put together by Alex Yartsev: Sorry if i used your images or data and forgot to reference you. Tell me who you are. aleksei.igorevich@gmail.com

Myocardial Infarct 1.03

History of presenting illness (HPI)

CRUSHING CHEST PAIN, radiating to back, shoulder, Lt. Arm, neck and/or jaw
AGGRAVATED by exercise,
RELIEVED by rest

List of differential diagnosis

- Transient ischaemic attack,
- **Acute myocardial infarction,**
- ventricular hypertrophy or hyperplasia,
- aortic dissection,
- aneurysm
- stenosis,
- embolism,
- restricted cardiomyopathy,
- congenital septal defects,
- endocarditis,
- valve dysfunction
- angina,
- cancer,
- GI problems –reflux, ulcers, tears, infections, obstructions,
- Respiratory – pneumothorax, embolism, cancer, infection/infestation,
- Lymphatic- blood trauma, cancer, infection/infestation,
- Musculoskeltal – intercostals strain, blunt trauma, fracture,
- NS – referred pain, slipped disc, cervical impingment,
- Mental- anxiety, stress, personality, occupation, palpitations, ectopic beats

List of pertinent findings on history (Hx)

Past history

High blood pressure
Elevated total cholesterol
SMOKING = MAJOR FACTOR

Personal history

high physical work load,
emotional stress
eat out at least 4 times per week
20 cigarettes per day since the age of 20
1 -2 glasses of beer every night

Family history

Of heart disease

Cardiovascular risk factors found in HISTORY:
- **High blood pressure**
- **Smoking**
- **Family history**
- **Hypercholesterolemia**
- **Stress**
- **Heavy exertion workload**

Findings on examination

Distressed, pale, sweating slightly

Physical exam

- *Overweight 100kg*

Vital signs

- ***Blood pressure: 160/90*** *Pulse rate: regular*

Cardiovascular exam

- **Soft heart sounds**
- **4th heart sound present**
- **Soft bruit over right carotid artery and left femoral artery** due to stenosis

Respiratory exam

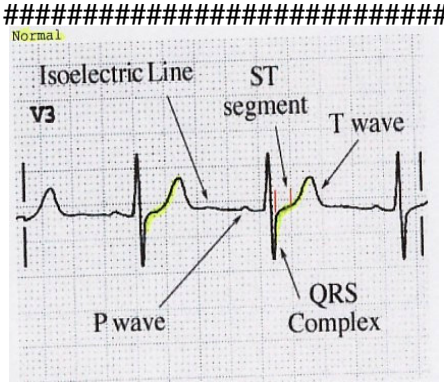
- **Scattered crepitations at base of both lung fields** due to pulmonary hypertension

Investigations

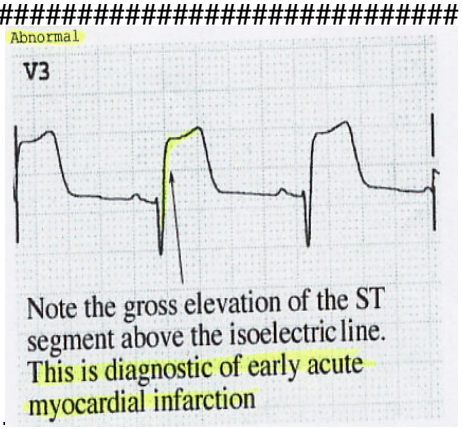
ECG

- **Looking for characteristic ST segment changes with axis deviation**

##



THE ST SEGMENT
is the relevant point for examination:
ST segment elevation of >2 mm in two contiguous chest leads (V1-V6) indicates
anterior myocardial infarction.
ST segment elevation of >1mm in two contiguous inferior leads (II, III, aVF) is indicative of
inferior myocardial infarction.



Myocardial ischaemia (NOT infarction)= **ST segment depression**.

Chest Xray

(**looking for Left Ventricle Hypertrophy** consistent with systemic hypertension)
also looking for **pulmonary congestion ("batwing sign")**

ALSO making sure that the crushing chest pain is NOT the result of a crushing chest injury (very embarassing)

→ eg. pneumothorax, broken rib, etc…

FBC

Looking for factors which may have predisposed to MI, eg. Anaemia
Blood Glucose might also be a useful test - considering diabetes

Serum Biochemistry

Looking for characteristic myocardial infarct enzymes, eg:

- **LDH (non-specific, would be elevated with strenuous physical activity)**
- **CK MB**
- **CK MB INDEX (i.e how much of the CK is the myocardium-specific CKMB)**
- **TEST EVERY 8 hrs! → serial CK**

Lipid profile

Less diagnostic and more an assessment of a risk factor …
…and indicator as to HOW MUCH LIFESTYLE ALTERATION IS NECESSARY

Management (heroic often useless measures)

Immediate (EMERGENCY ROOM)

- **NITRATES!! → give sublingual nitroglycerine to vasodilate!**
- **ECG Monitor** attached (**is the infarct ANTERIOR or POSTERIOR?**)
- **Oxygen** via mask to reperfuse myocardium
- **Intravenous cannula** inserted for easy delivery of fluids
- **5mg morphine** intravenously though cannula, for the excruciating pain
- **Thrombolytic rTPA- STREPTOKINASE** (**recombinant Tissue plasminogen activator-** converts PLASMINOGEN → **PLASMIN** → which **degrades FIBRIN**, the clot cement element)
  - commenced as it is less than 4 hrs since onset of pain and infarct is anterior

Medium-term Management

- **Turf to coronary care unit**
- **Angiography** to demonstrated coronary artery stenosis (BONUS if its what you expected from the ECG)
- **Coronary angioplasty** ⟸

~ANGIOPLASTY~

the KING of coronary artery salvage

…somebody turns up to ER with crushing chest pain and characteristic ST changes? → Wheel them straight down to the catheter lab to clear that coronary

Long term management + Follow Up

- **Medications**:
  - **150 mg asprin daily**,
  - **50 mg metoprolol three times per day (β blocker)**
  - **25 mg captopril ACE inhibitor**
- **low fat, low salt diet**
- **cease smoking**
- **graded increase in activity over the next 3 weeks**
- **have lipids checked in 3 months**

Extra management

- **Multidisciplinary approach** : **med, nursing, physio, OT, social worker**
- **Goal:**
  - to prevent another MI by patient education,
  - weight loss,
  - reduce/cease smoking,
  - increase exercise,
  - stress reduction

Disease definition: Acute occlusion of the left anterior descending coronary artery, resulting in infarction of the anterior myocardium, precipitating crushing retrosternal pain.

How is this diagnosis made

- ECG, chest x-ray and cardiac enzyme profile or troponin
- Later a lipid profile helps determine if cholesterol is a problem
- Diagnostic **red flags on presentation** –
  - **chest pain**, heaviness squeezing or crushing,
  - **dyspnoea** (shortness of breath),
  - **ankle swelling**,
  - **palpitations**,
  - **syncope** (transient loss of consciousness),
  - intermittent claudication (**limp**),
  - **fatigue, anxiety and restlessness** (from pain),
  - **pallor**, diaphoresis (**sweating**),
  - **cool limbs, fever** (not usually above 38°C)

Epidemiology

- **Angina and acute myocardial infarction are the major forms of cardiovascular disease causing death and illness in NSW** (9,479 deaths or **21% of deaths**, male deaths (25-74yrs) are 3.7 times higher than females in NSW 2000),
- **50% of those that suffer an acute MI survive**,
- **10% die in hospital**
- **10% die in the next 2 years,**
- **50% of initial survivors are alive at 10 years.**
- Increased risk factors for cardiovascular disease are : family history, old age, males and postmenopausal female, diabetics

Aetiology

- **Fixed risk factors**:
  - **increasing age,**
  - **male,**
  - postmenopausal females,
  - **family history,**
  - deletion polymorphism in the Angiotensin- converting enzyme ACE gene (DD genotype)
- **Changeable risk factors**:
  - **hyperlipidaemia,**
  - **smoking,**
  - **hypertension,**
  - **lack of exercise,**
  - **obesity,**
  - high fat or low antioxidant diets,
  - gout,
  - soft water,
  - **heavy alcohol consumption,**
  - contraceptive pill,
  - **diabetes mellitus,**
  - high levels of blood coagulation factors (fibrinogen, factor VII), C reactive protein CRP, hyper-homocysteinaemia)
  - type A personality
  - **salt consumption**

Prognosis

- **variable (related to age and size of infarct**). 10% of patients surviving the initial MI die within 2 years with 5 yr mortality approx 20%.
- In patients under 50 yrs risk of death is 3% per year compared to over 15% in over 70's.

Behavioural science

- Issues of diet and increased exercise need to be discussed with the patient and behavioural modifications need to occur for this to happen effectively.

Involvement of a **dietician, physio and OT** will need to occur to educate the patient on how to best begin this process without causing further health problems.

- ADVICE TO **QUIT SMOKING AND LOSE WEIGHT** : effective after 1st infarct; 50% of pts will quit even after short lecture (<3min) if they are STILL IN PAIN.

PAIN MAKES THEM REMEMBER

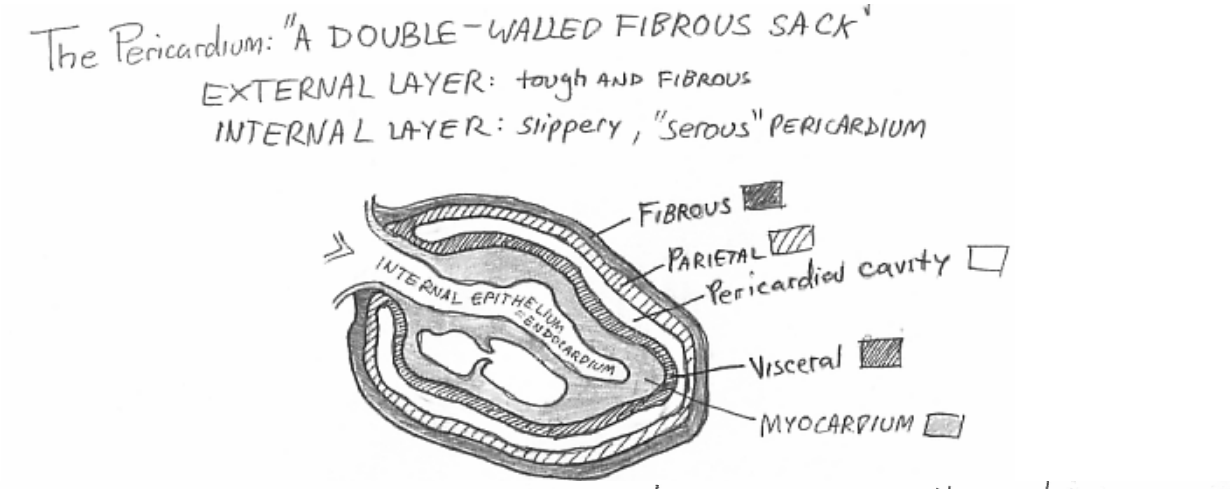
Basic sciences

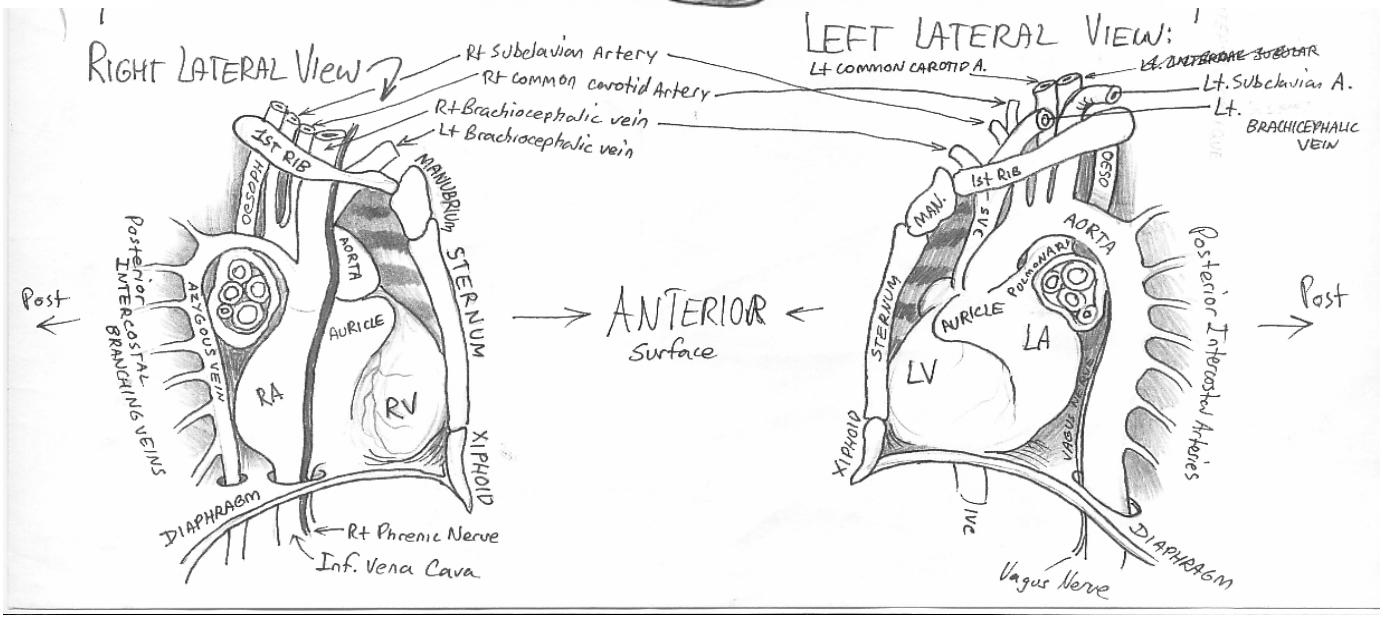
- Mycocardial ischaemia occurs when **CARDIAC NUTRITIONAL** **DEMAND EXCEEDS SUPPLY**
  Causes of this imbalance are:
  - **(a) obstructions** that reduce the blood flow
    (atheroma, thrombosis, spasm, embolus, coronary ostial stenosis, coronary arteritis)
  - **(b) decreased oxygenated blood flow**
    (anaemia, carboxyhaemoglobinaemia, hypotension causing decreased coronary perfusion pressure)
  - **(c) increased oxygen demand**
    due to increased cardiac output (thyrotoxicosis) or myocardial hypertrophy.

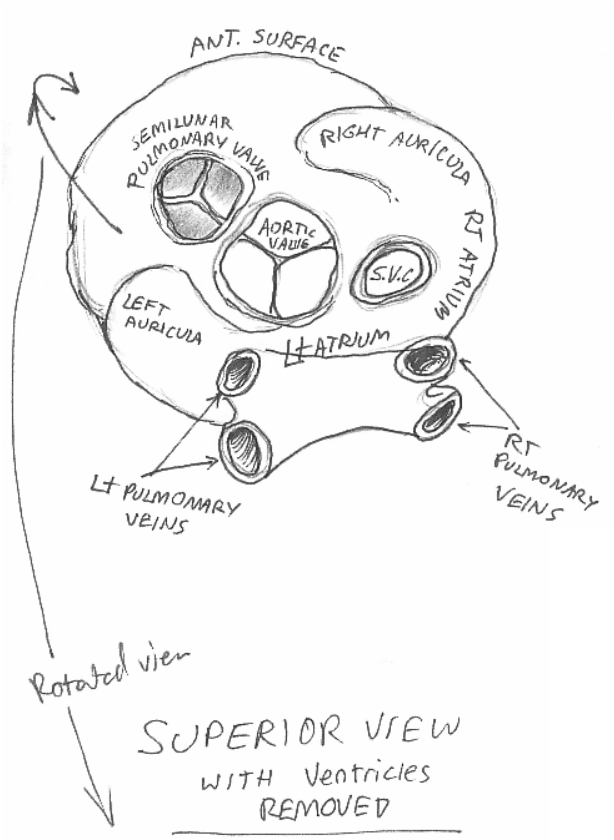
Relevant anatomy

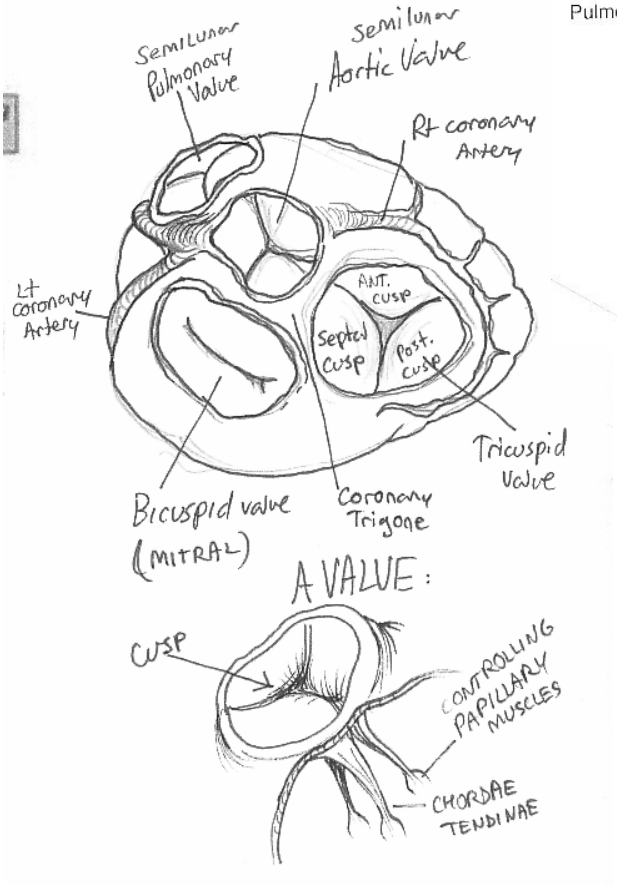
Normal Artery: 2 types: ELASTIC and MUSCULAR;

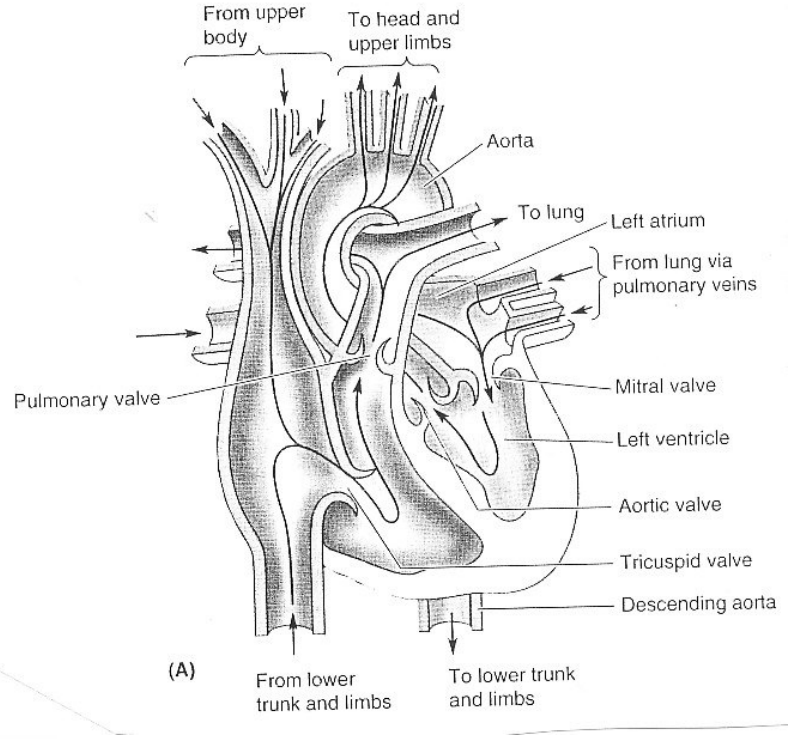
ENDOTHELIUM prevents coagulation by platlets contacting the collagen that lines the lumen, it **produces heparin**, **controls the constriction of muscle cells** and **is selectively permeable**
INTIMA (thin squamous epithelium)
INTERNAL ELASTIC LAMINA (elastic connective tissue)
TUNICA MEDIA (thickest layer with circumferential smooth muscle cells)
EXTERNAL ELASTIC LAMINA (elastic connective tissue)
TUNICA ADVENTITIA (outer connective tissue sheath)






ANT. SURFACE
SEMILUNAR PULMONARY VALVE
RIGHT AURICULA
RT ATRIUM
AORTIC VALVE
S.V.C.
LEFT AURICULA
LT ATRIUM
LT PULMONARY VEINS
RT PULMONARY VEINS
Rotated view
SUPERIOR VIEW WITH Ventricles REMOVED


Semilunar Pulmonary Valve
Semilunar Aortic Valve
Rt coronary Artery
Lt Coronary Artery
ANT. CUSP
Septal cusp
Post. cusp
Tricuspid Valve
Bicuspid valve (MITRAL)
Coronary Trigone
A VALVE:
CUSP
CONTROLLING PAPILLARY MUSCLES
CHORDAE TENDINAE


From upper body
To head and upper limbs
Aorta
To lung
Left atrium
From lung via pulmonary veins
Pulmonary valve
Mitral valve
Left ventricle
Aortic valve
Tricuspid valve
Descending aorta
(A)
From lower trunk and limbs
To lower trunk and limbs

Biochemistry

- Once the myocardium is deprived of oxygen and nutrients:
    - **the pH decreases, …thus**
    - **PFK1 decreases** (phosphofructokinase 1 which is inhibited by an acid pH).
    - **phosphatidyl creatinine and glycogen DECREASES**
      as the myocardium uses the energy stores available.

  Myocardium can last <u>up to 4 hrs</u> with occlusion before damage occurs.
  <u>THEN:</u> The *<u>cells burst releasing</u>*
  - **LDH H4 ,** (Lactate Dehydrogenase 1 and 2; **LDH1 rises after myocardial injury**)
  - **CK MB,** (Creatine Kinase MB is specific to myocardium)
  - **troponin I and T**
  - **myoglobin.**
  - **<u>ALL OF WHICH ARE CLINICALLY DETECTABLE POST-INFARCT!</u>**

- In mild ischemia oxidation of fatty acids occurs which increases lactate and H^+ however in severe ischemia glycolysis occurs from glycogen producing the ATP required increasing the lactate and H^+
- Aerobic reperfusion of the area to minimise cell damage:
  - **by angioplasty**, (mechanically opening the vessel)
  - **CAGS** (Coronary Artery Graft **Surgery**)
  - **thrombolytic therapy** (chemically reducing the occlusion)

After infarction there is
increase in fatty acid metabolism which requires <u>increased oxygen consumption</u>
THUS: If there is inadequate oxygen supplied then there is
- a decrease in pyruvate dehydrogenase (PDH),
- an increase in glycolysis,
- a decreased pH
- **an increase in Na^+ and Ca^{+2}**
- which means death for cells after 4 hrs because the calcium levels become too high

(apoptosis is activated by increased Ca^{2+})

Cell biology

- The consequences of endothelium injury in atherosclerosis (As) are:
- enhanced permeability of lipid from the blood to the intima,
- platlet and monocyte adhesion at the injury site with the release of
    - **platlet derived growth factor (PDGF)** and other similar factors which **stimulate smooth muscle cells migration** from the media to the intima.
    - Once the **smooth muscle cells** migrate to the intima they
        - **lose their contractile properties and become proliferative/synthetic**
        - **undergo mitosis** producing connective tissue mucins, **collagen and elastin** which contributes to the **intimal thickening.**
        - Together with monocytes the smooth muscle cells ingest lipids becoming **FOAM cells.**
- The **thickening of the intima can lead to narrowing (stenosis**) of the lumen which changes the blood flow **from laminar to turbulent.**

Genetics

- Genetic factors are involved in the predisposition to this disease – families of MI victims are at risk

Pathology

- Atherosclerosis causes prolonged endothelial injury where intimal thickening is a major feature.
- MI almost always occurs in patients with coronary atheroma as a result of plaque rupture with superadded thrombus.
- The occlusive thrombus consists of
    - a white clot (**platlet rich core**) and
    - a bulkier surrounding red clot **(fibrin rich outer surface).**

MI occurs when a coronary artery thrombus develops rapidly at a site of vascular injury. In most cases, infarction occurs when an **atherosclerotic plaque fissures, ruptures, or ulcerates** and when conditions (local or systemic) favor thrombogenesis, so that a mural **thrombus forms at the site of rupture** and leads to coronary artery occlusion (See diagram). Histologic studies indicate that the coronary plaques prone to rupture are those with a rich lipid core and a thin fibrous cap. After an initial **platelet monolayer forms at the site** of the ruptured plaque, various agonists (**collagen, ADP, epinephrine, serotonin**) **promote platelet activation**. After agonist stimulation of platelets, there is production and release of **thromboxane A_2** (a potent local vasoconstrictor), further platelet activation, and potential resistance to thrombolysis.

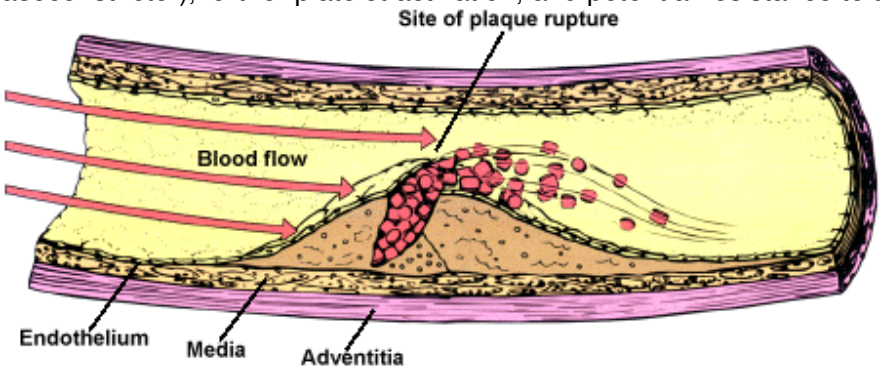


Diagram of arterial thrombus responsible for acute myocardial infarction..*[From NS Kleiman: Antiplatelet therapy, in RM Califf (volume ed): Acute Myocardial Infarction and Other Acute Ischemic Syndromes, in E Braunwald (series ed): Atlas of Heart Diseases, Philadelphia: Current Medicine, 1996, p. 8.2.]*

The coagulation cascade is activated on exposure of tissue factor in damaged endothelial cells at the site of the ruptured plaque.

Factors VII and X are activated, ultimately leading to **the conversion of prothrombin to thrombin, which then converts fibrinogen to fibrin**.

THUS:The **culprit coronary artery eventually becomes occluded by a thrombus** containing platelet aggregates and fibrin strands

- In rare cases, MI may be due to coronary artery occlusion caused by coronary emboli, congenital abnormalities, coronary spasm, and a wide variety of systemic-particularly inflammatory-diseases. The amount of myocardial damage caused by coronary occlusion depends on
    - **the territory supplied** by the affected vessel,
    - whether or not the **vessel becomes totally occluded**,
    - the **duration** of coronary occlusion,
    - the quantity of blood supplied by collateral vessels to the affected tissue,
    - the **demand for oxygen** of the myocardium whose blood supply has been suddenly limited,
    - native factors that can produce early spontaneous lysis of the occlusive thrombus, and
    - the adequacy of myocardial perfusion in the infarct zone when flow is restored in the occluded epicardial coronary artery.

Physiology

Cardiac Output = Heart Rate X Stroke Volume

– **STROKE VOLUME is dependent on:**

- **Preload =** Left ventricular end diastolic volume

  i.e. amount of stretch of left ventricle = *volume overload*

- **Afterload =** Total peripheral resistance = *pressure overload*

- **Contractility =** Capacity of myocardium to 'respond to' preload and afterload

Pathophysiology

- A number of **responses are associated with the failing myocardium**.

Initially these improve cardiac output but as the disease progresses,

these **responses become maladaptive** and contribute to a progression of the disease.

Cardiac dilatation - Cardiac output increases as length of muscle fibre is increased (Frank-Starling Law)

Sympathetic overdrive - Direct increase in contractility (positive inotropic effect), Indirect effects (increase preload - constriction of capacitance vessels and increase afterload - PVR) , Blood is diverted from liver, kidneys and skin to the heart and brain.

Renin-angiotensin system activated - Aldosterone causes Na^+ retention and thus increase blood volume (increase preload), Angiotensin causes peripheral vasoconstriction (increase TPR)

The effectiveness of the circulation becomes impaired due to:

- Elevated TPR that increase cardiac work, wall tension and hence O_2 requirements;
- Excess Na^+ and H_20 retention together with raised venous tone increase ventricular filling pressure.

Clinical consequences – *Fatigue, Peripheral oedema, Shortness of breath/pulmonary oedema*

- 2- 3 days post MI **cardiac arrhythmias, cardiac failure and pericarditis** are the most common complications. Later recurrent infarction, angina, thromboembolism, mitral valve regurgitation and ventricular septal or free wall rupture can occur. Late complications include post-MI syndrome (Dressler's syndrome), **ventricular aneurysm** and **recurrent cardiac arrhythmias.**

Immunology

- The plaque that develops contains a **large soft core** which **usually contains necrotic debris** and lipid with a **high density of MACROPHAGES** covered by a thin fibrous cap.
  - **Degradation of the collagen** by **metalloproteinases expressed by macrophages contributes to the rupture of the plaque**.

Pharmacology

Analgesia:

MORPHINE SULPHATE: Opioid:

Targets **opioid receptors** → Inhibition of Adenylate Cyclase → decrease cAMP; open K, close Ca channels, which leads to **General Inhibition of CNS and PNS**
dosage: ~5mg IV
Contraindications: hypersensitivity to opioids, respiratory depression, **cor pulmonale,** alcohol, intracranial pressure, labour.
Side Effects: sedation, constipation, nausea, resp. depression, euphoria **+ tolerance and dependance**
HARMFUL IN PREGNANCY

PARACETAMOL(acetaminophen): Simple Analgesics

Same as NSAIDs; inhibits COX isoenzymes
Minimal anti-inflammatory action
Minimal Side-effects at therapeutic dose
Dosage 1.0 g every 3-4 hours, **max 4 g a day** or else NECROTIC HEPATITIS (!!)
Contraindications: liver dysfunction, renal impairment
Side effects: hepatotoxicity, kidney failure, dyspepsia, nausea.
NO ADVERSE EFFECTS IN PREGNANCY

Thrombolytic Drugs:

STREPTOKINASE:

Converts Plasminogen to PLASMIN, which in turn degrades FIBRIN thus lysing the thrombus
COMPLICATED DOSAGE
Contraindications: Surgery, bleeding, trauma, severe hypertension
Side effects: bleeding in GIT, allergic reaction, Fever, Hypotension
HARMFUL IN PREGNANCY

β-Blockers (beta-adrenoceptor antagonists)

METROPROLOL

Decrease adrenoceptor function and thus decrease myocardial sensitivity to Adrenaline
THUS decrease heart rate and cardiac output
Dosage 50mg 3 times daily
Contraindications: right ventricular hypertrophy, sinus bradycardia
Side Effects: hypotension, bradycardia, cold extremities, headache, bronchial constriction
HARMFUL IN PREGNANCY

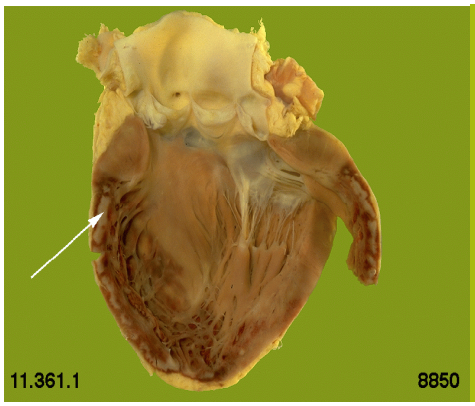
ACE Inhibitors (Angiotensin Converting Enzyme)

CAPTOPRIL

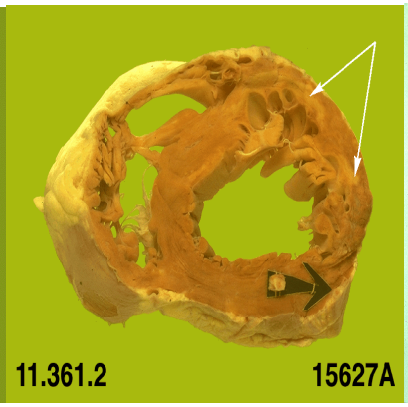
Block ANGIOTENSIN 2 generation from Angiotensin 1 (an inactive plasma protein)
THUS reduces vasoconstriction; THUS increases blood perfusion in stenosed arteries
Dosage 25mg twice daily
Contraindications angioedema, pregnancy
Side Effects: Hypotension; Angioedema; Hepatic Impairment; Dry Cough;
VERY HARMFUL IN PREGNANCY

NSAIDs:

ASPIRIN is cheapest and most effective;
Inhibits COX 1 and COX 2 isoenzymes; therefore blocking production of prostaglandins.
ALSO (most importantly) INHIBITS CLOTTING; thus useful to control emboli
contraindicated in asthmatics and people with existing gastric ulcers or haemorrhages
Dosage is dependant on many factors- BUT: Post-MI pts benefit from prophylactic with **very low doses (80mg orally, daily, indefinitely)**



Recent myocardial infarct



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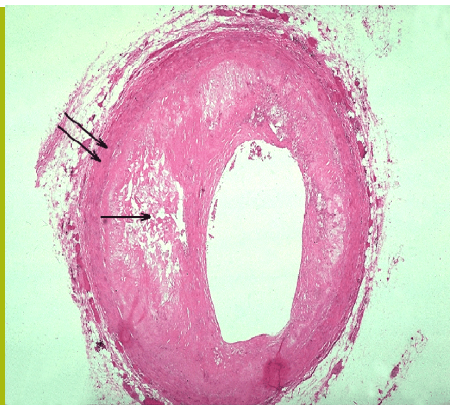
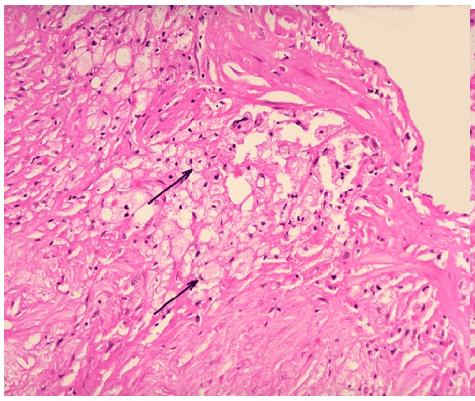


Atheromatous artery



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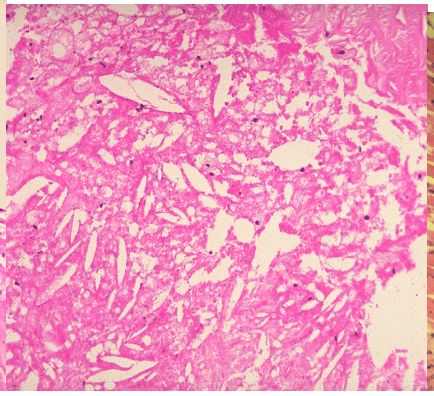
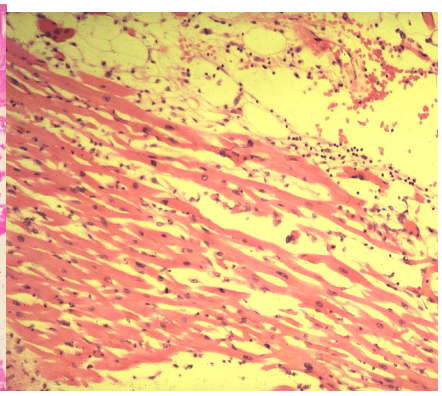
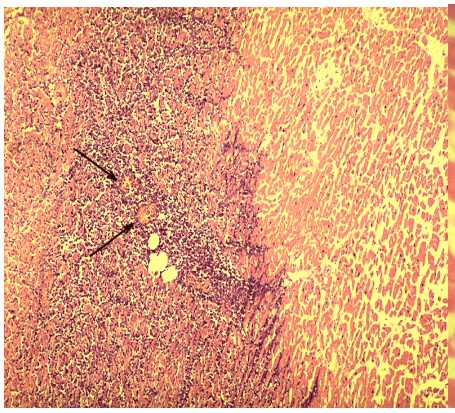


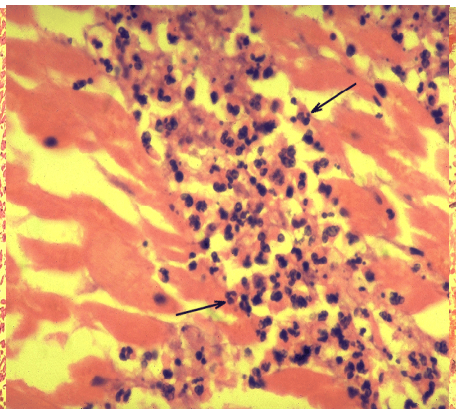
Atheromatous artery



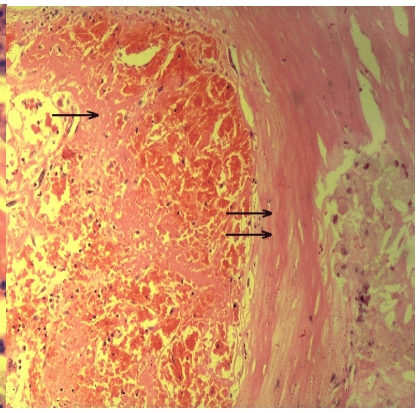
Recent myocardial infarct



Recent myocardial infarct



Recent myocardial infarct



Artery – atherothrombosis