C
2. hypoxia, acidaemia, hyperkalaemia
3. coronary embolism - air, thrombus
4. coronary / IMA spasm
5. infarction
6. defibrillator dysfunction

- ***Postoperative Hypotension***

a. hypovolaemia
b. tamponade
c. pneumothorax
d. IPPV with high mean intrathoracic pressures
e. arrhythmias
f. ***myocardial dysfunction***
   i. functional depression for ~ 24 hours post-bypass is "normal"
      → "***stunned myocardium***"
   ii. prolonged bypass time, coronary or ***IMA spasm***, air embolism
   iii. ischaemia, infarction
   iv. valvular dysfunction
   v. metabolic disturbance
      - hypoxia, hypercarbia, acidosis
      - hypocalcaemia
   vi. drugs
      - anaesthetic agents
      - β adrenergic blockers
      - Ca^{++} entry blockers

- ***Postoperative Bleeding***

1. surgical
2. thrombocytopaenia / ***platelet dysfunction*** → most common cause
3. incomplete reversal of heparin
4. dilutional coagulopathy
5. preoperative anticoagulants - aspirin, heparin, warfarin, NSAIDs
6. liver dysfunction
7. incompatible blood transfusion
8. CPB induced - DIC, thrombocytopaenia

NB: I_X: APTT, PT, platelet count, Hb ± skin bleeding time

R_X: platelet transfusion, protamine, FFP, DDAVP
return to theatre if loss → **> 400 ml/hr**
→ > 200 ml/hr for 3/24

Aprotinin

• recent studies have shown large doses of aprotinin reduce blood-loss associated with CPB
• originally studied in the 60's & 70's with no significant effect, but using much smaller (~ 50%) doses than present studies
• Royston *et al.* 1987 reported a significant reduction in blood-loss associated with CPB for repeat valve replacement procedures
• the aim of this study was to assess the effects upon postoperative ***pulmonary function***, the results on blood-loss were unexpected
• other studies have extended these findings to patients with,

a. septic endocarditis
b. recent aspirin ingestion

• detrimental effects of CPB on ***haemostasis*** include,

1. platelet dysfunction / consumption
   i. loss of membrane structure & granule contents
   ii. generation of activation markers on the cell surface
2. activation of the fibrinolytic & contact systems
3. activation of granulocytes → degranulation

• the likely, not proven, site of action of aprotinin is platelet ***membrane GPIb***

a. loss of GPIb is one of the early events during CPB which is prevented by aprotinin
b. GPIb contains the binding site for ***thrombin***-induced platelet activation
c. enzymatic hydrolysis of GPIb may result in platelet activation

• GPIb is a transmembrane ***hetrodimer***, readily cleaved by plasmin, elastase and calpain
• all of these agents are direct ***platelet agonists*** and are inhibited by aprotinin,

1. ***plasmin*** - activity 2° tPA or contact system activation
   * induced fibrinolysis results in ***increased*** platelet activity
   - this is why thrombin inhibition is required post-thrombolysis
2. ***elastase*** - generated from activated neutophils during CPB
   - inhibition requires greater concentrations cf. plasmin
3. ***calpain*** - cysteine protease present on thrombin stimulated platelets
   - ? also plasmin stimulated platelets

NB: inhibition of ***tPA-induced plasmin*** on the platelet surface could account for much or all of the observed effect

Post-CABG - Tamponade versus LVF		
Feature	Tamponade	LVF
Physiology	diastolic dysfunction	systolic dysfunction
Aetiology	decreased pericardial vol.	myocardial ischaemia
BP	low	low
Paradox	present	present but small
JVP	marked elevation	normal or high
Kussmauls	present ? but patient on IPPV usually	absent
PCWP	normal or high diastolic pressure equalisation	high
HR	tachycardia	tachycardia
Heart sounds	soft	S_3, S_4, gallop
ECG	small complexes	ischaemic changes
Lungs	clear	congestion ± oedema
CXR	cardiomegally present normal lung fields	cardiomegally often absent pulmonary congestion

CARDIAC FAILURE

Def'n: that state which occurs when the heart fails to maintain an adequate circulation for the metabolic needs of the body, despite an ***adequate venous return***

- ***Classification***

1. low-output failure
   high-output failure - anaemia, AV fistulae, sepsis
   - beri beri, hyperthyroidism, Paget's
2. RV failure
   LV failure
3. diastolic failure - ↓ LV compliance, LVEF usually normal
   systolic failure - ↓ LVEF

- ***Causes Infant***

1. ***cardiac***
   i. congenital valvular disease
   ii. congenital myocardial/endocardial disease
   iii. myocarditis
   iv. arrhythmias
2. ***non-cardiac***
   i. respiratory disease
   ii. sepsis
   iii. acidosis
   iv. anaemia
   v. CNS disease

- ***Causes Child***

a. congenital myocardial disease
b. congenital valvular disease
c. myocarditis
d. rheumatic fever
e. vasculitis - Kawasaki's disease

- ***Causes*** ***Adult***

NB: endocardium
valves
conducting system
myocardium
vessels
pericardium

1. coronary artery disease & ischaemic cardiomyopathy
2. hypertensive heart disease
3. cardiomyopathy
   - i. idiopathic
   - ii. alcoholic
   - iii. post-infective
   - iv. familial
   - v. nutritional deficiency - Mg^{++}, Ca^{++}
     - $HPO_4^{=}$, selenium, thiamine
   - vi. drugs - chloroquine
     - adriamycin, daunorubicin, etc
   - vii. pregnancy
   - viii. infiltrations - amyloid, sarcoid
   - ix. endocrine diseases - thyrotoxicosis, hypothyroidism
     - phaeochromocytoma, diabetes, acromegaly
4. myocarditis
   - i. viral, bacterial
   - ii. unusual infections - AIDS related
     - fungal, protozoal
5. SBE
6. valvular disorders
7. endocardial diseases - atrial myxoma
   - fibroelastosis, etc.
8. vasculitis - PAN, SLE, scleroderma
9. pericardial disease
   - i. idiopathic
   - ii. infective
   - iii. inflammatory / immunogenic
   - iv. infiltrative
   - v. irradiation

- ***Cardiac Failure with "Clear Lungs"***

  NB: hypotension, high CVP, peripheral oedema

  1. right ventricular infarction
  2. cardiac tamponade
  3. constrictive pericarditis
  4. restrictive cardiomyopathy
  5. CCF with CAL

- ***Precipitating Factors***

  1. ischaemia
  2. arrhythmias
  3. drugs, anaesthesia
  4. anaemia
  5. infection, trauma
  6. pregnancy, exercise
  7. pulmonary embolism
  8. fluid overload
  9. hyperthyroidism
  10. biochemical abnormality
      - hypoxia, hypercarbia, acidosis
      - hypokalaemia, hyperkalaemia, hypocalcaemia
      - hypernatraemia, hypophosphataemia, hypomagnesaemia

- ***Investigation***

  1. CXR - cardiac size & shape, pulmonary congestion, pleural effusions
  2. ECG - rate, rhythm, ischaemia, inflammation, pericarditis
  3. Echo - chamber size, wall thickness, RWMA, LVEF
     - valvular function, pericardial effusion
  4. Catheterisation
  5. Other - FBE, ESR, EC&U, CK-MB, TFT, AGA

- ***Management***

1. correction of underlying pathology
2. reduction in ***cardiac work***
   - i. general - rest, weight loss
   - ii. venodilators - isosorbide dinitrate etc.
     - nitrates reduce filling pressures & diastolic volumes
     - long-term ***no improvement*** in exercise tolerance or CCF symptoms
   - iii. nitrovasodilators - hydrallazine, minoxidil
     - no benefit with respect to symptoms or exercise tolerance
     - in moderate-severe CCF (NYHA III, IV) when added to digoxin/diuretics result in a reduction in ***mortality*** at 2 years (38 to 25%)
   - iv. calcium channel blockers
     - no improvement in exercise tolerance / symptoms
     - significant negative inotropic effects
     - may ***increase mortality*** post-MI
   - v. ACE inhibitors
     - both short & long-term clinical improvement, greater than other agents
     - reduction in ***symptoms***, improved exercise tolerance, improved ***survival***
     - reduced need for diuretics, K^+ supplementation & other agents
     - captopril may not elevate the creatinine to the same degree cf. enalapril
     - synergistic with positive inotropic agents
3. enhanced ***myocardial contractility***
   - i. cardiac glycosides
     - sustained improvement in CI and LVEF in patients with chronic CCF
     - beneficial predominantly in ***systolic dysfunction***
     - ineffectual if systolic function preserved & mainly diastolic dysfunction
   - ii. β-adrenergic & dopaminergic agonists
     - sustained benefit has been observed with twice weekly dobutamine infusions
     - generally ineffectual for chronic therapy due to tolerance
     - large study with xamoterol improved CCF but mortality increased
   - iii. PDE_3 inhibitors
     - produce good short-term benefit
     - chronic therapy associated with ***increased mortality*** & adverse cardiac events
4. reduction in salt & water retention
   - i. dietary restriction
   - ii. ***frusemide***
     - confliciting reports $\rightarrow$ $\downarrow\uparrow$ PAOP $\propto$ venodilation/vasoconstriction
     - $\therefore$ possible that IV may initially worsen CCF in some people due to $\uparrow$ SVR
     - this results from an acute release of ***renin*** & $\uparrow$ sympathetic tone
   - iii. ultrafiltration / haemofiltration
   - iv. venesection

Long-Term Management

- in patients with NYHA class I cardiac function, there is no data to support improved,
    1. quality of life
    2. survival

    NB: or any other beneficial effect irrespective of therapy options

- in NYHA classes II-IV, either ACEI alone, or in combination with digoxin/diuretics results in,
    1. reduced mortality
    2. improved exercise tolerance

Acute Pulmonary Oedema

- when LVF is the underlying cause only a small reduction in LAP is required
    a. in adults the vascular volume required to be removed ~ 200-300 ml
    b. this equates to a diuresis of ~ 1000-2000 ml

- when APO is 2° to IV volume excess the vascular volume reduction required ~ 1500 ml
- management includes,
    1. elevation of the head of the bed
    2. oxygen
    3. morphine
    4. GTN
    5. diuretics
    6. digoxin
    7. SNP
    8. venesection ~ 500 ml over 30 mins
    9. CPAP / IPPV

PULMONARY OEDEMA

Starling's Forces

• this equation predicts the net flux of water across a membrane;

$$J_v = K_f.[(P_c - P_i) - \sigma(\pi_c - \pi_i)]$$

where,
- J_v = net water flux
- K_f = the filtration coefficient
  - = flux coefficient x capillary area
- $P_{c,i}$ = hydrostatic pressures
- $\pi_{c,i}$ = oncotic pressures
- σ = Staverman reflection coefficient

• the Staverman reflection coefficient is a measure of capillary permeability to protein,

$\sigma = 1$ → completely ***impermeable***

• most studies assume a value of 1, ignore K_f, and simply refer to the net balance of forces which determine flow across the capillary
• this is invariably an over-simplification, quoted figures for lung varying from,

a.	lung capillary	2 to 12	mmHg
b.	lung interstitial	-7 to 1	mmHg
c.	plasma oncotic	20 to 35	mmHg
d.	interstitial	5 to 18	mmHg

→ this gives a total range of net driving pressure -29 to 17 mmHg

• the pulmonary interstitial pressures are probably slightly ***subatmospheric***
• interstitial protein concentrations vary considerably between tissues
• those in the lung are probably ~ 70-80% of plasma (Nunn ~ 50%)

Cardiac Vs. Non-Cardiac

- this differential is a common problem in ICU
- many can be differentiated on the basis of history, examination, ECG & CXR
- PA catheter & echocardiography are not always necessary
- mixed pictures can occur, LVF with a low PAOP, or sepsis with a high PAOP

Cardiogenic Oedema	Non-Cardiogenic Oedema
History	
• acute cardiac event • PHx cardiac disease	• non-cardiac event, sepsis, drugs • no cardiac PHx, age < 40 yrs
Examination	
• low CO state • cardiomegally • S_3, gallop • high JVP • crepitations	• hyperdynamic, bounding pulses • normal heart size • dual rhythm • evidence of underlying disease • crepitations ± wheeze
Investigations / PA catheter	
• PCWP > 18 mmHg • Q_S / Q_T small • (PCWP - COP) > 2 mmHg	• PCWP < 12 mmHg • Q_S / Q_T large • (PCWP - COP) < -2 mmHg
ECG	
• ischaemic changes ± AMI • ventricular arrhythmias	• usually normal • atrial tachyarrhythmias
CXR	
• perihilar distribution • ± cardiomegally • pleural effusions • venous congestion common	• more peripheral/uniform • cardiomegally unusual • effusions rare • venous congestion uncommon
Other	
• high P_{PC} • elevated cardiac enzymes • neutrophilia • oedema:plasma protein ratio: < 0.5	• high K_f & low σ • evidence of septicaemia, DIC • complement activation • oedema:plasma protein ratio: > 0.7

- ***Aetiology***

a. ***cardiogenic***

i.	↑ LAP	- mitral valve disease - atrial myxoma - thrombus - fluid overload - high output cardiac failure
ii.	↑ LVEDP	- acute LVF, AMI - myocardial ischaemia - aortic valve disease - cardiomyopathy - arrhythmia

b. ***pulmonary capillary defect***

i.	↑ permeability	- anaphylaxis - sepsis - aspiration pneumonitis - pancreatitis - multi-trauma, shock, DIC, burns - transfusion reaction
ii.	drug reactions	
iii.	chemicals	- O_2, CO, smoke, N-oxides
iv.	emboli	- air / fat / amniotic
v.	alveolar proteinosis	

c. ***neurogenic***
- sudden ↑ PVR, P_{PC}
- CNS trauma
- SAH, CVA
- epilepsy
- cerebral oedema

d. ***pulmonary venous disorder***
- congenital anomalous veins
- pulmonary veno-occlusive disease
- fibrosing mediastinitis
- methysergide
- mediastinal tumour
- ? high altitude residence

e. ***pulmonary lymphatic disease***
- lymphangitis carcinomatosis
- lymphoma, other tumours
- silicosis
- lymphangiogram dye
- DXRT

f. large negative ***interstitial hydrostatic pressure***
- post-upper airway obstruction
- ? re-expansion of collapsed lung
  eg. post-pneumothorax, thoracotomy

CARDIOGENIC SHOCK

Def'n: syndrome of severe impairment of ***tissue perfusion***,
secondary to ***primary pump failure***, and usually associated with,

1. systolic BP < 90 mmHg, MAP < 60 mmHg, or a decrease > 30 mmHg
2. rapid, small volume, 'weak' pulse ± alternans or paradox
3. ↑ JVP ± pulmonary oedema - ie. absence of hypovolaemia
4. cardiomegaly * acute → normal size
5. low urine output < 0.3 ml/kg/hr for ≥ 2 hrs
6. peripheries cool & pale, or mottled & sweaty
7. impaired mental function

- ***Aetiology***

1. ***myocardium***
   - i. AMI
     - 12-20% of all infarcts and has a high mortality 50-95%
     - represents a large infarct ³ **40%** loss of myocardium
     - or a complicated infarct ± valvular incompetence
       ± an acute VSD
   - ii. cardiomyopathy - restrictive, obstructive
   - iii. myocarditis
   - iv. transplant rejection
   - v. post cardiac surgery
   - vi. ventricular aneurysm
   - vii. trauma - myocardial contusion (RV > LV)
   - viii. abnormal conduction - severe brady/tachyarrhythmia
   - ix. drugs / toxins - CEB's, adrenergic antagonists

b. ***endocardium***
   - i. endocarditis
   - ii. severe valvular disease
   - iii. atrial myxoma
   - iv. fibroelastosis
   - v. endocardial fibrosis

c. ***pericardium***
   - i. cardiac tamponade
   - ii. restrictive pericarditis

- ***Pathophysiology***

  a. in AMI usually represents ≥ 40% loss of myocardium
  b. tachycardia
  c. CI < 1.8 l/min/m^2
  d. high SVR
  e. pulmonary oedema
  f. PAOP usually ≥ 18 mmHg
  g. CXR features of pulmonary oedema

- ***Causes of Cardiogenic Shock & LVF with a Low PAOP***

  1. RV dysfunction
  2. post-diuretic use
  3. relative hypovolaemia ? is this "cardiogenic"

- ***Diagnosis***

  a. history & examination
  b. ECG, CXR
  c. cardiac enzymes
  d. echocardiogram
  e. myocardial B_X
  f. catheter study

- ***Management***

a. ABC resuscitation

b. O_2 therapy

c. ventilatory support
   i. CPAP
   ii. IPPV

d. optimise preload → fluid challenge if PAOP < 18 mmHg

e. drugs
   i. inotropes - adrenaline, dobutamine, digoxin
   ii. vasodilators - captopril, SNP, GTN, hydrallazine
   iii. venodilators - GTN
   iv. antiarrhythmics - digoxin, amiodarone, lignocaine
   v. specific - streptokinase, steroids, cyclosporin

f. LV assist devices - IABP

g. specific
   i. emergency CABG
   ii. surgical repair of functional defects
      - valvular dysfunction
      - muscular defects - VSD, aneurysm, rupture
   iii. transplantation

NB: in general terms need to optimise,

   i. preload / afterload
   ii. rate & rhythm
   iii. contractility
   iv. O_2 demand / supply

Oxygen Delivery

Def'n: ***shock***: state of impaired tissue oxygenation, due to either,

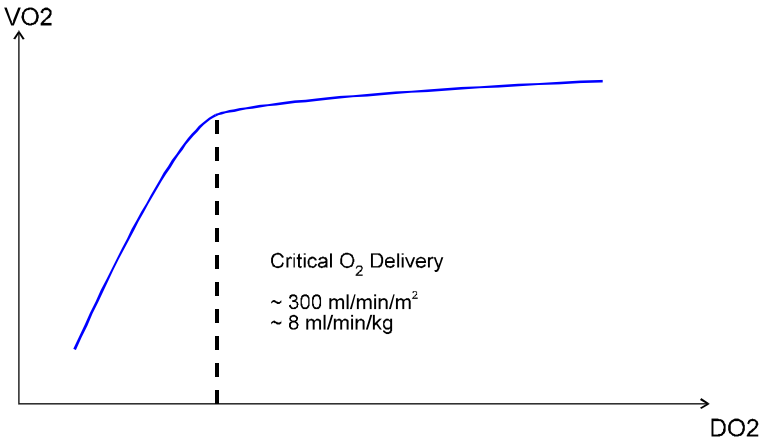
1. inadequate O_2 ***delivery***
2. inadequate O_2 ***utilisation***

- ***Oxygen Transport***

Def'n: **O_2 Flux**		~	CO x {(1.34 x [Hb] x 10 x S_{pO2}) + (0.003 x P_{aO2})}
	at rest	~	**1000** ml/min
		~	15 ml/kg/min
		~	520-720 ml/min/m^2
VO_2		=	(C_{aO2} - C_{vO2})/CO
	at rest	~	**250** ml/min
		~	3.5 ml/kg/min
		~	100-180 ml/min/m^2
C_{a-vO2}		~	4.0-5.5 ml/100 ml blood
O_2 ER		~	22-33%

1. "health" → DO_2 = 5.0 x 15 x 0.99 x 1.34 x 10 ~ 1000 ml/min
2. "ICU" → DO_2 = **4.0** x **10** x **0.95** x 1.34 x 10 ~ **500** ml/min

- ***Delivery Utilisation Relationship***



• the critical VO_2 may be less in humans ~ 3.5 ml/kg/min (Ronco *et al.*)
• normal VO_2 is determined by tissue metabolism & ***does not*** vary providing delivery is above a ***critical threshold***
• normal VO_2 ~ 140 ml/min/m^2 → maximum global O_2 extraction ~ 50%

Supranormal Resuscitation Goals

1. CI > **4.5** l/min/m^2
2. DO_2 > **600** ml/min/m^2
3. VO_2 > **170** ml/min/m^2 (Shoemaker, Surg Clin Nth Am 1985)

• increased survival in high risk general (not cardiac) ***surgical patients***
• methods used to attain these goals, (Shoemaker, Chest 1988)

1. colloids, blood T_x
2. inotropes - dobutamine
3. vasodilators

• 3 arms in study, with respective ***mortality*** rates,

1. CVP control ~ 23%
2. PAC control ~ 33%
3. PAC ***protocol*** ~ 4%

NB: significance levels 2 v 3 → $p < 0.01$
1 v 3 → $p > 0.05$

• other prospective studies have demonstrated ***no survival benefit*** →

Gattinoni, *et al.*	NEJM 1995	Tuchschmidt, *et al.*	Chest 1992
Hayes, *et al.*	NEJM 1994	Yu, *et al.*	CCM 1993

Limitations of Covariance Studies

1. mathematical coupling of shared variables
2. changes in VO_2 need to be controlled
3. thermogenic effects of catecholamines
4. require multiple data pairs per subject, over a wide range of DO_2 values to ascertain actual covariance

• shared variables,

1. DO_2 = CO x [Hb] x 1.34 x 10 x SaO_2
2. VO_2 = CO x [Hb] x 1.34 x 10 x (SaO_2 - **SvO_2**)

• subsequent studies that have addressed these limitations have ***never*** demonstrated pathological supply dependency,

1. Phang AJRCCM, 1994
2. Ronco ARRD, 1991
3. Manthous JCC, 1993

■ ***Hayes NEJM 1994***

- randomised controlled trial, 2 ICU's, ***109 patients*** > 16 years
- 9 excluded as reached targets with fluid alone → 50/50
- both high risk surgical and severely ill patients, matched for age & APACHE II
- predicted mortality for both groups ~ 35%

1. control ~ 34%
2. protocol ~ **54%** ($p < 0.05$)

- problems with study,

1. some of "control" group received ***dobutamine*** (n = 21)
2. both groups also received ***noradrenaline***
3. fluid resuscitation patients ***excluded*** from study
   - NB: Shoemaker included 66% of patients in this group

- conclusions that "use of dobutamine to boost CI, ... etc. failed to improve outcome"

NB: they ***did not*** extend the significant result to state,
"use of dobutamine ... etc. ***worsens*** outcome"

■ ***Gattinoni SvO2 Collaborative Group NEJM 1995***

- PRCT of 10,726 admissions, with ***762 patients*** with predefined treatment categories,

1. control CI group ~ 2.5-3.5 l/m/m^2
2. SvO_2 group > 70% SvO_2 or
   < 20% A-V difference
3. CI group > 4.5 l/m/m^2

- principal diagnostic groups included,

a. multiple trauma
b. high risk post-operative
c. massive blood-loss / transfusion
d. septic shock or sepsis syndrome
e. acute respiratory failure, or ARF with COPD

- treatment modalities included volume resuscitation, inotropes (dopamine, dobutamine), vasodilators (SNP, GTN), vasopressors (adrenaline, noradrenaline) as per Shoemaker *et al.*

NB: ***no differences*** in number of dysfunctional organs, length of ICU stay,
or ***mortality*** between the groups,
or for ***subgroup*** analysis of any of the diagnostic categories

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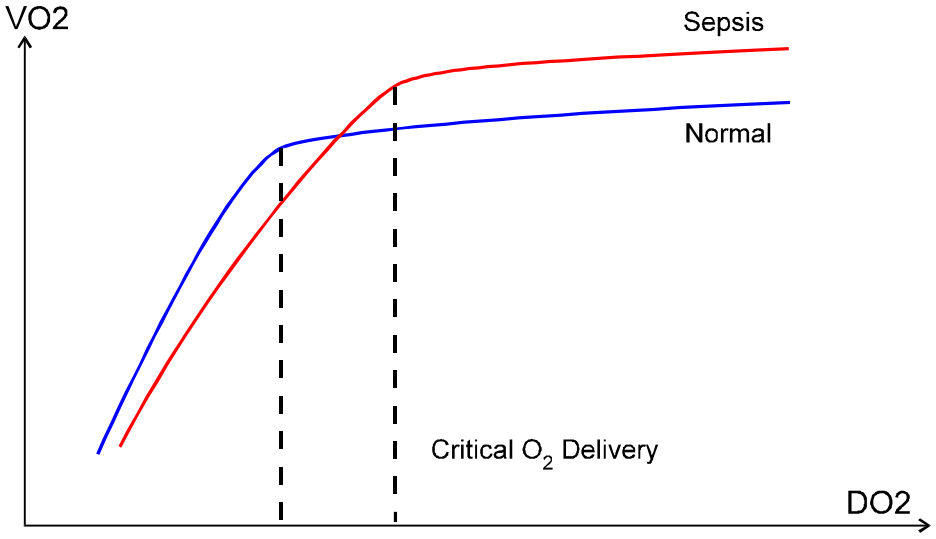
Critical Oxygen Delivery

Def'n: the O_2 delivery value below which VO_2 becomes supply/flow dependent,

1. varies between ***patients***
2. varies between ***organ systems*** in any one patient
3. varies in any one patient in the presence of severe ***disease***



- the "normal" value at rest, critical DO_2 ~ 8 ml/kg/min
  ~ 300 ml/min/m^2
  ~ P_{aO2} < 30 mmHg
- above from pooled human data
- the value found by Ronco *et al.* in dying patients was less than this (R: 3.8-4.5 ml/kg/min)
- but, in a 70kg adult, if VO_2 remained at 250 ml/min, ERO_2 would be 85% !!
- other studies in sepsis have not supported the right-shift of the inflexion point

- theories why this value 'should' increase with surgical stress, ARDS, trauma, sepsis, burns

→ ↑ ***flow dependency*** may be due to,

a. inadequate CO

b. decreased C_{aO2}
   - anaemia, hypoxaemia
   - haemoglobinopathy

c. impaired HbO_2 dissociation
   - hypothermia
   - alkalosis
   - low 2,3-DPG

d. maldistribution of tissue flow
   - AV shunts
   - loss of autoregulation
   - microvascular thromboses

e. impaired tissue O_2 extraction (? ARDS, sepsis)

- this critical DO_2 will be evident by,
    a. no increase in mixed P_{vO2} with increased DO_2
    b. increasing metabolic acidosis, anion gap, plasma lactate
        - the supposition that an increased plasma lactate equates to intracellular hypoxia is not necessarily true (see Pinsky)

- DO_2 can be increased by,
    a. ↑ CI
    b. ↑ [Hb]
    c. ↑ F_IO_2
    d. ↓ the effective shunt fraction
    e. optimizing HbO_2 dissociation - treat metabolic alkalosis
       - correct hypothermia, hypophosphataemia, etc

- a low VO_2 has been shown to be associated with a ***decreased survival***,
    a. < 10 ml/kg/min ~ 20% 12 month survival (? population)
    b. < 10 ml/kg/min - for thoracic surgery

Mixed Venous Oxygen Saturation

- ***Fick Equation***

$$CO = \frac{\dot{V}O_2}{C_{aO_2} - C_{vO_2}}$$

therefore,

$$C_{vO_2} = C_{aO_2} - \frac{\dot{V}O_2}{CO}$$

- the S_{vO2}, and mixed venous P_{vO2} are used for the calculation of,
  a. cardiac output
  b. oxygen flux
  c. pulmonary shunt fraction

- S_{vO2} may be used as a rough guide to CO,
  a. normal ~ 75%
  b. acceptable ~ 60%
  c. cardiac failure < 60%
  d. shock **< 40%**

Low S_{vO2}	High S_{vO2}
• low cardiac output	• high CO & low VO_2
• increased VO_2	• sepsis & shunting
• low P_{aO2}	• hypothermia
• anaemia	• CN^- poisoning

- ***Problems with SvO2***

  a. technical - wedged PA catheter
  b. global not regional
  c. multiple influencing factors
  d. trend more useful than single measurement

CARDIAC TAMPONADE

Def'n: haemodynamically significant cardiac compression, usually due to accumulation of pericardial fluid, resulting in impaired ***diastolic*** ventricular filling

• the amount of pericardial fluid required to produce tamponade varies with the ***rate*** of development,

a. acute ~ 250 ml

b. chronic ~ 250 - 1000 ml

• classically described by ***Beck's triad***,

1. ↑ JVP
2. hypotension
3. a quiet heart

• compensatory changes include,

a. ↑ ejection fraction → ~ 70-80%

b. tachycardia

c. vasoconstriction

▪ ***Aetiology***

a. acute pericarditis - *see later*
   i. viral pericarditis
   ii. other infective - tuberculosis
   - meningococcus, brucellosis
   iii. uraemia, renal failure during dialysis

b. haemorrhagic - traumatic, post-surgery
   - aortic dissection
   - post-infarction
   - anticoagulants & pericarditis
   - malignancy

c. malignant infiltration - lung, breast, lymphoma

d. idiopathic

▪ ***Symptoms***

a. dyspnoea

b. tachypnoea

c. orthopnoea

- ***Clinical Signs***

a. tachycardia with a small volume pulse

b. cool, clammy peripheries

c. hypotension with a large ***pulse paradox***

d. elevated JVP
   - prominent ***x-descent*** (no 'y-descent' as no rapid ventricular filling)
   - ***negative*** Kussmaul's sign

e. muffled or absent heart sounds

f. pericardial rub

g. clear lungs ± LLL bronchial breathing & collapse (Ewart's sign)

h. engorged liver ± spleen

- ***Investigations***

a. ECG: - tachycardia, ***low voltages***, non-specific ST changes
   - ***electrical alternans*** with large effusions

b. CXR: - large globular heart, clear lung fields
   ≥ 250 ml to be visible on CXR

c. Echo: - RA collapse, effusion volume, LV function

d. Swan-G
   - prominent ***x-descent*** in RAP, ie. forward venous flow only in ***systole***
   - equalization of diastolic pressures → RAP, RV, PA, PAOP within 5 mmHg
   - "square-root" pattern ***is not*** prominent

e. AGA's: - metabolic acidosis

f. U&E's

g. FBE

- ***Treatment***

a. 100% O_2

b. large bore IV + colloids to maintain filling pressures

c. ***isoprenaline*** / dobutamine infusion
   - isoprenaline has been shown to ↓ cardiac size, ↓ effective tamponade & ↑ CO

d. monitoring - IABP, ECG, SpO_2
   ± PA catheter

e. pericardiocentesis - emergency under LA
   - in theatre with CPB for haemorrhage

- ***Pericardiocentesis - Indications***

  a. pericardial effusion

  b. pericarditis

  c. trauma → producing ***tamponade***

- ***Complications of Pericardiocentesis***

  1. pneumothorax
  2. coronary artery perforation
  3. ventricular wall perforation
  4. arrhythmias - ectopics common
     - VT, VF
  5. haemorrhage
  6. laceration of the liver
  7. decompressive syndrome - with rapid removal of large volumes
     - pulmonary oedema & LVF
     - usually seen with rapid removal of volumes > 500 ml
     - ∴remove ≤ 200 ml acutely & remainder slowly using indwelling catheter
  8. secondary infection

- features differentiating ***pericardial blood*** aspirate,

  1. does not clot
  2. separates with peripheral halo on a gause swab

Pulsus Paradoxus

Def'n: > 10 mmHg ***decrease*** in systolic BP during ***inspiration***

- ***Mechanisms Spontaneous Ventilation***

  a. ↑ LV afterload

  b. ↓ LV filling
     - ventricular interdependence ∝ ↑ RV filling

  c. negative pressure transmitted to intrathoracic aorta

  NB: greater (-)'ve intrathoracic pressure with respiratory distress

- ***Mechanisms Mechanical Ventilation***

  a. ↓ venous return

  b. ↑ RV afterload → ? ventricular interdependence

- ***Causes***

a.	mechanical ventilation plus	- high P_{IP} - relative hypovolaemia
b.	"obstructive" lung disease	- CAL - asthma - upper airway obstruction
c.	"restrictive" cardiac disease	- tamponade - constrictive pericarditis - restrictive cardiomyopathy

NB: under GA, systolic pressure variation more sensitive for ***hypovolaemia*** than CVP

PERICARDITIS

Def'n: an inflammatory disorder of the pericardium, subdivided by duration,

1. ***acute*** < 6 weeks
   - fibrinous
   - effusive / haemorrhagic
2. ***subacute*** ~ 6 weeks to 6 months
   - constrictive
   - effusive / constrictive
3. ***chronic*** > 6 months
   - constrictive
   - effusive
   - adhesive (non-constrictive)

ECG Changes

1.	stage I	- concave ***ST elevation*** in most leads - V_1 & aVR "spared"
2.	stage II	± return to baseline ST ± ***PR prolongation***
3.	stage III	- widespread ***T-wave inversion*** ? may mimic myocarditis
4.	stage IV	- slow return to baseline ECG

- variations include,
  1. no change
  2. PR segment depression = "apparent" ST segment elevation
  3. ST elevation confined to several leads
  4. electrical alternans with large effusions

- ***Aetiology***

1. ***infectious***
   - i. viral - coxsackie A & B, EBV, HSV
     - influenza, mumps, chickenpox, echoviruses, adenoviruses
   - ii. bacteria - gram +'ves, Staph., *Strep. pneumoniae*
   - iii. TB
   - iv. mycotic
   - v. parasitic - toxoplasmosis, syphilis
2. ***non-infectious***
   - i. idiopathic
   - ii. neoplasm - 1°, 2°, DXRT
   - iii. myocardial ischaemia - AMI, Dressler's synd.
   - iv. iatrogenic - trauma, surgery
     - anticoagulants
   - v. irradiation
   - vi. familial - familial pericarditis, f. Mediterranean fever
   - vii. associated diseases - severe anaemia, ASD
   - viii. others - sarcoidosis
     - leaking aortic aneurysm
3. ***hypersensitivity / autoimmune***
   - i. acute rheumatic fever
   - ii. collagen-vascular disease - SLE, RA, scleroderma, PAN
   - iii. drugs - procainamide, hydrallazine, isoniazid, phenytoin
     - amiodarone, methysergide, practolol, phenylbutazone
4. ***metabolic***
   - i. uraemia
   - ii. myxoedema
   - iii. hypercholesterolaemia
   - iv. ? gout

- ***Investigations***

a. history & examination

b. baseline investigations
   - i. ECG
   - ii. FBE & ESR
   - iii. U&E's, Ca^{++}
   - iv. cardiac enzymes
   - v. CXR — ≥ **250 ml** for visible effusion
   - vi. echocardiogram

c. special investigations
   - i. MC&S — - blood, urine, sputum
   - ii. viral titres — - paired sera
   - iii. mantoux
   - iv. autoantibodies — - ANF, RA, ASOT, monospot
   - v. TFT's
   - vi. serum lipids
   - vii. serum ***ACE level***
     - ↑ levels — - active sarcoid, TB, leprosy, silicosis, asbestosis
   - viii. CT chest — ? tumour
   - ix. pericardiocentesis
     - MC&S
     - AFB's
     - wet prep
     - cytology
   - x. pericardial biopsy

Treatment

a. underlying disease process

b. NSAID's — - aspirin, Indocid, Brufen

c. steroids

d. antimetabolites — - Azathioprine

e. dialysis

f. pericardiocentesis

g. pericardial window

Constrictive Pericarditis

- occurs following acute pericarditis, especially,
    a. chronic idiopathic
    b. chronic renal failure
    c. rheumatoid arthritis
    d. neoplastic
    e. tuberculosis
    f. irradiation

    NB: ***male***:female ratio ~ 3:1

- small pericardial sac restricts filling during end-diastole → ***diastolic pump failure***
- systolic function is usually normal, in contrast to ***restrictive cardiomyopathy***

Symptoms

a.	dyspnoea	~ 85%
b.	headaches	~ 85%
c.	swollen ankles	~ 70%
d.	abdominal symptoms	~ 65%
e.	weakness/fatigue	~ 30%

Clinical Signs

NB: those of ***right heart failure***

a.	↑ JVP	~ 90%	
b.	hepatomegaly	~ 90%	
c.	ascites	~ 70%	
d.	peripheral oedema	~ 70%	
e.	pericardial 'knock'	~ 40%	(abrupt cessation of diastolic filling)
f.	Kussmaul's sign	- ↑ JVP on ***inspiration***	
g.	splenomegaly		
h.	clear lungs	± left pleural effusion	
i.	Broadbent's sign	- retraction of left chest with systole	
j.	pulsus paradoxus	* ***uncommon*** unless tamponade also exists	
k.	hypoalbuminaemia	- protein losing enteropathy & nephrotic syndrome	

- ***Investigations***

1. CXR
   - pericardial calcification, especially lateral
   - widened mediastinum (venous engorgement)
   - left pleural effusion
2. ECG
   - nonspecific ST changes
   - low voltages
   - tachycardia ± AF
3. PA Catheter
   i. prominent 'x' & 'y' descents
      - ***x-descent*** - rapid filling with atrial relaxation & RV contraction
      - ***y-descent*** - most prominent
        - due to rapid filling in early diastole
        - ie. impaired filling is only in ***late diastole***
      - Friedrich's sign → 'M' / 'W' shaped RAP tracing

   ii. RV diastolic dip & plateau, or "square root" sign
      - this is usually ***not*** observed in tamponade

   iii. positive ***Kussmaul's sign***

   iv. diastolic equalization of pressures

LIGW	Tamponade	Constrictive Pericarditis
• effusion	present	absent
• calcification	absent	frequent
• RA pressure trace	↑ x-descent	↑ x & y-descent[1]
• RV dip / plateau pattern[2]	minimal	prominent
• pulsus paradoxus	prominent	minimal
• Kussmaul's sign	absent	frequent
• diastolic knock	absent	frequent

[1] 'M' or 'W' shaped trace → Friedrich's sign

[2] "Square-root" sign

NB: major haemodynamic difference between ***tamponade*** & contrictive pericarditis is that in the former, restriction to filling occurs ***throughout*** diastole, whereas in the later, restriction is in the later half of diastole

CARDIOMYOPATHY

- ***Aetiology***

1. ***Dilated Congestive Cardiomyopathy***
   - i. idiopathic
   - ii. ischaemic
   - iii. alcoholic
   - iv. familial
   - v. infective
     - viral ~ **40% *Coxsackie B***, Coxsackie A, echoviruses - Influenza A, B, CMV, HBV, HCV, HSV, rubella
     - bacterial - septicaemia, SBE, Strep., diphtheria exotoxin, mycoplasma
     - fungal
     - protozoal - Chagas disease, toxoplasmosis, psittacosis
   - vi. metabolic - hyperthyroidism, phaeochromocytoma, uraemia - glycogen storage disease (type II)
   - vii. nutritional deficiency - thiamin, selenium, ?H_2PO_4
   - viii. autoimmune - RA, PAN, SLE, Kawasaki's disease - scleroderma, dermatomyositis
   - ix. drugs
     - toxicity - adriamycin, daunorubicin, doxorubicin
     - sensitivity - sulphonamides, phenothiazines, lithium - sympathomimetics
   - x. valvular incompetence - chronic AI or MI
   - xi. irradiation
   - xii. peripartum - 36/40 to 5 months post-partum
2. ***Restrictive Cardiomyopathy***
   - i. idiopathic
   - ii. infiltrations - amyloid, sarcoid, neoplasms
   - iii. endomyocardial fibrosis
   - iv. eosinophilic endomyocardial disease - Loeffler's syndrome
   - v. endocardial fibroelastosis
   - vi. glycogen storage disease
3. ***Hypertrophic Cardiomyopathy***
   - i. idiopathic - HOCM, IHSS
   - ii. familial - autosomal dominant
   - iii. Friedrich's ataxia ~ 50%

- ***Clinical Features***

a. persistent / resistant CCF

b. embolic phenomena

c. sudden death - VF / VT

- ***Management***

1. optimisation of CCF
2. anticoagulation - warfarin
3. antiarrhythmics - amiodarone
4. ***transplantation***
   - most patients with LVEF < 25% are dead within 2 years
   - post-operative: 1 year survival ~ 80%
     5 year survival ~ 60%

- ***Transplant Contraindications***

1. age > 55 years
2. widespread vascular disease
3. pulmonary hypertension- PVR > 800 dyne/cm^5/s (R: 150-250)
4. recent pulmonary infarction
5. IDDM
6. active infection
7. neoplastic disease

HOCM / IHSS

- ***Features***

  a. hypertrophic cardiomyopathy

  b. marked ***asymmetrical*** septal hypertrophy

  c. ***autosomal dominant*** inheritance ~ 50% familial

- ***Pathophysiology***

  a. anatomical septal hypertrophy- ASH

  b. markedly reduced LV ***compliance***

  c. ↑ LAP - frequently with LA dilatation & hypertrophy

  d. hypercontractile LV with ***dynamic*** subaortic muscular ***stenosis***
     - only **~ 25%** of patients with ASH demonstrate an outflow tract gradient

  e. systolic anterior motion of anterior MV leaflet ± ***mitral regurgitation***
     - virtually ***all*** LV obstruction is 2° to the mitral valve apparatus

  f. pre & postsurgical involvement of the conducting system with ***arrhythmias***

  NB: the majority of patients present with symptoms of ***diastolic dysfunction***

- ***Symptoms***

  a. exertional angina

  b. effort syncope

  c. palpitations

  d. SOBOE

- ***Clinical Signs***

  a. sharp upstroke, often ***bifid pulse***

  b. double or triple apical impulse (also seen with LV aneurysm)

  c. ESM maximal at the LSE - also at apex
     - increased by valsalva manoeuvre → ↓ LV preload & LVESV

  d. ***mitral regurgitation*** **~ 50%** due to abnormality of the anterior mitral leaflet

  e. normal S_1 and normal or split S_2 ± S_3 and $\mathbf{S_4}$

  f. ↑JVP & prominenent 'a-wave'

  g. post-ectopic ***decrease*** in systolic pressure - Brokenbrough's sign
     ~ pathogmonic

- ***Complications***

a.	sudden death	**~ 2-3%** due to VF/VT
b.	arrhythmias	
c.	syncope	
d.	LVF	*murmur decreases markedly
e.	CAD, angina	

- ***Investigations***

a.	ECG	- LVH + strain changes - septal ***Q-waves*** simulate AMI ± LA hypertrophy
b.	CXR	- often no LVF or cardiomegally
c.	Echo	- anterior septal hypertrophy, large degree of variation - ratio of ***septum:free wall*** ^{3} **1.5:1** ± increase in size of LA ± mitral regurgitation

- ***Exacerbating Factors***

a.	↑ contractility	- sympathomimetics - digoxin & (+)'ve inotropes - tachycardia
b.	↓ preload	→ reduction in ventricular size - hypovolaemia - venodilators (GTN) - ↑ PVR, high airway pressures (Valsalva)
c.	↓ afterload	- vasodilators - regional sympathectomy

- ***Factors Decreasing Dynamic Obstruction***

a.	↓ contractility	- β adrenergic blockers - Ca^{++} entry blockers - volatile anaesthetics
b.	↑ preload	- hypervolaemia - bradycardia
c.	↑ afterload	- vasoconstrictors - metaraminol, phenylephrine

- ***Management***

a. β-adrenergic blockade
   - aim to reduce angina and syncopal episodes
   - effective in ~ 50% of patients

b. Ca^{++} entry blockers

c. diuretics
   - need to be used cautiously, as LV is preload dependent

d. management of arrhythmias * amiodarone ***not*** digoxin

e. partial surgical resection of the septum - myotomy, myomectomy
   - high immediate surgical ***mortality*** **~ 5%**
   - CCF is common in the late post-operative period

- ***Anaesthetic Considerations***

NB: → "***full, slow and tight***"

1. SBE prophylaxis
2. maintain ***filling pressures***
   - the hypertrophied LV is poorly compliant
   - ↓ preload → ↓ LVESV → ↑ dynamic obstruction
3. maintain a slow ***heart rate***
   - tachycardia → ↑ velocity of contraction, ↓ LVESV
     ↓ diastolic perfusion time & coronary perfusion pressure
   - avoid factors likely to precipitate ***atrial fibrillation***
   - detrimental due to loss of atrial contribution to LV filling (≤ 40%) and potentially rapid ventricular response
4. maintain ***afterload***
   - reductions increasing the LV-aortic pressure gradient & obstruction
   - reductions in mean aortic diastolic pressure required for coronary perfusion
5. avoid increases in ***contractility***

NB: the management of ***mitral regurgitation*** in the presence of IHSS varies, in that pharmacological interventions affect MR+IHSS in the ***opposite*** manner to the isolated case

ie. management of ***IHSS*** takes ***precedence***

Anthracycline Cardiotoxicity

- toxicity appears to be ***non-reversible***
- may occur,
    a. early - within the course of therapy, or
    b. late - usually 1-6 months
        - rarely up to 7 years post therapy
- agents include,
    a. adriamycin
    b. ***doxorubicin***
        - toxicity proportional to the ***cumulative dose***
        i. < 500 mg/m^2 ~ 1%
        ii. 500-600 mg/m^2 ~ 11%
        iii. > 600 mg/m^2 > 30%
        - usual doses range from 450-550 mg/m^2
        - concomitant use of cyclophosphamide & DXRT increases incidence
        - some animal work suggests NAC may reduce incidence
    c. duanomycin
    d. duanorubicin

AFTERLOAD

Def'n: the load placed upon the left ventricle during contraction, or,
the input impedance of the systemic circulation;

this is ***directly proportional*** to the myocardial
wall tension at the onset of the systolic ***ejection phase***

- the direct determinants are,
  1. aortic input impedance
  2. aortic valvular resistance
  3. myocardial wall thickness
  4. ventricular diameter

- where myocardial wall ***tension*** is determined by,

$$T \propto \frac{\text{Pressure x Radius}}{\text{Thickness (h)}}$$

- increasing afterload decreases the maximal rate of shortening of the muscle fibres
- ***increased*** afterload results from,
  a. ↑ LV pressure
  b. ↑ LV diameter
  c. ↓ LV wall thickness
  d. aortic valvular disease
  e. ↑ SVR
  f. ↓ aortic compliance → ↑ resistance for constant CO/HR
  g. ↓ mean intrathoracic pressure

- ***decreased*** afterload results from,
  a. ↓ LV pressure
  b. ↓ LV diameter
  c. ↑ wall thickness
  d. ↓ SVR
  e. ↑ aortic compliance
  f. ↑ mean intrathoracic pressure

■ ***Afterload Reduction***

• methods to ***reduce LV afterload*** include,

a. ↓ SNS tone
   i. treatment of hypoxia | hypercarbia | acidosis
   ii. analgesia & sedation
   iii. α_2-agonists - clonidine, dexmedetomidine
   iv. anaesthetics

b. vasodilators
   i. SNP, GTN, trimethaphan, hydrallazine
   ii. prazosin, α-antagonists, captopril
   iii. β_2-agonists

c. CPAP, PEEP

d. ↑ cardiac ejection fraction
   i. mechanical assistance - IABP, LV assist
   ii. surgical correction - AS, coarctation
   iii. correction of dynamic outflow obstruction (HOCM, IHSS)
   - β-blockers
   - Ca^{++} entry blockers

• methods to ***reduce RV afterload*** include,

a. correction of acidosis, hypoxia
b. pulmonary vasodilators - NO, GTN, PGE_1
c. maintain RV perfusion pressure
d. inotropes - isoprenaline, dobutamine
e. decrease mean airway pressure - ↓ PEEP, ↓ V_T, APRV, IRV(?), HFJV
f. treat specific conditions
   - PE
   - Fallot's
   - pulmonary stenosis, mitral stenosis

Normal Cardiovascular Pressures

Right		Left	
CVP & RA	~ 0-3 mmHg diastole ~ 4-8 mmHg systole	PCWP & LA	~ 3-7 mmHg
RV	~ 22-25 / 0 mmHg	LV	~ 120 / 0 mmHg
PA	~ 22-25 / 8 mmHg	BP	~ 120 / 80 mmHg
PA mean	~ 13 mmHg	BP mean	~ 93 mmHg

AORTIC DISSECTION

- ***Aetiology***

a. traumatic

b. mesenchymal abnormalities - cystic medial necrosis

c. atherosclerotic - minimal role

d. ***predisposition***

i. systemic hypertension > **50%** of cases
ii. pregnancy
iii. coarctation of the aorta
iv. aortic valvular disease - AS, bicuspid valve
v. coronary & aortic surgery
vi. Marfan's
vii. Turner's syndrome
viii. Giant cell arteritis
ix. Ehlers-Danlos syndrome
x. polycystic kidney disease
xi. male:female ratio ~ **4:1**

- ***Classification: Stanford***

1. ***type A***
   - DeBakey's - type 1 (64%) with spread to descending aorta
     - type 2 (4%) localised to ascending aorta
   - involve the ascending aorta
   - often younger patients
   - associated with inherited defects
   - commonly involves → ***right*** coronary
     left intercostal, left renal, and left iliac arteries
   - high mortality - tamponade, massive AI, acute LVF
     - compromised cerebral circulation
   - better prognosis treated ***surgically***
2. ***type B***
   - DeBakey's - type 3 (30%), localised to descending aorta
   - older patients
   - associated with hypertension, atherosclerosis
   - die from intrapleural rupture
   - better prognosis treated ***medically***

NB: irrespective of medical/surgical management **~ 50% *mortality*** at 2 days

Clinical Features

1. symptoms
   - i. pain - sudden, severe, "tearing"
     - radiation to back and/or legs
   - ii. mechanical - neurological deficit, TIA/RIND
     - haemoptysis, dyspnoea, dysphagia
   - iii. anxiety, restlessness, "impending doom"
2. signs
   - i. CVS - tachycardia/bradycardia, hypertension/hypotension
     - absent, reduced, assymetrical pulses
     - AI, tamponade
     - SVC syndrome
     - ischaemic limb
   - ii. RSP - pulmonary oedema
     - pleural effusion
     - assymetrical AE
   - iii. CNS - obtundation, hemiparesis, paraparesis

Investigations

1. FBE - leukocytosis, anaemia (haemolysis[§])
2. MBA - renal or hepatic dysfunction
   - metabolic acidosis, ↑ LDH[§]
3. ECG - ischaemia, tachycardia
   - small volts with tamponade, electrical alternans
4. CXR - ***normal***
   - widended superior mediastinum (erect, NGT)
   - loss or normal aortic contour
   - left haemothorax, pleural cap
   - tracheal deviation, inferior displacement of LMB
5. ***contrast CT*** - mediastinal haematoma, false lumen, intimal flap
   - sensitivity > 90%, specificity ~ 100%
6. aortography - low incidence of false positive/negative
7. ***TEE***
   - NEJM 1995, completed studies in 93/101 within 29 ± 12 min
   - 11 positives → sensitivity = 100%
     specificity ~ 98%
   - additional information - LV function, valvular competence
     - tamponade
   - ***but*** operator dependent & blind spots in ascending aorta & other arteries
   - transthoracic echo of no use in diagnosis

AORTIC STENOSIS

- ***Aetiology***

1. congenital bicuspid valve
2. calcific or degenerative
3. rheumatic

NB: may be valvular, subvalvular or rarely supravalvular

- ***Pathophysiology***

a.	normal valve area	**~ 2.5 - 3.5 cm^2**
	• symptoms usually appear	< 0.8 cm^2
b.	chronic ***pressure overload***	- concentric LVH & ↑ LV mass - ↑ QRS voltages - LV failure / decompensation
c.	↓ LVEF and CO	- fixed low output state
d.	LV / aortic root pressure gradient	
e.	↑ LVEDP & ↑ PAOP	- eventually ↑ LAP
f.	↓ coronary perfusion pressure	
g.	↑ myocardial VO_2	
h.	eventually pulmonary hypertension	

- ***Symptoms***

NB: ***late onset*** and indicate ***severe stenosis***

a.	angina	- life expectancy ~ 5 yrs ~ 50% have CAD
b.	effort syncope	- life expectancy ~ 3-4 yrs - eventually LVF ± arrhythmias
c.	SOBOE	- life expectancy ~ 2 yrs

NB: without surgical correction ~ 80-100% of patients with AS are dead within 4 years of developing symptoms (LIGW)

- ***Clinical Signs***

a. pulse - regular, slow upstroke, ***plateau***, small volume

b. BP - narrow pulse pressure

c. heart
   - ↑ LV impulse + pre-systolic ***lift*** → palpable S_4
   - sustained, basal systolic ***thrill***
   - harsh SEM → carotids
   - decrease in A_2/S_2 ± reverse splitting (P_2-A_2)
   - * normal heart size until late
   - S_3 with onset of LVF and severe stenosis

NB: AS + cardiomegaly → AI, MI, CCF & severe end-stage disease

- ***Problems***

1. the murmur may decrease / disappear with the onset of LVF & ↓ CO
2. the pressure gradient is low with LVF
3. in the ***elderly***
   i. murmur is often louder at the apex / LSE
   ii. ***arteriosclerosis*** → ↓ compliance which obscures pulse changes
   iii. other causes of LVF are common

- ***Predominance of AI / AS***

a. pulse characteristic & pulse pressure

b. heart size

c. echocardiography

d. catheterisation

- ***Investigations***

a. ECG
   - SR or AF
   - LVH ± strain
   - LBBB ~ 10%

b. CXR
   - usually normal heart size with convex LV border
   - may have post-stenotic dilatation of ascending aorta
   - valve calcification

c. Echo
   - AV disorganization
   - LVH, LV size and contraction
   - LA size
   - ***not*** good at quantifying severity

d. Catheterisation
   - Ao/LV gradient
   - assessment of LV function and other valves
   - coronary anatomy

Catheter	AV gradient		AV size	
normal	~ 0	mmHg	2.5-3.5	cm^2
mild[1]	0-25	mmHg	1.2-2.0	cm^2
moderate	25-50	mmHg	0.8-1.2	cm^2
severe	**> 50**	mmHg	**< 0.8**	cm^2

[1] "aortic sclerosis"

- ***Medical Treatment***

a. SBE prophylaxis

b. digoxin & diuretics for LVF
   - hypertrophied LV is preload dependent

c. balloon dilatation

d. vasodilators are ***contraindicated***, except in severe LVF

e. cardioversion for sudden onset AF

Anaesthetic Considerations

NB: → ***"full, normal rate & tight"***

1. higher ***filling pressures*** are required for the non-compliant ventricle
   - these are transmited into the pulmonary circulation with the risk of pulmonary oedema, therefore monitoring of PAOP may be necessary
   - in the non-compliant ventricle, mean PAOP ***underestimates*** LVEDP, which more closely approximates the "a-wave" of the tracing
2. avoid factors likely to induce ***atrial fibrillation***
   - atrial contribution to LV filling may be **~ 40%** cf. 15% normally
   - acute onset AF may be associated with LV failure & requires prompt treatment
   - cardioversion in the presence of acute failure may be difficult
3. ***heart rate*** ~ 70-90 bpm is optimal, maintaining ***sinus rhythm***
   - avoid tachycardia / bradycardia as these result in decrease coronary perfusion
4. minimise myocardial ischaemia, ie. maintain ***coronary perfusion pressure***
   i. ↑↑ myocardial VO_2 ∝
      - ↑ muscle mass
      - ↑ pressure work

   ii. ↓↓ myocardial DO_2 ∝
      - ↓ diastolic interval ∝ longer ejection phase
      - ↓ mean aortic diastolic pressure
      - ↑ LVEDP & ↓ subendocardial perfusion
      - ↓ muscle capillary density
      - accelerated atherosclerosis

   iii. avoid decreases in ***SVR*** as these decrease aortic ***mean diastolic pressure***

AORTIC REGURGITATION

	Acute	Chronic
Aetiology:	• bacterial endocarditis • aortic dissection • traumatic • artificial valve failure	• SBE • Marfan's • rheumatic fever • RA, ankylosing spondylitis • psoriasis, Reiter's • UC, Crohn's • myxomatous degeneration • syphilis • osteogenesis imperfecta
Symptoms:	• abrupt onset • pulmonary oedema • cardiogenic shock	• asymptomatic period • palpitations • fatigue • SOBOE • angina (5-10%)
Signs:	• rapid low volume pulse • hypotension • ***normal*** heart size • soft or absent S_1 • loud S_3 • EDM (soft)	• 'water hammer' pulse • low diastolic pressure • LV enlargement • decrescendo DM at LSE • ESM with high CO • apical MDM (***Austin Flint***)
ECG:	• normal • ± ischaemia	• LVH • ± ischaemia
CXR:	• LVF, pulmonary oedema • ± dilated aorta	• ↑ LV & aortic shadow

- ***Aetiology & Physical Examination***

a. rheumatic
b. syphilitic - Argyll-Robertson pupils, tabes dorsalis
c. Marfans - stature, hands, palate
d. SBE - fever, splenomegaly, embolic phenomenon, haematuria
e. rheumatoid - hands, joints, nodules
f. psoriasis - skin, nails, hand joints
g. Reiter's - large joints, urethritis, uveitis
h. Crohn's/Ulcerative colitis - abdomen, nails
i. ankylosing spondylitis - kyphosis, SI joints
j. myxomatous degeneration
k. traumatic dissection

- ***Severity of Incompetence***

a. pulse character - bounding, collapsing, bisferens
b. BP - systolic > 140 & diastolic < 60
c. cardiomegaly & LV heave
d. Austin-Flint murmur * loudness of the murmur is ***not*** a useful guide
e. ECG - LVH & strain
f. aortic root ***angiography*** → 4 grades,
   i. small amount of contrast enters LV during diastole, clearing in systole
   ii. LV faintly opacified during diastole, but not cleared in systole
   iii. LV progressively opacified
   iv. LV completely opacified during first diastole & remains for several beats
g. assessment of ***regurgitant volume***
   i. mild ~ 1-2.9 l/min
   ii. moderate ~ 3-5.9 l/min
   iii. severe ≥ 6.0 l/min
   - volumes up to 25 l/min have been recorded
h. indicators of severe chronic AI are,
   i. cardiomegaly and onset of CCF
   ii. associated ***mitral incompetence***

NB: JLM states early closure of mitral valve an early sign for decompensation

- ***Eponymous Signs***

1.	Corrigan's pulse	→	water hammer pulse
2.	Corrigan's sign	→	neck pulsation
3.	Quincke's sign	→	capillary pulsation in fingers
4.	Muller's sign	→	pulsation of the uvula & palate
5.	de Musset's sign	→	head jerks with systole
6.	Duroziez's sign	→	femoral bruits
7.	Landofi's sign	→	pupils ***dilate*** in ***diastole*** & constrict in systole
8.	Hill's sign	→	increased BP in the legs cf. the arms

NB: these are ***not*** pathognomic of AI, and may be seen with other high output states, sepsis, anaemia, thyrotoxicosis, AV shunt

- ***Anaesthetic Management***

NB: → ***"full, dilated and fast"***

1. ***heart rate*** slightly higher than normal > 80 bpm
   - ↓ LV size as less time is available for diastolic regurgitation
   - reduction in LV size & wall tension offsets VO_2 effects of ↑ HR
   - ↑ subendocardial flow due to higher aortic diastolic pressure and ↓ LVEDP
   - conversely, bradycardia must be avoided
2. BP is often labile & very responsive to vasoactive drugs
   - with appropriate monitoring, vasodilators may be used to,

   i. ↓ SVR & ↑ "forward" pump flow

   ii. ↓ LV distension, 2° mitral regurgitation & pulmonary pressures
   - diastolic hypotension & reduced coronary blood flow must be avoided
   - avoid excess vasoconstriction due to reverse effects
3. myocardial ***contractility*** is usually impaired in both acute & chronic AI
   - VO_2 is increased only moderately as ***volume loads*** increase LV work ~ 10-15%
   - LV ***wall tension*** is only marginally increased until the later stages of the disease

MITRAL STENOSIS

- ***Aetiology***

  a. ***rheumatic***
  b. congenital
  c. rare causes - calcific accumulation

- ***Pathology***

  a. thickened leaflets ± shortening of chordae tendineae
  b. commissural fusion
  c. subvalvular scarring
  d. LA enlargement ± hypertrophy
     ± thrombosis
  e. pulmonary hypertension

- ***Pathophysiology***

  a. diastolic pressure gradient LA-LV determined by - mitral valve flow/area
     - normal area ~ **4.0-6.0 cm^2**
     - symptoms appear at > 50% reduction
     - ↑ LAP to ~ 25 mmHg at ~ 1.0 cm^2
     - ***NB:*** the δP in AS is much greater at this diameter due to shorter systole
  b. ↑ LAP, ↑ pulmonary venous pressure ± pulmonary oedema
  c. ↑ PVR → passive, reversible ***pulmonary hypertension***
     → irreversible pulmonary hypertension later
  d. ↓ CO
  e. ↓ LV filling & LV ***dysfunction***

  NB: the natural history is of a long ***asymptomatic phase***,
  followed by a long symptomatic phase → ***slow progression***

- causes of ***sudden*** deterioration include,

  a. new onset AF
  b. fever, infection, trauma
  c. exercise, pregnancy
  d. SBE
  e. pulmonary embolus

- ***Symptoms***

  a. dyspnoea, orthopnoea, PND

  b. fatigue ∝ ↓ CO, development of PAH

  c. recurrent respiratory infection

  d. acute pulmonary oedema

  e. ***haemoptysis*** - may be severe

  f. chest pain ~ 10%

  g. systemic ***thromboembolism***

- ***Clinical Signs***

  a. malar flush, peripheral cyanosis

  b. small volume pulse ± AF

  c. normal JVP ± loss of 'a' wave

  d. heart - "tapping" apex beat
     - palpable RV impulse & loud P_2

  e. ***auscultation*** * 4 cardinal signs (LIGW → no S_3)

     i. opening snap - implies pliable valve

     ii. mid-diastolic rumble

     iii. presystolic accentuation - in SR ***only***

     iv. loud S_1 - leaflets wide open at onset of systole

- ***Investigations***

  a. ECG - bifid p-wave (p mitrale)
     - biphasic p-wave in V_1 of LA hypertrophy
     - RV hypertrophy (PAH)
     ± AF

  b. CXR - pulmonary venous congestion
     - Kerley B lines ± pulmonary oedema
     - enlarged LA
     - large pulmonary outflow tract
     - mitral valve calcification (lat.)

  c. Echo - assessment of severity
     - exclusion of ***atrial myxoma***
     - LA size and presence of ***thrombus***
     - LV size and function
     - RA / RV size & function

Cardiac Catheterization				
Severity	MV Area		Gradient	
normal	4.0-6.0	cm^2	~ 0	mmHg
mild	1.5-2.0	cm^2	0-5	mmHg
moderate	1.0-1.5	cm^2	5-10	mmHg
severe[1]	**< 1.0**	cm^2	**> 10**	mmHg
Additional Information	• PVR and pulmonary hypertension • LV function • ***coronary artery anatomy*** • other valvular lesions			

[1] gradient often > 20 mmHg at area < 1.0 cm^2

- ***Clinical Assessment of Severity***

a. systolic BP and pulse volume

b. signs of PAH
- RV heave
- ↑ JVP, TR
- loud P_2

c. murmur
- short ***interval*** between $S_2 \rightarrow$OS
- ***loudness*** of murmur

d. loud S_1 and OS represent pliable valve

e. CXR - calcification, LAH, LVH, PA prominence

- ***Treatment Medical***

1. SBE prophylaxis
2. AF
   - digoxin
   - quinidine, cardioversion, warfarin
3. systemic emboli - warfarin
4. dyspnoea - diuretics

- ***Treatment Surgery***

1. valvotomy
2. valve replacement
   - 5-8% mortality
   - only indicated for
     - severe stenosis, ie. MV area < 1.0 cm^2
     - NHYA class III or IV symptoms

- ***Anaesthetic Considerations***

NB: → ***"normal rate, full and tight"***

1. ***heart rate*** is the primary consideration
   - bradycardia markedly reduces CO as the SV is limited by the stenotic valve and the small size of the LV
   - tachycardia is more detrimental, as it decreases LV filling time, hence preload & cardiac output
   - acute pulmonary oedema may occur if AF with a rapid ventricular response occurs
   - this requires aggressive R_X → DCCV, digoxin, verapamil, atenolol
   - digoxin should be continued throughout the operative period in the presence of atrial arrhythmias (? amiodarone)
2. near maximal ***preload*** should be maintained
   - within constraints of pulmonary congestion
   - precise monitoring of LAP or PAOP is desirable, however due to the elevated PVR and pulmonary hypertension,
   i. the PAOP ***is not*** a reliable index of either LAP or LVEDP
      - although ***trends*** may show similar degrees of change
   ii. floating the catheter into the PA may be difficult
   iii. a PAOP tracing may not obtainable
   iv. increased risk of ***PA rupture*** during balloon inflation
   - ∴ insertion of a LA catheter at the time of surgery may be preferrable
   - δLAP-LVEDP ~ 4-7 mmHg across the prosthetic valve is normal
3. progression of disease to ***pulmonary hypertension*** also results in,
   i. ↑ PVR - may limit LA & LV filling
   ii. the RV may fail if its workload is too great
   iii. ***ventricular interdependence*** may also limit LV filling with RV failure
   - ∴ factors tending to ↑ PVR should be avoided,
     ie. hypercarbia, hypoxia and the use of N_2O
4. ***pulmonary hypertension***, RVF and tricuspid regurgitation usually improve over the days to weeks following correction of mitral stenosis, however, the structural changes due to longstanding disease limit the extent of long-term improvement

MITRAL REGURGITATION

	Acute	**Chronic**
Aetiology	• spontaneous chordae rupture • papillary muscle rupture • LV ischaemia • SBE • trauma • prosthetic valve malfunction	• mitral valve prolapse • papillary / LV infarction • rheumatic fever • cardiomyopathy, HOCM • chronic AI • calcific annulus • Ehlers-Danlos, Marfan's synd. • Hurler's syndrome
Pathology		
LV:	• normal sized	• eccentric hypertrophy • dilatation • increased compliance
LA:	• normal ± small increase • ***large*** pressure increase	• dilatated & thin walled • increased compliance
Symptoms	• abrupt onset severe dyspnoea • pulmonary oedema • cardiogenic shock • RVF, peripheral oedema • SOBOE • orthopnoea, PND	• long asymptomatic phase • palpitations • fatigue
Signs	• often in SR • sharp small volume pulse • AB not displaced • RV^{++} & LV hyperdynamic • variable murmur • $S_4 \pm S_3$, $\uparrow P_2$, split S_2 • RVF ***early***	• often in AF • AB displaced & hyperdynamic "thrusting" • soft S_1, apical PSM + thrill • added sounds, S_3 • RVF ***late***
Investigations		
ECG:	• SR or SVT • AMI changes	• AF • p mitrale & biphasic p-V_1 • LVH, RVH
CXR:	• normal LA, LV • pulmonary oedema	• increase LA^{++} ***and*** LV^{++} • later not seen with pure MS

- ***Pathophysiology Acute***

  a. severe MR into relatively non-compliant LA → ***high pressure***
  b. marked ↑ PAOP with large 'v' wave
  c. PVH & PAH → ***early RVF***
  d. compensatory ↑'s in SNS tone → ↑ regurgitant fraction & worsens failure
  e. normal LV function - unless infarction & rupture is origin of MR
  f. early onset of clinical heart failure

- ***Pathophysiology Chronic***

  a. gradual increase in the regurgitant fraction
  b. gradual increase in LA size & ***compliance***
  c. late onset of significant increase in LVEDP & PAOP
  d. irreversible LV dysfunction occurs ***before*** deterioration of ejection phase and clinical heart failure

- ***Other Investigations***

a.	Echo	- aetiology, other valves - LV size and contractility - LA size
b.	RNVG	- EF, LV volumes
c.	Catheter	- severity of regurgitation - haemodynamic effects - LV function - ***coronary anatomy*** & other valves

- ***Assessment of Severity***

a.	clinical	- heart size, LV heave, diffuse AB - S_3 & signs of CCF, ***length*** of murmur - PAH
b.	CXR	- ↑ LA, LV * degree of LVF
c.	ECG	- AF, LVH
d.	Catheter	> 0.6 ***regurgitant*** fraction → CCF

NB: BP, pulse, loudness of murmur of ***no*** significance
differentiation of MI vs MS → ***pulse volume*** and ***heart size***

Treatment

- ***Medical***

1. CCF / dyspnoea - diuretics & vasodilators, ACEI
2. AF - digoxin
3. SBE prophylaxis
4. systemic emboli - warfarin

- ***Surgery***

1. valve repair
2. valve replacement

- ***Anaesthetic Considerations***

NB: → ***"full, fast and loose"***

1. ***heart rate*** should be maintained at normal to tachycardic levels
   - bradycardia → ↑ LV volume, ↑ regurgitant fraction, ↓ CO
2. factors ***decreasing*** the regurgitant fraction,
   - ↓ afterload
   - vasodilators
   - regional anaesthesia
3. factors ***increasing*** the regurgitant fraction,
   - ↑ afterload
   - ↑ SNS tone - pain, hypoxia, hypercarbia, acidosis
   - slow HR
   - N_2O
4. myocardial ***contractility*** is decreased
   - the myocardium is more sensitive to depressant drugs
   - increasing ***preload*** → LV dilatation & increased regurgitant flow
5. following valve replacement there is the risk of ***ventricular rupture***
   - especially in elderly patients
   - usually transverse & ? due to loss of ventricular support by the valve mechanism
   - measures to reduce the risk include,
     i. continued CPB
     ii. IABP to decrease afterload
     iii. vasodilators & antihypertensive agents

Mitral Valve Prolapse

- ***Incidence***

  a. ***females*** ~ 17% at 20-30 yrs
  - decreasing with age

  b. males ~ 2-4%
  - constant with age

  c. overall ~ 4-5%

- ***Aetiology***

  a. ? dominant inheritance in some families

  b. connective tissue abnormality

  c. congenital / embryological

  d. neuroendocrine disease

- ***Congenital Associations***

  a. ostium secundum defects

  b. HOCM, IHSS

  c. long QT syndrome

  d. WPW syndrome

  e. Marfan's syndrome

  f. Ehler's-Danlos

  g. Ebstein's anomaly (TI)

  h. Turner's syndrome

- ***Complications***

NB: usually very low,
however, occur more commonly in the presence of,

1.	symptoms	- syncope, palpitations
2.	LV dilatation	> 5.9 cm male > 5.5 cm females
3.	abnormal resting ECG	
4.	increasing age	≥ 40 yrs
5.	female > male	
6.	murmur	* MR not MVP
7.	redundant valve leaflets	

NB: LIGW states, symptomless patients with a mid-systolic click only ***are not*** at increased risk of sudden death,

those with a mid-systolic click and late systolic murmur, with ***symptoms*** of LV dysfunction and significant mitral regurgitation, often have valve leaflet thickening > 5 mm and are at ***increased risk*** of,

i. sudden death
ii. endocarditis
iii. stroke

- complications include,
  a. ***arrhythmias**** - AE's/VE's ~ 55%
     - SVT ~ 6%
     - VT ~ 6%
     - sudden death ~ 1.4%
  b. sudden death
  c. thromboembolism
  d. mitral insufficiency
  e. bacterial endocarditis
  f. aortic dissection
  g. chordae rupture

- * these are increased by,
  a. increases in SNS tone
  b. administration of catecholamines
  c. type I antiarrhythmics
  d. prolonged QTc

- ***Clinical Presentation***

  a. chest pain - atypical
  b. palpitations / arrhythmias
  c. rarely progress to MI
  d. systemic thromboembolism

- ***Clinical Findings***

  a. mid-systolic click
  b. mid/late systolic murmur → apex & LSE
     - increased by reducing afterload - valsalva, vasodilators
  c. ECG - ST/T wave changes inferiorly
     - arrhythmias
  d. Echo - very sensitive = "gold standard"

PULMONARY STENOSIS

- ***Aetiology***

1. congenital
   - most common ~ 10% of CHD
   - often complicated ± Fallot's tetralogy, PDA, VSD
     - rubella
2. rheumatic fever*
3. carcinoid syndrome* *rare causes
4. IV drug users

- ***Clinical Findings***

a. symptoms - dyspnoea, fatigue, syncope, angina

b. signs
- small volume pulse
- cannon 'a' wave
- RV heave & pulmonary thrill
- ESM at LSE $\rightarrow$ left shoulder
- increases with inspiration
- split S_2, soft P_2

± pulmonary ejection click
- hepatic pulsation, peripheral oedema, etc.

c. ECG - RAH, RVH ± strain, RBBB

d. CXR
- enlarged pulmonary outflow (post-stenotic dilatation)
- oligaemic lung fields

- ***Indications of Severity***

1. symptoms
2. cannon 'a' wave
3. opening click proximity to S_1
4. ***length*** of murmur
5. RV hypertension ?RV > 70 mmHg

ATRIAL SEPTAL DEFECT

	Ostium secundum	**Ostium primum**
Frequency:	• **95%**	• 5%
Features:	• usually uncomplicated • often asymptomatic • low incidence endocarditis • high incidence of late AF	• ± MI, TI, VSD • symptomatic • frequent endocarditis
ECG:	• RAD, partial RBBB • RVH • AF	• LAD - superior axis • RVH - ↑ $R\text{-}V_1$ • conduction defects

- ***CXR***

  a. ↑ RA, RV

  b. plethoric lungs, PA truncus may be very large

  c. small aortic shadow

- ***Clinical Features***

  a. congenital anomaly ~ **7-10%** of CHD

  b. small volume pulse

  c. RV heave

  d. pulmonary flow murmur * ***not*** due to flow through ***defect***

  e. fixed splitting of S_2

  f. R→L communicaton demonstrated by 2D-echo in **~ 80%**

  g. other signs with ostium primum

- ***Complications***

  a. ↑ PBF - pulmonary hypertension
  - frequent infections
  - obstructive airways pattern

  b. AF

  c. TI

  d. endocarditis

  e. R→L shunt ? up to 80% (Harvey, AIM'86)

- ***Indications for Surgery***

1. R:L flow ratio ³ **2:1** (> 1.5:1 *HPIM)
2. the presence of other valve lesions
3. before reversal of shunt
   - ie. ***absence*** of marked pulmonary hypertension
   - high risk of postoperative RV failure
4. ***operative mortality***
   - i. patients < 45 years without CCF < 1%
   - ii. peak PA pressures < 60 mmHg < 1%
   - iii. higher risk patients ~ 5-10%
     - age > 60 yrs
     - PAP > 60 mmHg
     - CCF - ↑ JVP, S_3, SOBOE

Patent Foramen Ovale

- incidence of ***probe patent*** foramen ovale at autopsy in adults **~ 25%**
- R→L shunting may occur in conditions of,

1. acute pulmonary hypertension
   - i. pulmonary embolism - other embolic disorders (AFE, FAT, etc)
   - ii. RV infarction
   - iii. ARDS
   - iv. post-pneumonectomy
2. chronic pulmonary hypertension
   - i. CAL - any cause
   - ii. primary pulmonary hypertension
   - iii. recurrent PTE

- PFO and R→L shunting characterised by,

1. ***platypnoea*** - dyspnoea on assuming upright posture
2. ***orthodexia*** - arterial desaturation accentuated by upright posture

- these signs are also seen in ***hepatopulmonary syndrome***
- predominance of abnormal AV communication in bases results in worsening hypoxaemia with upright posture

PATENT DUCTUS ARTERIOSUS

a. incidence ~ 1:2,500 overall
~ 10% of CHD

b. clinical significance *effects depend upon,
   i. size of communication
   ii. difference in SVR & PVR

c. predisposing factors,
   i. prematurity
   ii. IRDS
   iii. fluid overload
   iv. hypoxia, acidosis
   v. congenital rubella
   vi. familial

Clinical Features

a. dyspnoea, SOBOE, CCF

b. widened pulse pressure

c. delay in A_2 ∝ degree of shunt flow → single S_2 | reverse split S_2

d. continuous ***"machinery" murmur*** with systolic accentuation
   • maximal at 2nd ICS, LSE

e. LV heave ∝ volume overload

f. recurrent respiratory infections

g. risk of SBE
   • lesions more common on the ***pulmonary side*** of the ductus

Investigation

a. CXR - ↑ LA, LV, PA & large aorta
* pulmonary plethora

b. ECG - LVH

c. PAC - "step-up" in SO_2 from RV to PA

d. echo - helpful but best visualised by ***aortography***

- ***Treatment***

a. neonatal
   i. correction of hypoxia, acidosis
   ii. diuretics to counter fluid overload/gain
   iii. ***indomethacin*** ~ 0.1 mg/kg

b. child/adult
   i. surgical closure - ***all*** shunts L→R without pulmonary hypertension
   ii. catheter closure - may be procedure of choice for most patients

Prosthetic Valves

1. SBE prophylaxis
2. anticoagulation
3. routine "line" care
4. haemolysis
5. mechanical dysfunction

NB: 1. ALL ***regurgitant murmurs*** are abnormal
2. outflow obstruction is difficult to assess

COARCTATION OF THE AORTA

- ***Essential of Diagnosis***

1. presentation
   - i. infants - present with ***severe CCF***
   - ii. children / adults - usually asymptomatic
     - present with upper body ***hypertension***
2. absent or weak femoral pulses
3. ***systolic*** pressure gradient between upper/lower limbs (diastolic BP similar)
4. harsh systolic murmur heard in the back
5. investigation
   - i. ECG - LVH
     ± ischaemic changes
   - ii. CXR - rib notching
     ± "3-sign": abnormal aortic knuckle
     enlarged subclavian artery
     post-stenotic dilatation
   - iii. echo-doppler is diagnostic

• stenosis is virtually always just distal to the origin of the left subclavian artery
• ***bicuspid aotric valve*** is present in **~ 25%**
• this group may have an associated murmur of ***aortic incompetence***
• most untreated adult patients die before age 40 yrs due to complications,

1. hypertension induced LVF
2. cerebral haemorrhage due to associated ***cerebral aneurysms***
3. aortic dissection / rupture
4. infective endarteritis

• surgical resection has an operative mortality **~ 1-4%**
• post-repair ~ 25% remain hypertensive
• ***balloon angioplasty*** has been performed and may be procedure of choice, especially for recurrent stenosis, but aortic tears have been described

CARDIOPULMONARY RESUSCITATION

- ***Indications for Prolonged Resuscitation***

  a. children
  b. hypothermia
  c. drowning
  d. drug overdose
  e. electrocution

- ***Causes of Reversible 'Asystole'***

  a. fine VF
  b. hyperkalaemia
  c. severe acidosis
  d. high parasympathetic tone
  e. artefactual - ie. lead misplacement

- ***Causes of Electromechanical Dissociation***

  1. "nothing to fill with"
     i. hypovolaemia - absolute | relative
     ii. anaphylaxis
  2. "inability to fill"
     i. pericardial tamponade
     ii. tension pneumothorax
     iii. ruptured heart
     iv. massive pulmonary thromboembolism
     v. other embolic - air embolism, CO_2
  3. "inability to pump"
     i. massive ischaemia / infarction
     ii. severe metabolic disturbance
        - hypoxia
        - hypothermia
        - hypokalaemia, hypocalcaemia, hypermagnesaemia
     iii. post cardiopulmonary bypass
     iv. drug overdose - Ca^{++} entry blockers
        - β-adrenergic blockers

- ***Causes of Ventricular Tachycardia***

a. ischaemic heart disease
b. biochemical derangement - hypokalaemia, hypomagnesaemia
c. drugs - antiarrhythmics, tricyclics
   - catecholamines, cocaine, local anaesthetics
   - anticonvulsants, volatile anaesthetics
d. cardiomyopathy - idiopathic, drug induced, infective
e. prolonged QT syndrome
   i. congenital
   ii. acquired - biochemical, drug induced
f. electrocution

- ***Complications of Resuscitation***

a. complications related to ***intubation***
   i. failure to intubate, oesophageal intubation
   ii. aspiration
   iii. airway trauma
b. complications related to ***ECM***
   i. chest wall - fractured ribs
      - fractured sternum
   ii. lungs - pneumothorax, haemothorax
      - pulmonary contusion
      - pulmonary oedema, ARDS
      - bone marrow, fat emboli
   iii. abdominal - ruptured diaphragm, liver or spleen
      - especially in children
c. complications related to ***defibrillation / cardioversion***
   i. failure of cardioversion
   ii. induction of a worse rhythm
   iii. myocardial damage
   iv. skin burns
   v. bystander electrocution
d. complications related to ***organ ischaemia / hypoxaemia***
   i. cerebral infarction, encehpalopathy, oedema
   ii. ischaemic hepatitis, ischaemic colitis
   iii. acute renal failure
   iv. myocardial infarction
e. drug side-effects

Open Chest Cardiac Massage

a.	cardiac diseases	- severe aortic stenosis* - valvular incompetence* - tamponade* - aortic dissection, rupture* - massive pulmonary embolus - ventricular wall or septal rupture - dilated cardiomyopathy
b.	chest wall injuries	- flail chest* - penetrating chest injuries* - barrel chest* - diaphragmatic rupture*
c.	pulmonary disease	- pneumothorax - emphysema - large lung cysts
d.	cardiothoracic surgery*	
e.	severe hypothermia*	

NB: * situations where open massage ***may*** be effective when closed massage is not

Cardioversion / Defibrillation

Def'n: ***Cardioversion***: synchronised electrical discharge used in the treatment of tachyarrhythmias, in the presence of cardiac output

Defibrillation: asynchronous electrical discharge for the treatment of pulseless VT / VF

- ***Indications for Cardioversion***

1. AF ≤ 6 months duration ~ 80% successful
2. atrial flutter*
3. SVT* *~ 95% successful
4. VT with pulse*

Initial Energies	
SVT & atrial flutter	~ 30-50 J
VT with pulse	~ 50-100 J
AF	~ 100-200 J
VT (without pulse) / VF	~ 200^{+} J (3-5 J/kg)

- ***Complications***

a. those associated with ***anaesthesia***,
   i. pain / awareness
   ii. respiratory depression, aspiration
   iii. hypotension, hypoxaemia
   iv. myocardial ischaemia
   v. hyperkalaemia - SCh

b. ***electrical*** complications,
   i. burns
   ii. cardiac arrest - especially if unsynchronized
   iii. myocardial damage

c. those associated with a new ***rhythm***,
   i. failure of version
   ii. establishment of a worse rhythm - bradycardia, VT/VF
   iii. recurrence of the original arrhythmia
   iv. systemic emboli (AF → SR)
   v. hypotension
   vi. pulmonary oedema

- ***Contraindications - Relative***

  a. chronic arrhythmia > 6 months

  b. metabolic or toxic cause for the arrhythmia
     - ? this would include almost ***all*** ICU patients

  c. full stomach

  d. no consent

- ***Contraindications - Absolute***

  a. high risk of systemic ***emboli***

  b. digoxin toxicity

  c. inadequate resuscitation facilities

- ***Factors Associated with Failure***

  a. pericarditis

  b. myocarditis / cardiomyopathy

  c. septicaemia

  d. left atrial enlargement

  e. sick sinus syndrome

  f. thyrotoxicosis

  g. biochemical disturbance

  h. drug toxicity

  NB: in these cases management with ***antiarrhythmics*** should be pursued

Bicarbonate Administration

NB: "unanimous feeling that the routine administration of bicarbonate was counterproductive" (AHA, JAMA 1986)

- ***no*** studies demonstrate a benefit in outcome, most show deleterious effects
- 100 mmol of HCO_3^- produces 2.24l of CO_2, therefore the P_{aCO2} will rise if ventilation is fixed
- is only the R_X of choice where the origin of the acidaemia is loss of bicarbonate
- the dose of HCO_3^- is usually calculated on the empirical assumption that the ion has a V_D ~ 50% of body weight
- this takes into account diverse buffer reactions in both ECF & ICF, however becomes inaccurate with severe metabolic acidosis
- initial correction should be aimed at ≤ ½ this amount as the initial action is in the ECF
- the AHA recommendations for administration include;

1. CPR > 10 minutes
2. an increase in V_M possible (ie. ventilated)
3. AGA's → pH < 7.2
4. R_X ≤ 1 mmol/kg slowly IV

- theoretical problems associated with administration include;

1. paradoxical ***ICF acidosis*** - CO_2 → ICF
2. excess may produce an ***ECF alkalosis***;
   i. shifts the Hb-O_2 curve to the ***left***, decreasing O_2 availability at a cellular level
   ii. shifts K^+ into cells and may result in:
   - hypokalaemic cardiotoxicity in K^+-depleted patients
   - tetany in renal failure or Ca^{++} depletion
3. excessive ***Na^+ load*** → cardiovascular decompensation ± CCF
   - solution is 1M, ie. 50 ml = 50 mmol of both Na^+ & HCO_3^-
4. CSF equilibrates slowly with $[HCO_3^-]_{pl}$, therefore ventilation may be maintained despite the increase in $[HCO_3^-]_{pl}$, resulting in a ***respiratory alkalosis***
5. where the acidaemia is due to organic acids, the subsequent metabolism of such acids and regeneration of HCO_3^- will produce a ***metabolic alkalosis***

Indications for Calcium

a. ionized hypocalcaemia
b. hyperkalaemic cardiotoxicity
c. overdose with Ca^{++} entry blockers
d. post-CPB
e. massive transfusion - citrate toxicity

- ***Disadvantages***

a. myocardial irritability → pro-arrhythmic
b. coronary vasospasm
c. increased intracellular VO_2
d. sustained contraction
e. increased post-anoxic brain damage & cerebral vasospasm
f. ? increased reperfusion injury

NB: there is ***no*** evidence Ca^{++} is of benefit in CPR,
conversely, there is some animal evidence for benefit with CEB's

Hypomagnesaemia and Cardiac Arrhythmias

- Mg^{++} follows K^{+} closely in the ICF
- hypomagnesaemia < 0.7 mmol/l
- useful in the treatment of,

a.	tachyarrhythmias	- VT, AF - torsade de pointes VT - digoxin overdosage
b.	suspected Mg^{++} depletion	- ETOH abuse - malnourished - chronic diuretic use

- there is evidence in the treatment of SVT, see recent paper by TQEH group in CCM 1995
- the standard 5 ml ampoule = 10 mmol = 2.5 g
- 1 gram of $MgSO_4$ ~ 4 mmol of Mg^{++}

TQEH Protocol

a.	correct K^{+} to > 4.0 mmol/l and wait for 1 hr			
b.	loading dose	=	0.037 g/kg	~ 2.5g / 70kg mmol IV / 5 mins
c.	infusion	=	0.025 g/kg/hr	~ 3.5 ml/hr / 70kg
d.	target plasma Mg^{++}	~	1.8-2.0 mmol/l	

NB: halve rate if plasma [Cr] > 200 µmol/l or U/output < 30 ml/hr

if rate not controlled in 12 hrs, cease infusion and commence ***amiodarone***

CENTRAL VENOUS CATHETERIZATION

- ***Indications***

a. measurement of central venous pressure
b. infusion of hypertonic | irritant fluids - TPN, inotropes, HCl
c. large volume infusions
d. difficult vascular access
e. other therapy
   - pacemaker
   - PA catheter
   - haemodialysis / haemoperfusion
   - plasmapheresis

- ***Complications***

1. during ***insertion***
   i. failure to site in SVC
      - cephalic ~ 55%
      - basilic ~ 35%
      - EJV ~ 10%
      - subclavian ~ 5% (± up to 25%)
      - IJV ~ 0-4%
   ii. pneumothorax
      - subclavian ~ 2%
      - IJV ~ 1-2%
   iii. arterial puncture
      - subclavian ~ 5%
      - IJV ~ 1-2%
   iv. haematoma
   v. structural damage
      - nerves - vagus, recurrent laryngeal, stellate ganglion, cervical plexus
      - trachea
      - thoracic duct
2. during ***use***
   i. colonization, infection, bacteraemia / septicaemia
   ii. venous thrombosis
   iii. embolism - thrombus, septic thrombus, air, catheter tip
   iv. venous perforation - especially older stiff catheters
   v. AV fistula
   vi. accidental removal
   vii. migration - fluid administration to pleural cavity
3. during ***removal***
   i. haemorrhage / haematoma
   ii. air embolism

Anatomy IJV

- continuation of the ***sigmoid sinus***
- passes down the neck in the ***carotid sheath*** with the carotid artery and vagus nerve
- lies lateral and superficial to the internal and common carotid arteries
- the ***left*** joins the subclavian to form the ***innominate vein*** at the medial margin of ***scaleneus ant.***
- the ***right*** joins the subclavian vein behind the sternoclavicular joint
- there is one valve present at the junction

Anatomy EJV

- formed by the junction of the ***posterior facial*** and ***posterior auricular*** veins at the angle of the mandible, inside the parotid gland
- runs deep to the platysma and superficial to sternomastoid
- pierces the deep cervical fascia just above the mid-clavicular point
- usually enters the ***subclavian vein*** at an acute angle, rarely enters the IJV
- there are two valves present

Anatomy Subclavian

- formed as a continuation of the ***axillary vein*** at the outer border of the first rib
- joins with the IJV at the medial border of scaleneus anterior
- courses behind the clavicle and subclavius muscle

a.	structures behind and above	- the subclavian artery - scaleneus anterior - the phrenic nerve
b.	structures posterior	- first rib - Sibson's fascia - pleural dome - the lung

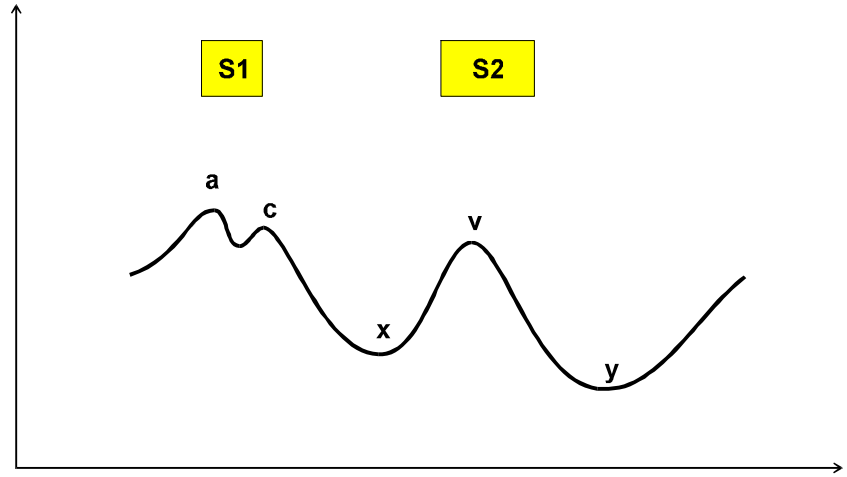
- tributaries include the EJV and occasionally the anterior jugular or cephalic veins
- the left subclavian vein receives the ***thoracic duct***
- the right receives the right lymphatic duct
- usually has two valves

Central Venous Pressure

Def'n: hydrostatic pressure measured in the SVC or at the SVC/RA junction
normal range ~ **3-10 cmH_2O**

- the ***zero point*** (supine) is the 4th ICS, mid-axillary line ~ 5 cm below the sternum
- usual waveforms, only assessable on ***recorded*** pressure tracing,

1. 'a' wave - ***atrial*** contraction (absent in AF)
2. 'c' wave - ***closure*** & bulging of tricuspid valve in isovolumetric contraction
3. 'x' descent - atrial relaxation & descent of tricuspid valve annulus with contraction
4. 'v' wave - atrial filling ± ***valvular*** bulging
5. 'y' descent - tricuspid valve opening & rapid ventricular filling phase



- ***Abnormal Waveforms***

a. cannon waves
- AV dissociation | junctional rhythm
- VT *important clinical sign versus SVT
- VVI pacing

b. large 'a' waves
- TS, PS
- pulmonary hypertension
- RVF
- RA myxoma

c. large 'v' waves
- TI

d. rapid 'x' descent
- tamponade
- constrictive pericarditis

e. rapid 'y' descent
- constrictive pericarditis

NB: in ***tamponade***, rapid filling only occurs with descent of the AV annulus in systole

- ***Raised CVP > 10 cmH_2O***

  a. acute hypervolaemia
  b. congestive cardiac failure
  c. RV infarction / ischaemia
  d. cor pulmonale, RV failure
  e. tamponade
  f. constrictive pericarditis, restrictive cardiomyopathy
  g. pulmonary embolus
  h. SVC obstruction
  i. IPPV
  j. tricuspid incompetence

- ***Lowered CVP < 3 cmH_2O***

  a. acute hypovolaemia - haemorrhage
     - GIT / renal losses, burns
  b. high output cardiac failure
     i. septicaemia / SIRS
     ii. thyrotoxicosis
  c. decreased sympathetic tone - spinal shock, anaphylaxis
     - spinal / epidural anaesthesia
  d. drugs - vasodilators, histamine release

- ***Correlation CVP ^{1} LAP***

  NB: ***poor*** correlation with,

  1. impaired LV function
     i. EF < 40%
     ii. LV dyskinaesia
     iii. myocardial ischaemia
     iv. LAP > 15 mmHg
     v. right heart disease
  2. severe pulmonary disease
     i. cor pulmonale
     ii. acute lung injury
     iii. pulmonary vascular disease / hypertension

PA CATHETERS

- ***West Zone 3 Criteria***

1. 'a' & 'v' waves visible on PAOP trace
2. mean PAOP ≤ PADP (except with large 'v' waves)
3. blood freely aspirated from distal port
4. aspirated blood has a high $P_{O2} \sim P_{aO2}$

• changes from zone 3→2→1 occur with,

a. hypovolaemia
b. high PEEP > 10 cmH_2O
c. poor catheter position
d. poor patient position

- ***Effective Pulmonary Capillary Pressure***

$$P_C = P_{LA} + 0.4 \times (P_{mPA} - P_{LA}) \qquad \textbf{Garr Equation}$$

• P_C is determined by,

a. mean PA pressure
b. LAP
c. alveolar pressure
   - PEEP → ↑ LAP & PAP
     → ↑ $P_C \sim 0.5 \times$ PEEP

NB: but surely the important pressure is ***transcapillary pressure***,
ie. pulmonary capillary - pulmonary interstitial pressure,
∴"extrinsic" causes of raised P_C should be clinically less important

- the pulmonary capillary pressure (P_C) = the dynamic pulmonary capillary hydrostatic pressure
- this is the pressure responsible for ***hydrostatic pulmonary oedema***,

PAOP ~ LAP, but PAOP ¹ P_C

® PAOP < P_C

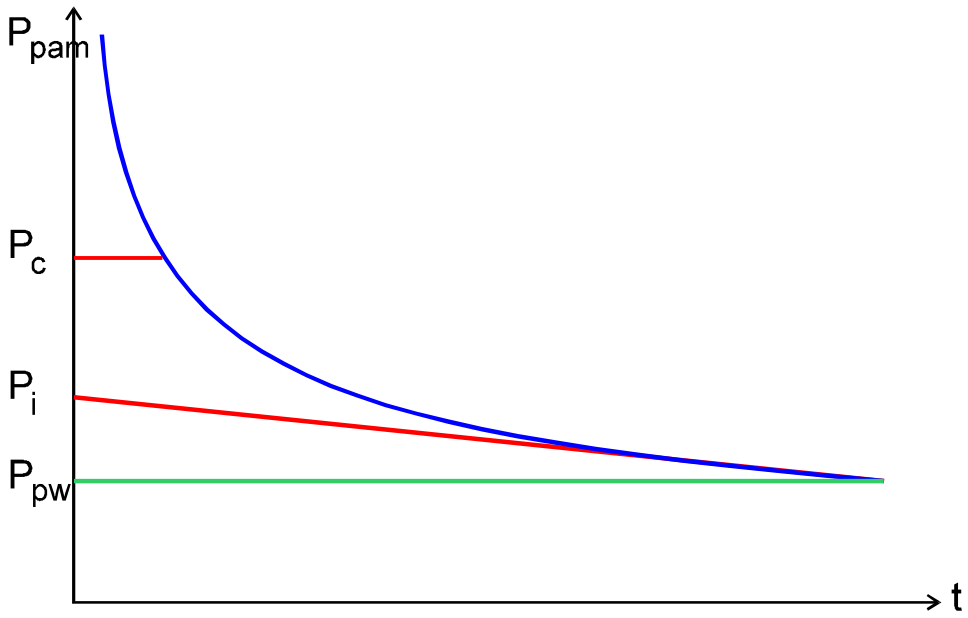
- this can be calculated upon occlusion of the PA tracing → bi-exponential decay
- ***extrapolating*** the second phase to time zero gives an ***intercept pressure***, P_i where,

P_C ~ PAOP + P_i

- alternatively, the pressure at the ***inflexion point*** of the decay curve ~ P_C
- by these techniques it is possible to determine the predominant site of PVR in health and disease states,

1. PAP >> P_C ~ PAOP → most PVR is ***precapillary***
2. PAP > P_C >> PAOP → most PVR is ***postcapillary***

- using this technique it has been demonstrated that most of the increase in PVR,
  1. with ***histamine*** is postcapillary (ie. venous)
  2. with 5HT is precapillary



PA Catheters - Complications

1. complication rate similar to CVC catheters
2. minor complications common
   - arrhythmias
   - haematoma
   - catheter thrombosis
3. major complications rare
   - carotid puncture ~ 1-4%
   - pneumothorax ~ 0.5%
   - infection ~ 1-2%
   - PA rupture ~ 0.1%
   - pulmonary infarction < 7%
4. major problems = ***misuse & misinformation***

Author	Shah *et al*[1]	Davies, Cronin	Other
Patients	6,245	220 (1982)	
Carotid artery puncture	1.9 %	3.6 %	
Pneumothorax	0.5 %	-	
Arrhythmias	**72 %**	**25 %**	**17-28 %**
• **VEB's**	**67 %**	**24 %**	
• persistent VEB's	3.1 %	-	
• AEB's	1.3 %		
• SVT	0.5 %		
• transient RBBB	0.05%		
• 3°HB	0.016%		
Bacteraemia/Sepsis	**~ 5 %**	1.4 %	0-2 %
PA rupture	0.064%		
PE/pulmonary infarct	0.064%	0.5 %	≤ 7%
Balloon rupture		0.5 %	

[1] Shah, Rao, El Etr Anaesthesiology, 1984 61:271-5

- ***Other Complications***

1. complications of insertion
2. thrombotic endocardial vegetation ≤ 1%
3. valvular damage / papillary muscle damage
4. catheter knotting
5. erroneous or misleading information

PA Catheters - Misleading Information

- the primary assumption, that **PAOP ~ LVEDP**, holds true for 90-95% of "normal" subjects
  → tolerance limits **± 0-4 mmHg**

- on balloon inflation, at time = 0, the systolic component is lost and PAOP ~ PADP
- the pressure then falls away ***bi-exponentially*** to approach LAP, the rate of decay depending upon,

a. diastolic time
b. pulmonary vascular resistance* **time constant* = R.C
c. pulmonary vascular compliance*

- the value should be taken at ***end diastole*** and ***end expiration*** (SV & IPPV)

- ***Potential Problems***

1. **PAOP > P_CP** up to 11 mmHg
   i. tachycardia - inadequate time for EDP to equilibrate with LAP
   ii. PA hypertension - hypoxia, hypercarbia, acidosis
   - CAL
   - 1° PAH
   → prolongation of time constant

2. **PAOP < P_CP** up to 7 mmHg
   i. RBBB - RV systole delayed, and
   - septal movement interferes with PAEDP
   ii. hypovolaemia - increase non-zone 3 area

3. **P_CP > P_VP** (or LAP)
   i. pulmonary venous disease (fibrosis, tumour, anomalies)
   ii. PEEP > 10 cmH_2O

4. **LAP > LVEDP**
   i. mitral valve disease
   ii. prosthetic valve
   iii. atrial myxoma

5. **LVEDP ≈ LVEDV**
   - accuracy with which LVEDP represents LVEDV depends upon LV compliance
   - this is ***non-linear*** in normals and displaced in disease states
   - determinants of LV compliance include,

   i. LV chamber diameter
   ii. LV wall thickness
   iii. fibre stiffness
   iv. pericardial pressure* *juxtacardiac pressure
   v. intrathoracic pressure*

   - ↓ compliance occurs in - IHD, AMI
     - IHSS
     - fibrosis, infiltration
     - LVH
   - ↑ compliance occurs in - dilated LA or LV

6. **LAP < LVEDP** - aortic regurgitation
7. West's zone of placement

- other problems reading PA catheters are encountered with,

a. rapid heart rates - difficult to judge end-diastole
   - insufficient time for equilibrium
b. respiratory pattern - rapid rate, large tidal volumes
   - large intrathoracic pressure swings
   - difficult to judge end-expiration
c. digital readouts → - average pressure
   - where mean ≈ end-diastolic pressure
d. underdamping - small air bubbles < 0.25 ml
e. overdamping - large air bubbles
   - narrow, long tubing
   - catheter blockage

■ ***Correlation - Reasons why LVEDP ≈ LVEDV (Sibbald, Raper)***

a. myocardial fibre stiffness, ***compliance***, varies
b. myocardial wall thickness varies
c. alterations in juxtacardiac pressures

NB: ∴ "LVEDP (and PAOP) must be regarded as an ***unreliable*** index of LVEDV"

- ***Correlation - PAOP & LAP***

• generally a good correlation in postsurgical patients with no respiratory disease
• the correlation is poor with,

1. high levels of PEEP
2. hypovolaemia
3. acute respiratory failure

- ***Circumstances Where PAOP ¹ LAP***

1. incorrect catheter placement
2. non-zone 3 position
3. incorrect transducer placement
4. over/under-damping
5. respiratory pressure artefact, PEEP
6. eccentric balloon inflation
7. balloon overinflation
8. obstructive airways disease (autoPEEP)
9. valvular heart disease
10. increased pericardial pressure
11. altered myocardial compliance
12. pulmonary venous obstruction

- ***Circumstances Where LAP ¹ LVEDP***

1. altered myocardial compliance
   - IHD, AMI
   - IHSS
   - fibrosis, infiltration
   - aneurysm
   - LVH
   - dilated LA or LV
2. b. mitral valve disease
3. c. atrial myxoma
4. d. aortic regurgitation - falsely high PAOP

NB: no animal studies have shown a consistent correlation between LVEDP & LVEDV, hence, PAOP can only be considered as a rough measure of ***LV preload***

▪ *Circumstances Where ↑LVEDP ≠ ↑LVEDV*

• factors which influence this include,

1. LV compliance
2. RV diastolic volume - ventricular interdependence
3. pericardial compliance
4. intrathoracic pressures

NB: normal curvilinear relationship between EDP/EDV is ***volume dependent***
→ steep vs. flat portion of the curve

▪ *LV Compliance ® LV Pressure/Volume Curve*

• decreased compliance → left shift
• increased compliance → right shift

a. LV preload
b. LV mass
   - LVH decreases compliance
   - chronic dilatation increases compliance
c. myocardial fibre stiffness
   - ischaemia
   - fibrosis, scar
   - infiltration, amyloid
d. RVEDV
   - cor pulmonale
   - ↑ PVR
e. hypoxia, temperature, osmolality, HR
f. vasopressors, vasodilators, inotropes, adrenergic blockers

• ***ventricular interdependence*** depends upon,

a. RV size
b. septal shift
c. juxtacardiac pressure change
   - tamponade
   - high PEEP
   - effusion

PAOP and PEEP

$P_C = LAP + 0.4 \times (P_{PA} - LAP)$ Garr Equation

- P_C is determined by,
  a. PA pressure
  b. LAP
  c. alveolar pressure
  d. PEEP
     - increases LAP & PAP
     - increase in $P_C \sim 0.5$ x PEEP
     - the PAOP ~ LAP which are both less than P_C
     - thus, PEEP will affect PAOP, the important factors being,

     i. the level of PEEP
     ii. lung and chest wall compliance
     iii. airways resistance → "autoPEEP"

$$\delta P_{IP} = \delta P_{AW} \times \frac{C_L}{C_L + C_{CW}}$$

P_{IP} - interpleural pressure
P_{AW} - airways pressure
C_L - lung compliance
C_{CW} - chest wall compliance

- in the normal physiological state, C_L & C_{CW} are approximately ***equal***, therefore,

$\delta P_{IP} \sim \frac{1}{2} \times \delta P_{AW}$ or,

$\Delta P_C \sim \Delta PCWP \sim \frac{1}{2} \times \Delta PEEP$

• in pathological lungs with decreased compliance, $C_{CW} >> C_L$, thus,

$$\delta P_{IP} \sim \delta P_{AW} \times C_L/C_{CW}$$

where, $C_L/C_{CW} << 1.0$

so, $\delta P_{IP} << \delta PEEP$

or, $\mathbf{dP_C \sim dPCWP << dPEEP}$

• that is, the "wedge pressure" is relatively protected
• the reverse occurs with either highly compliant lungs, or a pathologically stiff chest wall,

→ $C_L >> C_{CW}$

thus, $\mathbf{dPc \sim dPCWP \sim dPEEP}$

PAOP and Preload

• the correlation of CVP with LVEDP is poor when,

1. EF < 40%
2. LV dyskinaesia
3. myocardial ischaemia
4. LAP > 15 mmHg
5. conditions of raised PVR
6. right heart disease

• the correlation of PAOP and LVEDP,

1. is fair in "normal" individuals ± 4 mmHg in 95%
   ?? ± 1 mmHg in 90%
2. is poor where,
   i. LAP > 15 mmHg
   ii. PEEP > 10 cmH_2O
   iii. tachycardia

• the correlation of PAOP and LVEDV,

1. ***very poor*** correlation in the presence of ***sepsis***, or cardiac disease → "scatter graph"
2. relationship between LVEDV and LVEDP is ***non-linear***
3. LV compliance is abnormal in a number of disease states

- ***Causes of Increased LV Compliance***

1. ↑ LVEDV - low EF, volume overload
2. dilated cardiomyopathy
3. vasodilators - SNP, GTN, β-blockers

- ***Causes of Decreased LV Compliance***

1. ↓ LVEDV - improved EF, relief from volume overload
2. ischaemia / infarction
3. infiltration, fibrosis
4. PEEP
5. ↑ RV afterload
6. hypotensive shock - hypovolaemia
   - sepsis
7. pericardial effusion
8. positive inotropes - β_1-agonists

- ***Factors Affecting PAOP in Critically Ill (Sibbald)***

1. CVP and RVEDV - 80%
2. LVEDV - 10%
3. PVR - 10%

- ***PA Catheter - Clinical Aspects***

a. ***no*** absolute indications

b. ***no*** improvement in ***outcome*** in CCU patients

c. ***no*** improvement in outcome in severe respiratory disease

d. some suggestive evidence for improved survival,
   i. in major post-operative and severely septic patients (Shoemaker)*
   ii. perioperative MI < 3 months (Rao, El Etr)[§]

e. results depend upon the use of information derived

NB: *this improvement was not necessarily related to PA catheter
[§]this was a none peer reviewed paper, claimed benefits subsequently withdrawn

- ***Relative Indications***

1. optimisation of fluid resuscitation in the presence of poor myocardial function
2. haemodynamic & O_2 flux monitoring in patients with cardiorespiratory disease, unresponsive to conventional therapy
3. preoperative assessment of patients prior to,
   i. major vascular
   ii. cardiac
   iii. neurological procedures
4. specific diagnostic categories,
   i. angiography in PE
   ii. air embolism
   iii. preoperative assessment of post-pneumonectomy risk
   iv. analysis for intracardiac shunt - VSD, PDA
5. research

- ***Primary Data***

NB: individual values are of little use, ***trends*** are more useful

a. PAOP as an indicator of oedemagenesis
   - essentially a ***poor*** indicator of preload

b. PA pressures indicate degree of PAH

c. P_{vO2} indicates global O_2 supply/demand

- ***Derived Data***

a. haemodynamic variables
   - CI, LVSWI, SVRI
   - qualitative information re cardiac and vascular function
   - some quantitative information with trends
   - response to ***therapeutic intervention***

b. DO_2 & VO_2
   - rough guide to O_2 supply and utilization
   - assessment of the effect of therapy

CARDIAC PACEMAKERS

- ***Complications of Temporary Pacing***

  a. electrical
     i. under/over-sensing
     ii. failure to capture
     iii. induction of arrhythmias
  b. those of central venous cannulation
  c. infection, endocarditis, bacteraemia
  d. thrombosis and pulmonary emboli
  e. myocardial perforation
  f. diminished cardiac output

- ***Adverse Effects of Ventricular Pacing***

  a. loss of atrial contribution to filling
  b. intermittent mitral / tricuspid regurgitation
  c. V-A conduction in some patients
  d. potential tachyarrhythmias requiring atrial pacing
  e. hypotension

- ***Haemodynamic Changes with Ventricular Pacing***

  a. ↓ LV stroke volume
  b. ↓ CO
  c. vasodilatation from vasodepressor reflexes
  d. ↑ LAP & RAP
  e. mitral / tricuspid regurgitation
  f. cannon 'a' waves

INTRA-AORTIC BALLOON COUNTERPULSATION

Def'n: a cardiac assist device, placed in the descending aorta, which acts to,

1. ↓ LV afterload
2. improve coronary blood flow / myocardial perfusion
3. improve myocardial VO_2 balance

▪ *Indications*

1. AMI + surgically correctable complication
   - i. acute mitral regurgitation | papillary muscle rupture
   - ii. acute VSD
   - iii. contained free wall rupture
2. unstable angina - prior to emergency CABG
   - immediately post PTCA
3. preoperative CABG in high risk patient
   - severe LAD stenosis
   - low EF ≤ 35%
   - extreme myocardial irritability
4. CABG & weaning from CPB
5. prior to cardiac transplantation

▪ *Contraindications - Absolute*

1. aortic regurgitation / sinus of Valsalva rupture
2. aortic dissection
3. severe aorto-iliac atherosclerosis - aortic dissection, thoracoabdominal aneurysm
   - obliterative aorto-iliac disease
   - recent aortic surgery
4. irreversible disease (non-surgical)
   - no improvement in ***outcome*** when used in ischaemic cardiogenic shock

▪ *Contraindications - Relative*

1. thrombocytopaenia
2. contraindications for anticoagulation
3. CI > 1.4 l/min/m^2
4. uncontrolled tachycardia > 120 bpm

- ***Timing***

1. arterial pressure waveform
   - i. ***inflation***
     - aorta ~ dichrotic notch
     - femoral ~ pressure peak
     - radial ~ midway
   - ii. ***deflation*** - immediately prior to pressure rise
2. ECG
   - i. ***inflation***
     - aortic closure ~ the **T wave** peak
   - ii. ***deflation***
     - LV systole ~ start of QRS
3. external cardiac pacemaker

- ***Complications***

a. ***on insertion***
   - i. failure to pass ~ 5-15%
   - ii. aortic dissection / perforation ~ 1-2%
   - iii. bleeding, haematoma

2. ***during use***
   - i. failure to assist
     - balloon rupture
     - failure of timing / incorrectly set timing
     - hypotension, ↑ LV afterload, ischaemia
   - ii. systemic emboli
   - iii. limb ischaemia
   - iv. complications of anticoagulation
   - v. thrombocytopaenia
   - vi. amputation
   - vii. infection
3. ***on removal***
   - i. bleeding, haemorrhage, haematoma
   - ii. femoral artery thrombosis, ischaemia
   - iii. aneurysm formation

Normal Cardiovascular Pressures					
Right			**Left**		
CVP RAP	diastole ~ 0-3 systole ~ 4-8	mmHg mmHg	PAoP LAP	~ 3-7	mmHg
RV	~ 22-25 / 0	mmHg	LV	~ 120 / 0	mmHg
PA	~ 22-25 / 8	mmHg	Aortic	~ 120 / 80	mmHg
PA mean	~ 13-15	mmHg	MAP	~ 90-100	mmHg
PVRI	~ 150-250	$dyne/cm^5/s/m^2$	SVRI	~ 800-1800	$dyne/cm^5/s/m^2$

Mean Arterial Pressure

Def'n: integrated mean arterial pressure over unit time,
or a given number of cardiac cycles

• on a direct arterial trace, it is the integrated area under the pressure/time curve, usually averaged over ~ 3 cardiac cycles
• its main importance is that it determines organ ***perfusion***, with the exception of the LV

$$MAP = BP_{DIAS} + k \,.\, (BP_{SYS} - BP_{DIAS})$$

where, k = 0.2 to 0.45 depending upon the vascular bed
~ 0.33 mean

Mesenteric Ischaemia - Causes

a. severe atherosclerosis
b. hypotension ± pre-existing mesenteric vascular disease
c. post aortic resection
d. embolic
- SBE
- AMI, AF
- cardiomyopathy

e. mesenteric venous thrombosis
  - hypercoagulable states
f. malignant hypertension

HYPERTENSION

- ***Causes of Failed Therapy***

  a. inadequate drug / inadequate dose
  b. poor compliance
  c. drug interactions - pseudoephedrine / sympathomimetics
     - steroids / OCP
  d. high Na^+ intake
  e. secondary hypertension
  f. progressive renal or endocrine disease

- ***Causes in ICU***

  a. pain, anxiety, fear
  b. metabolic - fever
     - hypothermia
     - hypoxia, hypercarbia, acidosis
     - hypoglycaemia
  c. drug withdrawal - antihypertensives
     - sedatives, narcotics
  d. drug induced - inotropes
     - steroids
  e. secondary hypertension - thyrotoxicosis
     - phaeochromocytoma
     - Cushing's, Conn's
     - coarctation
     - MH, etc.
  f. aortic dissection
  g. AMI

- ***Causes Post-CEA***

  a. pain, anxiety, fear
  b. hypothermia, hypoxia, hypercarbia
  c. carotid baroreceptor denervation
  d. cerebral ischaemia
  e. myocardial ischaemia
  f. pre-existing hypertensive disease

- ***Causes of Hypertension & Hypokalaemic Alkalosis***

  a. essential HT & diuretics **most common* cause
  b. essential HT & secondary hyperaldosteronism
     i. malignant HT
     ii. renovascular HT
     iii. oestrogens, steroids
     iv. renin secreting tumour
  c. primary hyperaldosteronism
  d. Cushing's syndrome
  e. congenital adrenal enzyme deficiencies
  f. carbenoxolone
  g. Liddle's syndrome - pseudohyperaldosteronism (tubular autonomy)

- ***Bartter's Syndrome***

  a. hyper-reninaemic hyperaldosteronism
  b. due to failure of NaCl reabsorption in the ***ascending tubule***
     → ***secondary hyperplasia*** of the JGA cells
  c. generally ***does not*** result in ***hypertension***
     i. the JGA cells also secrete vasodilatory PGE_2 and PGI_2
     ii. ↓ vascular responsiveness to NA and AII
     iii. ↑ formation of bradykinin

HYPERDYNAMIC CIRCULATION

- ***Clinical Features***

  a. bounding pulse
  b. hyperaemia
  c. warm peripheries
  d. high CO / low SVR

- ***Physiological***

  a. exercise
  b. pregnancy
  c. high altitude

- ***Pathological***

a.	SIRS	- septicaemia - ARDS, pancreatitis
b.	high output LV failure	- severe anaemia - AV shunts - beri-beri - carbon monoxide & cyanide poisoning
c.	hypermetabolism	- burns - multiple trauma, MOSF
d.	thyrotoxicosis	
e.	hepatic failure	
f.	metabolic acidosis	- reperfusion injury - lactic acidosis
g.	hyperthermic states	- MH, MNS, high fever
h.	hypercarbia	

- ***Drug Induced***

a.	inotropic infusions	- isoprenaline, dobutamine, adrenaline
b.	alcohol	
c.	vasodilators in young	

HYPODYNAMIC CIRCULATION

NB: ** causes of low CO, high SVR, cool peripheries

a. cardiogenic shock
   i. myocardium - AMI, cardiomyopathy, myocarditis
   ii. valvular - acute MR, stenotic valvular lesions
   iii. pericardium - tamponade, constriction
   iv. RV failure - ↑ CVP, ↓ PAOP & clear lungs
   v. pulmonary embolus, air embolus, AFE

b. hypovolaemic shock

c. distributive shock

d. drug induced - overdose with β-adrenergic blockers, CEB's
   * any significant negative inotrope

e. pre-eclampsia ?

NB: ** causes of low CO, low SVR, warm peripheries

1. hypovolaemic septic shock
2. spinal cord injury/shock
3. CO poisoning
4. drug induced - vasodilators
5. Addison's disease

ENDOCARDITIS

Non-Infective Endocarditis

1. rheumatic fever
2. SLE - Libman-Sacks
3. eosinophilic endocarditis
4. non-bacterial, thrombotic endocarditis - 'merantic'
   - 50% have pulmonary emboli if right-sided endocarditis exists
   - found in ~ 1% of all autopsy specimens from patients with,
   i. neoplastic disorders
   ii. DIC / sepsis
   iii. burns
   iv. central venous cannulae

Infective Endocarditis

Def'n: infection by micro-organisms of a platelet / fibrin vegetation on the endothelial surface of the heart

a. incidence ~ 1:200-6,000 hospital cases, or
~ 1:17,000 normal population

b. mortality
   i. overall ~ 20-30%
   ii. elderly ~ 40-70%
   iii. severe CCF ~ 100%

NB: the later may be reduced to ~ 30% with surgery

■ ***Acute Bacterial Endocarditis***

- rapid, severe, destructive infection often with virulent bacteria
- often occurs on ***normal valves***, cf. SBE on abnormal valves, and has a high associated mortality
- causative organisms include,

a. *Staphylococcus aureus*

b. *Strep. pneumoniae* & *Strep. pyogenes*

c. *Neisseria gonorrhoeae*

- ***SBE: Causative Organisms***

NB: = "just about any"

a.	Strep.	*viridans*	30%	
		faecalis	10%	**~ 60%**
		other	15-30%	
b.	Staph.	*aureus*	20-30%	
		epidermidis	5%	**~ 25-35%**
c.	gram negatives			~ 1.5-13%
	i. *E. coli*			
	ii. *P. aeruoginosa*			
	iii. *H. influenzae*			
d.	anaerobes			~ 4%
e.	fungi	Candida		
		Aspergillus		~ 4%

NB: IV drug abusers → Staph. (~ 60%), Candida & gram negatives more common

- ***Predisposing Factors***

a.	none found	**~ 20-40%**
b.	rheumatic valvular disease	~ 25-60%
	• used to be most frequent cause	
	• more recent studies →	£ **15%**
c.	congenital valvular disease	~ 10-20%
d.	mitral valve prolapse	~ 10%
e.	cardiac surgery & prosthetic valves	~ 10-20%
f.	degenerative heart disease / valvular disease	
g.	IHSS, HOCM	
h.	Marfan's syndrome	
i.	peripheral AV fistulae, chronic haemodialysis	
j.	pacemakers, IV or IA lines	
k.	prosthetic aortic grafts	
l.	IV drug abuse	
m.	immunosuppression	
n.	severe burns	
o.	alcoholism	

- ***Predisposition***

a.	*Strep. viridans*	- dental procedures	~ 20%
b.	*Strep. faecalis*	- GIT, bowel surgery	~ 50%
c.	Staphylococci	- skin lesions, line sepsis ~ 40% IV drug abuse	

- ***Causes of Culture Negative Endocarditis***

a. prior treatment with antibiotics
b. Coxiella burnetti, Clamydia
c. pyridoxine requiring Streptococci
d. fungi
e. other unusual organisms

- ***Clinical Findings***

a. murmur ~ 90%
   - changing murmur ~ 12%

b. fever ≥ 38°C ~ 77%

c. embolic episodes ~ 30-50%
   - brain, spleen, kidney, heart

d. skin changes ~ 50%
   - petechiae - conjuntiva, buccal mucosa, palate
   - splinter haemorrhages - subungual, dark-red linear streaks
   - Osler's nodes - small tender finger & toe pad nodules
   - Janeway lesion - small haemorrhages, slightly nodular
     - palms & soles, most commonly in endocarditis
   - jaundice
   - poor dentition

e. splenomegaly ~ 25%

f. metastatic infection ~ 20%

g. clubbing ~ 12%

h. Roth spots ~ 5%
   - oval retinal haemorrhages + clear centre

i. immune complex phenomenon ~ 15%
   i. arthritis
   ii. acute GN

j. negative cultures **~ 5-40%**

- ***Laboratory Investigations***

a. ↑ ESR/CRP

b. ↑ WCC ~ 75%

c. normochromic, normocytic, low reticulocyte anaemia ~ 50%

d. biochemistry - renal function, LFTs

e. IV blood cultures x 3 - MIC, MBC ***essential***

f. features of GN & renal involvement - ***haematuria*** ~ 50%
- RBC casts & proteinuria

g. echocardiograph - confirms diagnosis
- assesses risk of emboli & degree of valvular dysfunction
* low sensitivity ≤ 50% for transthoracic

- ***Clinical Management***

NB: always consult ***microbiologist*** & ***cardiac surgeon***

a. empirical therapy *__all__ for 4/52

i.	penicillin	1.2g IV	q4h
ii.	flucloxacillin	2.0g IV	q4h
iii.	gentamicin	4.5 mg/kg IV	q24h

b. known organism,

i.	Staph.	- flucloxacillin/gentamicin as above	
ii.	Strep	- penicillin/gentamicin as above	
		- penicillin	1.8g if MIC > 0.2 mg/l
iii.	MRSA	- vancomycin	1.0g IV q12h 6/52
iv.	gram (-)'ve	- cefotaxime	1-2g q6h
		+ gentamicin	4.5 mg/kg IV q24h
v.	pseudomonas	- timentin	3.1g q4h
		+ gentamicin	4.5 mg/kg IV q24h

NB: patient allergic to penicillin → ***vancomycin***

indications for ***valvular surgery***,

i. acute valvular incompetence
ii. fever > 6/52
iii. persistent large vegetations
iv. infected prosthetic valve

• use of ***gentamicin*** as an adjuvant agent for *Strep. faecalis* has not been validated for single daily dose therapy → some microbiologists still use tds therapy in this scenario

MULTIFOCAL ATRIAL TACHYCARDIA

- ***Diagnosis***

1. atrial rate > 100 bpm
2. ≥ 3 'P' wave morphologies **not* of SA node origin
3. irregular PP, PR, RR intervals

NB: ?? rapid form of ***wandering atrial pacemaker***
the major differential is from AF
prodromal arrhythmias include atrial ectopics, AF and flutter

- ***Associations***

a.	elderly	≥ 70 yrs average
b.	chronic lung disease	~ 60% ≤ 17% of CAL in acute resp. failure - less frequent with PE or infection ?? RAH, hypoxia/hypercarbia, aminophylline
c.	ischaemic heart disease	- common in CCF - low CO, high PA/PAOP - rare in valvular disease
d.	post major surgery	~ 28%
e.	diabetes mellitus	~ 24%
f.	hypokalaemia	~ 14%
g.	uraemia	~ 14%
h.	children	- uncommon - of those affected 54% otherwise NAD - only 21% of CHD

- ***Management***

a. treat underlying 1° disease - exacerbation CAL
- CCF, etc.

b. check plasma electrolytes - K^+, *Mg^{++}
   - Mg^{++} was effective in 7/8 patients even when the plasma level was ***normal***

c. amiodarone - very useful at FMC/QEH but not widely reported

d. verapamil ~ 43% conversion to SR

e. β-adrenergic blockers - variable efficacy

f. digoxin
   - ***ineffective*** in treating arrhythmia
   - useful to improve LV/RV function
   - toxicity may occur more commonly - underlying problems

PROLONGED QT SYNDROMES

Def'n: $QT_C = QT / \sqrt{RR}$ < 0.44 s (F < 0.44, M < 0.40s)
- 'rule-of-thumb' < ½ RR interval, best measured in aVL

Inherited

a. over 500 cases up to 1981
   i. Romano-Ward syndrome
      - most common
      - autosomal ***dominant***
      - LQTS ***without*** deafness
   ii. Jervall, Lange-Neilsen synd.
      - 0.3% of deaf mutes
      - autosomal ***recessive***
      - LQTS ***with deafness***
   iii. familial ventricular tachycardia
      - LQTS only with ***exercise***
      - usually early childhood
      - recurrent syncope & sudden death

b. high ***mortality*** **~ 35%**

c. ECG
   - usually sinus bradycardia with marked ↑ QT_C **~ 0.5-0.7 s**
   - abnormal T waves, often inverted ± U waves
   - *any tachyarrhythmia*, but especially - VT, torsade, VF

d. pathophysiology * uncertain, possible mechanisms
   i. imbalance of ***sympathetic*** discharge
   ii. abnormal conduction
   iii. disturbance of transmembrane K^+/Ca^{++}

- ***Treatment***

a. b-***blockers*** - atenolol (no ISA)
   - no change in HR or QT
   * one study → ↓ ***mortality*** 73% → **6%**

b. phenytoin ± β-blockers

c. magnesium

d. lignocaine
   - class Ib → pure Na^+-channel blockade
     no K^+ cf. class Ia agents

e. ***left*** stellate ganglionectomy

f. ventricular overdrive pacing

g. implantable cardioverter-defibrillator

Acquired LQTS

a. slow HR — - SA disease, AV block

b. electrolytes
- $\downarrow Mg^{++}$ | $\downarrow Ca^{++}$
- $\downarrow K^{+}$ results in "apparent long QT", ie. ↓T + U-waves

c. myocardial
- ischaemia
- myocarditis, cardiomyopathy
- MVP
- ventricular tumour

d. drugs
- i. antiarrhythmics
  - classes Ia & Ic — * both Na^{+} & K^{+}-channel blockade; - ie. "class III" properties
  - class III — - amiodarone, sotalol
- ii. psychotropics
  - tricyclics — - classically described, but evidence ***equivocal***
  - phenothiazines
- iii. local anaesthetics — - bupivacaine, cocaine
- iv. antimicrobial agents
  - erythromycin, septrin, pentamidine, amantadine, chloroquine
  - ketoconazole, itraconazole
- v. others — - organophosphonates, vasopressin, arsenic

e. endocrine
- hypothyroidism
- hyperparathyroidism
- phaeochromocytoma
- hyperaldosteronism

f. miscellaneous

- generally occurs at ***rest*** rather than during exercise
- frequently in the elderly, average age > 50 years

NB: β-blockade is relatively ***contraindicated***, in contrast to inherited LQTS

- ***Treatment***

1. correct underlying cause
2. $MgSO_4$
3. lignocaine
4. isoproterenol
5. ventricular overdrive pacing

Treatment - Torsade de Pointes

a. ABC
b. CPR
c. DC cardioversion
d. $MgSO_4$ - 8.0 mmol/2g IV
e. isoprenaline - ↑ HR decreases QT interval
f. overdrive pacing

PULMONARY HYPERTENSION

Pulmonary Artery Pressures

State	Mean PAP	
Normal	~ 13	mmHg
PAH[1]	> 20	mmHg, or PA_{dias} - PCWP > 5 mmHg
• mild	20-25	mmHg
• moderate	25-35	mmHg
• ***severe***	**> 35**	mmHg

[1] LIGW states for diagnosis of pulmonary hypertension:

PAP	> 25 mmHg
PVRI	> 300 dyne/s/cm^5/m^2
PAP(x)-PAOP	> 15 mmHg

• may be clinically divided into,

1. active vs. passive
2. acute vs. chronic

- ***Acute Active***

a. hypoxia, acidosis
b. SIRS, septicaemia
c. ARDS
d. acute respiratory failure
e. pulmonary emboli
f. neurogenic pulmonary oedema
g. lung resection

- ***Acute Passive***

a. AMI
b. LVF - acute pulmonary oedema
c. hypervolaemia

- ***Chronic***

a. ↑ PVR
   i. primary pulmonary hypertension
   ii. recurrent pulmonary emboli
   iii. pulmonary veno-occlusive disease
   iv. CCF/LVF
   v. mitral stenosis

b. loss of pulmonary vasculature
   i. obstructive airways disease / emphysematous diseases
   ii. diffuse interstitial lung disease

c. hypoxic pulmonary vasoconstriction
   i. decreased central drive - sleep apnoea
      - CNS disease
      - drugs
   ii. chest wall disease - scoliosis
      - morbid obesity
      - neuromuscular diseases
   iii. parenchymal lung diseases
   iv. high altitude residence

• chronic pulmonary disease frequently results in pulmonary hypertension when,

1. P_{aO2} < 55 mmHg on air
2. FEV_1 < 1000 ml
3. VC | TLC < 50% predicted

- ***Complications***

1. recurrent respiratory infections
2. chronic hypoxia
3. polycythaemia
4. cor pulmonale ± RV failure
5. 2° LV dysfunction
6. sudden death * especially 1° PAH

Primary Pulmonary Hypertension

- rare ***idiopathic*** disorder, typically of ***females*** aged 20-40 years → F:M ~ 4:1
- diagnosis by demonstration of pulmonary hypertension & ***exclusion*** of other causes
- three histological patterns described,

1. ***plexogenic*** pulmonary arteriopathy
   - obliteration of the precapillary arteries
2. ***thrombotic*** pulmonary arteriopathy
3. pulmonary ***veno-occlusive*** disease
   - intimal proliferation and fibrosis of intrapulmonary veins & venules

- ***poor prognosis***, with an average 10 yr survival ~ 25%
- most cases are ***sporadic***, but associations with,

a. oral contraceptives

b. pregnancy

c. amphetamines

d. Raynaud's phenomenon ~ 7-30%

COR PULMONALE

Def'n: right ventricular ***enlargement*** secondary to pulmonary disease, in the ***absence*** of congenital or left sided heart disease

- ***Aetiology***

1. chronic ***parenchymal disease***
   i. CAL
   ii. interstitial lung diseases
   iii. chronic multiple emboli
   iv. primary pulmonary hypertension
2. lung ***pump failure***
   i. kyphoscoliosis
   ii. morbid obesity
   iii. neuromuscular diseases
3. ***central*** respiratory impairment
   i. morbid obesity
   ii. sleep apnoea syndrome
   iii. chronic mountain sickness

- ***Exacerbating Factors***

a. progression of primary lung disease
b. respiratory infection
c. bronchospasm
d. sedatives / opioids
e. increased work of breathing
f. hypercatabolic states - trauma, surgery, sepsis
g. pulmonary emboli
h. cardiac arrhythmias
i. pulmonary resection
j. RV ischaemia

NB: any factor which causes exacerbation of the primary disorder, or any additive factor from either of the groups (1-3 above) to which the patient will be more sensitive

■ ***Pathogenesis***

• cor pulmonale can be either,

1. acute → RV dilatation, or
2. chronic → RV hypertrophy, ± dilatation later
3. episodic
4. progressive

• initially PAH only occurs during ***exercise*** or stress
• there is episodic RV dilatation, with normal RVEDP and RV stroke volume
• later in the course, there is,

1. persistent PAH
2. RV hypertrophy and dilatation
3. sustained elevation of the RVEDP

→ RV failure *initially only during exercise, later at rest

• the mechanisms for these changes include,

a. loss of effective vascular bed
b. ***irreversible*** pulmonary vasoconstriction
   i. chronic hypoxia
   ii. chronic acidosis *pH < 7.2
   iii. chronic hypercapnia

■ ***Symptoms***

a. dyspnoea
b. weakness / fatigue
c. decreased exercise tolerance
d. peripheral oedema
e. other signs of RV failure later

- ***Clinical Signs***

a.	chronic lung disease	- dyspnoea, tachypnoea, ↑ WOB - central cyanosis - clubbing, asterixis - nicotine staining
b.	RV ***hypertrophy***	- RV thrust - ↑ split S_2 with loud P_2 ± RV S_4 - TI - AF, recurrent SVT's, MAT
c.	RV ***failure***	- ↑ JVP - peripheral oedema - hepatomegaly ± ascites

- ***Investigations***

a.	FBE	- polycythaemia - ↑ WCC if infective episode
b.	biochemistry	- EC&U, LFT's
c.	CXR	- changes of chronic lung disease - prominent PA shadows with decreased peripheral vasculature - usually ***no*** LVF or cardiomegaly
d.	ECG	- 'P' pulmonale - RVH (qv), RAD, RBBB - sinus tachycardia, AF, MAT
e.	Echo	- RV dilatation/hypertrophy, ± TI
f.	V/Q Scan	- to exclude chronic pulmonary emboli

- ***Complications***

a. recurrent respiratory infections
b. chronic hypoxia
c. polycythaemia
d. acute respiratory failure
e. RV failure
f. sudden death (1° PAH)
g. cardiac arrhythmias
h. cirrhosis
i. oedema | ascites

- ***Management***

a. treat primary lung disease & cease ***smoking***

b. optimise remaining lung function & minimise hypoxia,
   i. weight loss
   ii. bronchodilators
   iii. steroids
   iv. diuretics
   v. antibiotics
   vi. physiotherapy
   vii. O_2 therapy

c. prevention of pulmonary emboli

d. prompt & aggressive management of respiratory infections

e. respiratory stimulants - aminophylline

f. optimise cardiac function - digoxin, antiarrhythmics

g. pulmonary vasodilators
   i. nitric oxide ~ 10-40 ppm
   ii. PGI_2 ~ 5-25 ng/kg/min
   iii. adenosine ~ 50-500 µg/kg/min
   iv. ACEI
   v. GTN
   vi. β_2-agonists
   vii. Ca^{++} blockers

h. heart/lung ***transplantation***

Nitric Oxide

- endothelium dependent vascular relaxation demonstrated in 1980 → EDRF proposed
- *Furchgott* and *Ignarro* independently proposed NO as EDRF in **1986**
- production of NO by endothelium was confirmed by *Palmer et al.* in 1987
- ideal local ***transcellular messenger***,

1. rapid diffusion between cells,
   i. gaseous molecule
   ii. small size
   iii. lipophillic nature
2. short duration of action

- produced endogenously, predominantly in ***upper airways***, and is detectable at baseline levels in exhaled air

▪ ***Action***

- causes relaxation of arteries, arterioles, and veins
- inhibits platelet aggregation and adhesion
- synthesised from the terminal guanidino-nitrogen of ***l-arginine*** under the influence of ***nitric oxide synthase***
- binds to the haem complex of ***guanylate cyclase***
- the resulting ***nitrosyl-haem*** is a potent ***stimulator*** of this enzyme

→ ↑ production of **cGMP**

- effects of raised ICF cGMP are dependent upon the cell type
- biological activity is rapidly terminated due to avid binding to Hb
- it has a very brief $t_{½\beta}$ ~ 6-50 secs and is rapidly oxidized to NO_2^- and NO_3^-
- also inhibited by antioxidants and superoxide radicals
- its action is potentiated by superoxide dismutase and cytochrome C
- ***release*** is stimulated by,

1. ACh
2. bradykinin
3. substance P
4. thrombin
5. ATP
6. increased vessel flow → reflex dilatation

- enhances the action of cAMP mediated drugs, eg. β-agonists and prostacycline

Clinical Studies

• disease processes studied with inhalational NO include,

1. acute pulmonary hypertension
2. chronic pulmonary hypertension
3. acute bronchoconstriction
4. ARDS
5. respiratory distress of the newborn
6. congenital and acquired heart disease

Acute Pulmonary Hypertension

• in normal lungs, baseline PVR is very low and administration of NO has little effect
• USA OHS guidelines recommend < 25 ppm exposure for an 8 hour day
• 40-80 ppm rapidly reverses pulmonary hypertension associated with,

1. hypoxia
2. infusion of the thomboxane endoperoxide analog U46619
3. protamine-heparin reaction

• vasodilatation occurs preferentially in well ventilated alveoli
• this action appears unaffected by,

1. endothelial damage
2. prolonged exposure

NB: SVR remains unchanged

Bronchodilatation

• animal studies of 5-300 ppm show a dose related,

1. reduction in airway resistance
2. increase in dynamic compliance
3. reversal of bronchoconstriction in response to
   - LTD_4
   - histamine
   - neurokinin A
   - methacholine

NB: these effects are additive to terbutaline and other β_2 agents

ARDS

• as inhaled NO is distributed to ventilated alveoli, theoretically should result in "steal" toward these regions with a reduction in shunt fraction and A-aO_2 gradient
• *Rossaint et al.* used inhaled NO at 18-36 ppm in 9 patients with ARDS,

a. ↓ mean PAP → 37 to 30 mmHg
b. ↑ P_{aO2} ∝ ↓ Q_S/Q_T
c. ↑ P_{aO2}/F_IO_2 ratio → 152 to 199 mmHg

• in comparison, infusion of ***prostacycline*** resulted in,

a. ↓ mean PAP
b. ↓ P_{aO2} ∝ ↑ Q_S/Q_T

• subsequent studies have shown [NO] < 20 ppm effectively reduce PAP and improve PaO_2
• there is also an increase in RVEF
• in general, the baseline level of PVR predicts the degree of vasodilatation in response to NO
• ***tachyphylaxis*** has ***not*** been observed with administration up to 53 days
• however, PAP and P_{aO2} promptly return to baseline levels upon discontinuation of inhalation
• occasionally there may be an ***overshoot phenomenon*** on cessation, this may be due to,

1. ↓ NO synthetase activity
2. ↑ cGMP phosphodiesterase activity
3. progression of underlying lung disease

Neonatal Respiratory Distress

• ***persistent pulmonary hypertension*** of the newborn PPHN may be due to reduced endogenous production of NO
• several authors have shown dose dependent reductions in,

a. mean PAP
b. R→L shunting through the patent DA and the foramen ovale

• ***oxygenation*** improved from a mean,

a. PaO_2 43 → 185 mmHg
b. SaO_2 74 → 96 %

• systemic blood pressure was unaffected
• however, inhalation of NO ***did not*** alter ventilation/perfusion relationships caused by GBS sepsis, nor haemodynamic changes

• *Kinsella et al.* studied 15 patients with PPHN who fulfilled the criteria for ECMO, 13 of whom, were successfully treated with NO
• NO therapy for PPHN is currently being studied in a multicentre randomised trial

Toxicity of NO

• NO is a common atmospheric pollutant, being produced by burning of fossil fuels and lightning
• OHS TLV are 25 ppm over an 8 hour day (3 ppm/hr) or 5 ppm as an acute exposure
• NO is a ***free radical***, which reacts with O_2 to form NO_2, which in aqueous solutions,

a. is in equilibrium with N_2O_3 and N_2O_4
b. is converted to nitric and nitrous acids
c. reacts with superoxide radical to ***peroxynitrate***

• forms complexes with Fe^{++} containing species and iron-sulphur proteins
• in the circulation rapidly forms ***nitrosyl-Fe^{++}-Hb***, which then reacts with O_2 to form ***methaemoglobin*** plus nitrates and nitrites which are subsequently excreted in the urine
• very high concentrations of NO_2 are rapidly fatal due to,

a. gross destruction of lung tissue with severe pulmonary oedema
b. haemorrhage and desquamation
c. massive methaemoglobinaemia
   - up to 100%
   - hypoxia, acidosis and cyanosis

• significant methaemoglobinaemia at lower levels may result if production is increased or removal by ***methaemoglobin reductase*** (NADH-diaphorase) is reduced
• activity of NADH-diaphorase may be reduced as an inherited disorder and is low in newborns
• under normal conditions the conversion of NO to NO_2 is slow

■ ***Other Effects***

• inhibits platelet adhesion to endothelial cells and reverses platelet aggregation *in vitro*
• bleeding time may be prolonged *in vivo*
• may be involved in neuronal "memory" and spinal cord "wind-up"
• involved in ovulation

■ ***Tissue Regulation***

• vasodilatation may be regulated locally by endothelial cells which respond to flow or shear stress
• flow-dependent coronary artery dilatation has been demonstrated in humans *in vivo*
• local production of NO produces dilatation in response to hypoxaemia
• the coronary vessels of patients with atherosclerotic disease ***do not*** show flow-induced dilatation, and there is a decreased basal secretion of NO
• the regulatory effect of the vascular endothelium is impaired in animals with atherosclerotic disease
• disorders of NO metabolism are implicated in endotoxic shock, mediated by NO from an ***inducible*** form of NO synthase
• other hyperdynamic circulatory states, such as cirrhosis, may also be due to abnormal NO metabolism

Prostacyclin PGI_2

- has largely replaced PGE_1 which was less potent
- is an expensive systemic and pulmonary vasodilator
- usual dose ~ 5-25 ng/kg/min (ie. 20-100 µg/hr, vials are 500 µg)
- a PA catheter is required for monitoring
- may be used to evaluate the ***reponsiveness*** of the pulmonary circulation to vasodilators
- if PGI_2 does not result in a reduction in PAP & PVR, then vasodilators are of no use
- patients must be weaned slowly, ~ 3 ng/kg/min each 3-4 hrs
- noradrenaline at 1-2 µg/min may be used to overcome the systemic vasodilatory effects
- side effects include,
    1. systemic vasodilatation
    2. impairment of HPV $\rightarrow$ $\uparrow$ shunt fraction
    3. hypotension
    4. nausea and vomiting

- some recent work investigating ***inhaled prostacycline***

Right Heart Perfusion Pressure

- RVPP ~ MAP - RV_{mean}, $\therefore$

$$RV_{PP} = MAP - \left[RA_{\tilde{x}} + \frac{PA_{Sys.} - RA_{\tilde{x}}}{3} \right]$$

- the aim is to maintain a RVPP ^{3} **35 mmHg**
- management should include,
    a. $\uparrow$ MAP
    b. $\downarrow$ RV afterload
    c. $\downarrow$ HR - less critical than LV perfusion

PULMONARY EMBOLUS

- ***Virchow's Triad***

  1. ***venous stasis***
     - IV fibrin deposition ~ 30-40% of patients following AMI
       ~ 30-60% following stroke or postoperatively
     - postoperative incidence of DVT **~ 20%** overall
  2. ***endothelial damage***
  3. ***hypercoagulability***

- 66% of DVT's in the legs result in ***no symptoms***
- a half of these will be missed on examination
- complete lysis occurs in < 10%
- clinically significant thromboses usually have extended proximal to the popliteal vessels

Def'n: ***massive pulmonary embolus*** is defined as that which obstructs **> 50%** of the pulmonary vasculature

Co-existing Factors/Disease			
Major		Minor	
1. thrombophlebitis	~ 40%	1. arrhythmias	~ 16%
2. bed rest	~ 32%	2. recent fracture	~ 15%
3. recent surgery	~ 31%	3. varicose veins	~ 15%
4. obesity	~ 30%	4. AMI	~ 12%
5. CCF	~ 17%	5. malignancy	~ 7%

NB: ***no*** predisposing factor **~ 6%**

Symptoms		Signs	
1. dyspnoea	~ 80%	1. tachypnoea (RR > 16)	~ 90%
2. chest pain		2. auscultation	
• pleuritic	~ 70%	• crepitations	~ 60%
• non-pleuritic	~ 10%	• split S_2 & loud P_2	~ 50%
3. apprehension	~ 60%	• S_3 / S_4	~ 30%
4. cough	~ 50%	• friction rub	~ 10%
5. haemoptysis	~ 30%	3. ↑ JVP	~ 50%
6. sweats/diaphoresis	~ 30%	4. tachycardia	~ 44%
		5. fever > 37.8°C	~ 43%
		6. signs of DVT	~ 30%
		7. cyanosis	~ 20%
		8. cardiogenic shock	~ 5%

- ***Incidence***

  a. fatal PE < 0.5%

  b. non-fatal PE ~ 1-2%

- ***Mortality***

  a. untreated PE ~ 15%

  b. treated PE ~ 8%

- ***Problems***

  a. common disease and difficult to diagnose

  → < 10% of fatal PTE treated at autopsy

  b. no quick, easy, specific diagnostic test

  c. most are asymptomatic and self limiting

  d. most are preventable

- ***Haemodynamics***

a. acute pulmonary hypertension
b. RV dilatation ± ischaemia
c. tricuspid regurgitation
d. cardiogenic shock

- ***Diagnosis DVT***

1. venography
2. impedance plethysmography | - sensitive for occlusive DVT in femoral/iliac veins
   - best for ilio-femoral segment
3. ***doppler*** ultrasound | - sensitivity ~ 100% / specificity ~ 90%
   - best for femoro-popliteal segment
4. radiolabelled fibrinogen - sensitivity ~ 60-80%
   - less accurate above the knee

- ***Diagnosis PTE***

a. history and physical examination → ***clinical probability***
b. FBE, MBA ~ 60% ↑ LDH
   ~ 30% ↑ bilirubin
c. AGA's ~ 90% low P_{aO2} & P_{aCO2}
d. ECG - SR tachycardia, atrial flutter | fibrillation
   - transient rSR in anterior leads
   - clockwise rotation and RAD, rarely S_1-Q_3-T_3
   * exclusion of other pathology
e. CXR - peripheral oligaemia / hilar attenuation (Westermark's sign)
   - elevated hemidiaphragm, atelectasis, pleural effusion
   * most commonly ***normal*** → exclusion of other pathology
f. V/Q lung scan → %PE
   i. normal < 4%
   ii. low probability ~ 15%
   iii. intermediate probability ~ 20-33%
   iv. high probability ~ 87%
g. PA catheter
   - acute elevation of mean PAP > 30 mmHg correlates with > 50% obstruction
   - mean PAP rarely exceeds 40 mmHg
   - pressures > 50 mmHg → chronic pulmonary hypertension & RVH
h. ***pulmonary angiography*** = "gold standard" (see later)

- ***Indications for Angiography***

a. high index of suspicion ± V/Q scan equivocal
± high risk of anticoagulation

b. prior to thrombolytic therapy

c. differentiation between recurrent PE and fragmentation of an initial PE

NB: ***does not*** exclude PTE if performed > 5 days

- ***DVT Prophylaxis***

1. mechanical therapy
   i. leg exercises, early mobilisation
   ii. compressive stockings
   iii. pneumatic compression
2. low dose ***heparin***
   i. ↓ incidence of DVT ~ 60%
   ii. ↓ incidence of PTE ~ 50%
   iii. ↓ fatal PTE from 0.7 to ~ 0.2%
3. antiplatelet agents* are ***ineffective*** in prevention of DVT
4. IVC interruption
   i. caval filters - Greenfield / Bird's nest
   - useful when long-term anticoagulation contraindicated
   - also when recurrent emboli on Rx
   ii. caval ligation - ***not*** effective & severe lower limb oedema
   ~ 30-50% suffer PTE via colaterals

Treatment

- PTE either undergoes spontaneous fibrinolysis or organization
- substantial angiographic resolution usually occurs by 24 hrs, with further resolution at 4-6 wks
- only ~ 10% retain a significant pulmonary defect at 6/52
- 1-2% develop recurrent PTE with progressive pulmonary hypertension

a. general
   i. oxygen
   ii. CVS support *usually only required for massive embolism
      - small volume challenge may be beneficial ~ 500 ml
      - ↑ RAP > 20 mmHg may result in ↓ LV filling & acute TI
      - inotropic support with ***noradrenaline*** may have some advantage

b. ***anticoagulation***
- untreated PE has a mortality ~ 15%, cf. ~ 8% treated
- ∴ should be administered as soon as diagnosis suspected, unless contraindicated
- significant haemorrhage from heparin ~ 4% total
  ~ 0.5% fatal

i. heparin ~ 7-12 days
ii. warfarin ~ 3-6 mths

c. thrombolytic therapy
- massive PE
- persistent hypotension
- within 7 days of onset
- proven by angiogram
- absence of contraindications

- ***Streptokinase*** - 250,000 U over 30 mins
  - 100,000 U/hr for 24-72 hrs
- ***no*** proven decrease in mortality at 1 month cf. heparin alone
- improves early haemodynamics & improves angiographic resolution

d. IVC umbrella

e. surgical intervention
i. embolectomy
ii. IVC plication

f. management of RVF

- the indications for acute ***surgical embolectomy*** are unclear
- of patients with massive PTE ~ 66% die within 1st hr
  ~ 80% die with 2 hrs
- ∴if alive after several hrs → manage ***medically***
- consider embolectomy for those continuing to deteriorate after 1 hr,

a. cardiogenic shock- systolic BP < 90 mmHg despite inotropes
b. oliguria
c. hypoxia
d. failed medical therapy

- ***<u>Fragmin Infusion</u>***

a. loading dose ~ 5.0-10.0 U/kg *optional
b. infusion ~ 75-100 U/kg/day
i. concentration - 5000 U / 50 ml
ii. initially ~ 1.5-2.0 ml/hr
iii. maximum ~ 7.0 ml/hr *average size adult ≤ kg/10 ml/hr

V/Q Scan and Pulmonary Embolus

PIOPED Results[1]		
Scan Reading	% Pts.	% PTE
High Probability	13%	88%
Intermediate Probability	39%	33%
Low Probability	34%	15%
Normal	14%	2%

[1] JAMA 1990; 263:2753 ***prospective*** study
755 patients → pulmonary angiography & V/Q scans

- ***PIOPED***

1. a ***normal scan*** rules out clinically significant PTE, no further study required
   - however, this is exceeding rare in ICU setting
2. a ***low probability*** scan does not exclude PTE
3. ***clinical suspicion*** additive & important, with a low probability (~ 15%) scan
   i. high clinical suspicion **~ 40%** PTE
   ii. low clinical suspicion ~ 4% PTE
4. only ~ 40% of patients with PTE had ***high probability*** scans
   - ie. good specificity but ***poor sensitivity***

- prospective study of V/Q scan, angiography and venography,

1. high probability V/Q scan → positive,
   i. angiogram ~ 86%
   ii. venogram ~ 50%
   iii. either ~ 91%
2. non-diagnostic V/Q scans ~ 48% angiogram positive
   - ∴venogram/plethismography useful in this group
3. impedance plethismography = venography for DVT
   - however, ***neither*** is sensitive below the popliteal vessels
4. angiographically proven PTE →
   i. impedance plethismography DVT ~ 57%
   ii. venogram ***negative*** ~ 30%

NB: 90% of acute PTE originate from DVT

- ***Morrell et al. BMJ 1992***

1. high and low probability VQ scans are **~ 90%** specific and can generally be accepted
2. anticoagulants ***should not*** be given without good evidence for the diagnosis because the risk is in fact substantial
   - **5%** major bleed with 7 days heparin
   - **8%** major bleed with 3 months warfarin
   - ∴ always pursue a firm diagnosis rather than anticoagulating on clinical suspicion
   - other authors would ***disagree***, due to the 50% decrease in mortality with Rx
3. problem with ***intermediate probability*** scans, where **~ 40%** will actually have emboli, however,
   - ~ 90% of emboli come from the legs
   - ~ 90% of significant (ie popliteal or above) clots will show on ***doppler ultrasound***
4. although ~ 30% of PE patients have negative leg studies, the risk of further embolism in these patients appears to be small, so a case can be made to observe (perhaps with prophylactic-dose heparin) and re-scan if things change
5. if all of this is still inconclusive, then go to pulmonary angiography
   - if looking to exclude ***major*** emboli in ICU, use bedside pulmonary angiography

- ***Diagnostic Algorithm***

NB: do ***perfusion scan*** first,

a. ***normal Q scan***
   - i. & normal venogram → not PE
   - ii. & (+)'ve venogram above knee → treat as PE

b. ***abnormal Q scan***
   - i. & normal CXR → treat as PE
   - ii. & matching CXR changes, or
   - iii. subsegmental Q defects only → non-diagnostic

NB: non-diagnostic Q scan & CXR → ***ventilation scan***

- i. ***V scan normal*** (= V/Q mismatch) → PE (90%)
- ii. ***V scan abnormal*** → non-diagnostic
  → then do ***angiogram***

AIR / GAS EMBOLISM

- ***Aetiology***

  a. surgery involving major veins

  b. central venous cannulation

  c. pump infusions - CPB
     - haemofiltration

  d. pneumoperitoneum for laparoscopy or hysteroscopy

  e. LSCS ≤ 50% doppler proven VAE, especially with ***exteriorisation***

  f. orthopaedic surgery - especially THR

  g. neurosurgery - sitting position
     - patent dural venous sinuses

- ***Contributing Factors***

  a. volume / rate of infusion
     i. ³ **0.5 ml/kg/min** → results in symptoms
     ii. ³ **2 ml/kg/min** → generally fatal

  b. venous pressure * subatmospheric

  c. posture

  d. presence of an ASD - probe patent foramen ovale in ~ 10-25%
     - associated causes for ↑ PVR

- ***Associated Problems***

  a. ↑ PA pressure

  b. ↑ alveolar dead space and $P_{A\text{-}aO2}$ gradient

  c. acute RV failure

  d. systemic hypotension and tachycardia

  e. hypoxia

  f. arrhythmias, cardiac arrest

  g. systemic embolization *coronary & cerebral
     - occurs with or ***without*** PFO
     - ie. in massive embolisation, gas traverses the lung

  NB: the most likely cause of rapid death following massive embolisation is mechanical obstruction to ***RV outflow***

Monitoring		
• oesophageal stethoscope	~ 1.8	ml/kg/min
• systemic hypotension	~ 0.7	ml/kg/min
• ECG / tachyarrhythmias	~ 0.6	ml/kg/min
• $ETCO_2$	~ 0.42	ml/kg/min
• ETN_2 (better than CO_2)		
• PA pressure rise	~ 0.42	ml/kg/min
• continuous CVP	~ 0.4	ml/kg/min
• ***doppler precordial stethoscope***	~ 0.02	ml/kg/min
• transoesophageal echocardiography	sensitivity ~ 5-10x > doppler	

NB: ***precordial doppler*** can detect as little as **0.1 ml** of intracardiac air
& the correlation with TEE during caesarean section is ~ 100%

Management

a. prevent further air embolization
   i. inform surgeon → flood operative field
   ii. optimise position
   iii. neck vein compression

b. 100% F_IO_2 - ie. cease N_2O

c. ***right*** lateral position

d. withdraw air via multiorifice RA CVC line

e. IV fluids

f. drugs
   - pulmonary vasodilators
   - inotropes/vasoconstrictors ??
   - antiarrhythmics

g. hyperbaric oxygen

h. thoracotomy

i. intracardiac needle aspiration - right 4th ICS parasternally
   • ***NB***: must get RV & always get a ***pneumothorax***

RHEUMATIC FEVER

Def'n: an acute febrile ***systemic inflammatory disorder***,
following infection with ***group A,*** b-***haemolytic Streptococci***,
affecting predominantly the heart and joints

- ***Predisposition***

a. age 5-15 years
b. PH_X of rheumatic fever
c. recent Streptococcal infection
d. temperate climate

- ***Diagnosis***

Def'n: 2 major OR 1 major + 2 minor criteria

plus, recent evidence of *Streptococcal* infection

Major Criteria	Minor Criteria
1. endocarditis 2. myocarditis 3. pericarditis 4. polyarthritis 5. chorea 6. erythema marginatum (10-20%) 7. subcutaneous nodules	1. PH_X of rheumatic fever 2. fever 3. arthralgias 4. ↑ ESR, WCC, CRP 5. 1°HB on ECG 6. culture of β-haemolytic Strep.

- ***Other Features***

1. glomerulonephritis
2. scarlet fever
3. erythema nodosum
4. peritonitis
5. pleuritis

- ***Investigations***

1.	**ECG**	- tachycardia - 1°HB - T-wave inversion - pericarditis
2.	**CXR**	- cardiomegally - pleural effusion, pericardial effusion - LVF
3.	**FBE**	- neutrophilia, normochromic anaemia - ↑ ESR, CRP - ↑ ASOT - anti-DNA-ase B - muscle Auto-Ab's
4.	**Urine**	- proteinuria, haematuria - pyuria - casts

Treatment

a.	general supportive care	
b.	NSAID's	
c.	penicillin	- long term

COMPARTMENT SYNDROME

Def'n: ischaemic muscle damage caused by increased ***extravascular pressure***, usually occurring within a fascial compartment

- ***Aetiology***

a. prolonged ischaemia
   - thrombosis, embolism
   - surgery, torniquet

b. burns

c. trauma
   - crush syndrome
   - fractures
   - hypovolaemia / hypotension
   - vascular compromise

d. electrocution

e. rhabdomyolysis

- ***Clinical Features***

a. ***pain*** & tenderness

b. ***paralysis*** of the involved muscles

c. ***paraesthesiae*** - sensory & motor neuropathy of nerves within the compartment

d. impaired distal blood supply $\rightarrow$ "pulseless"

e. erythema, cyanosis, or discolouration of the overlying skin

- ***Management***

a. prevention

b. monitor high risk groups
   - compartmental pressures
   - doppler flow assessment
   - plasma CK/CPK
   - myoglobinuria

c. indications for fasciotomy
   i. pressure $\geq$ **40 mmHg**
   ii. $BP_D - P_{IC}$ < 30 mmHg
   iii. distal ischaemia

d. prevent myoglobinuric renal damage
   $\rightarrow$? forced ***alkaline diuresis*** - HCO_3^- / mannitol / saline

VASCULITIS

- ***Classification***

1. systemic ***necrotizing*** vasculitis
   - i. classical polyarteritis nodosa
     - small and medium sized vessels, especially at branch points
     - multiple organs involved, but usually ***lungs spared***
   - ii. allergic angiitis and granulomatosis *Churg-Strauss disease
     - multiple organ granulomatous vasculitis, especially involving lung
     - peripheral blood ***eosinophilia*** & eosinophillic tissue infiltration
     - association with severe asthma
   - iii. polyangiiitis overlap syndrome
2. ***hypersensitivity*** vasculitis
   - common feature is small vessel involvement, predominantly effecting skin
   - i. ***exogenous*** antigens proven or strongly suspected
     - drug induced vasculitis
     - infection induced vasculitis
     - Henoch-Schönlein purpura
     - serum sickness
   - ii. ***endogenous*** antigens probably involved
     - neoplasia associated vasculitis
     - connective tissue diseases
     - congenital complement deficiencies
     - other underlying diseases
3. Wegener's granulomatosis
   - upper & lower respiratory tracts, plus ***glomerulonephritis***
   - paranasal sinus involvement with pain and haemorrhage
   - mucosal ulceration, cartilage destruction (saddle nose)
4. giant cell arteritis
   - i. temporal arteritis
   - ii. Takayasu's arteritis
5. miscellaneous
   - i. mucocutaneous lymph node syndrome - Kawasaki's disease
   - ii. thromboangitis obliterans - Berger's disease
   - iii. isolated cerebral vasculitis

- ***Investigation***

1. history & examination
2. FBE, ESR, CRP
3. biochemistry - renal function, LFT's
4. urinalysis + sediment
5. serology
   i. RF
   ii. HBV Ab & Ag, HCV
   iii. autoantibodies
   iv. C' levels
   v. immune complexes
6. ECG
7. CXR
8. angiography
9. ***tissue biopsy***

Antibodies to:	**ANA**	**RF**	**Sm**	**Ro | La**	**SCL-70**	**centro-mere**	**ANCA**
RA	30-60	70-85					
SLE	95-100	20	10-25	5-20			
Sjogren's	95	75					
Scleroderma • limited (CREST) • diffuse	 80-95 80-95	 25-33 25-33			 20 33	 50 1	
Polymyositis	80-95	33			10		
Wegener's	0-15	50					93-96[1]

[1] principally ***cytoplasmic pattern*** in Wegener's
the ***perinuclear pattern*** is seen in patients with systemic vasculitis, or vasculitis limited to the kidney; the sensitivity of the later is undetermined & tissue diagnosis is still required