Heart Failure

History of Presenting Illness

The heart failure patient, upon presentation, will complain of

The patient will invariably be FAT, possibly DIABETIC, and almost certainly a SMOKER

- **EXTERTIONAL DYSPNOEA**
- **ORTHOPNOEA**
- **PAROXYSMAL NOCTURNAL DYSPNOEA**

LVF

- **ANKLE SWELLING**
- **ABDOMINAL SWELLING**
- **ANOREXIA**
- **NAUSEA**

RVF

…or, possibly, the bouquet of INFARCT SYMPTOMS +ANGINA

Differential Diagnoses

Acute Respiratory Distress Syndrome
Asthma
Cardiogenic Shock
Chronic Bronchitis
Chronic Obstructive Pulmonary Disease
Emphysema
Goodpasture Syndrome
Myocardial Infarction
Myocardial Ischemia
Pneumocystis Carinii Pneumonia
Pneumonia, Bacterial
Pneumonia, Community-Acquired
Pneumonia, Viral
Pneumothorax
Pulmonary Edema, Cardiogenic
Pulmonary Edema, High-Altitude
Pulmonary Edema, Neurogenic
Pulmonary Embolism
Pulmonary Fibrosis, Idiopathic
Pulmonary Fibrosis, Interstitial (Nonidiopathic)
Respiratory Failure

Pertinent Findings on History

- Orthopnea = early symptom;
  …how many pillows?…
  … occurs rapidly, often within a minute or two of recumbency
- Exertional dyspnea
- Non-productive cough
- Paroxysmal nocturnal dyspnea
  = sudden awakening of the patient, after a couple hours of sleep, with a feeling of severe anxiety, breathlessness, and suffocation. The patient may bolt upright in bed and gasp for breath.
  … may require 30 minutes or longer in this position for relief.
- Dyspnea at rest
- Nocturia
- Fatigue and weakness
- Cerebral symptoms:
  - Confusion,
  - memory impairment,
  - anxiety,
  - headaches,
  - insomnia,
  - bad dreams or nightmares,
  - rarely, psychosis with disorientation, delirium, or hallucinations may occur in elderly patients with advanced heart failure, esp. those with cerebrovascular atherosclerosis.
- ***Predominant right heart failure:***
  - Ascites,
  - congestive hepatomegaly,
  - increased abdominal girth
  - epigastric and right upper quadrant (RUQ) abdominal pain.
  - anorexia,
  - bloating,
  - nausea,
  - constipation.
  - In preterminal heart failure, inadequate bowel perfusion can cause abdominal pain, distention, and bloody stools. Distinguishing right-sided CHF from hepatic failure is often clinically difficult.
  - NO Dyspnea !! unlike LHF
  - NOT UNTIL LATER does dyspnea occur as a consequence of the reduced cardiac output, poor perfusion of respiratory muscles, hypoxemia, and metabolic acidosis

Findings on Examination

LVF

OBSERVATION:
Tachypnoea
Central cyanosis
Cheyne-Stokes breathing
Peripheral cyanosis
Hypotension
Cardiac cachexia
PULSE:
Sinus tachycardia
low pulse pressure
pulsus alternans
(alternating strong and weak beats)]
PALPATION:
displaced apex beat
AUSCULTATION
left ventricular S3
mitral regurg pansystolic murmur
lung fields will crackle coarsely @ bases

RVF

OBSERVATION:
Swollen ankles / abdomen
Peripheral cyanosis
PULSE:
low volume
JVP
Raised with large V waves
PALPATION:
"Rt ventricular heave"
tender hepatomegaly
(liver distended against the rigid capsule)
pitting oedema
AUSCULTATION
rt ventricular S3
tricuspid regurg pansystolic murmur

Tests and Investigations: its all about the UNDERLYING CAUSE

FBC: Looking for anaemia, which would in turn cause tachycardia in an underperfused heart

Electrolytes Looking for derangements of calcium and potassium (cause arrhythmia)

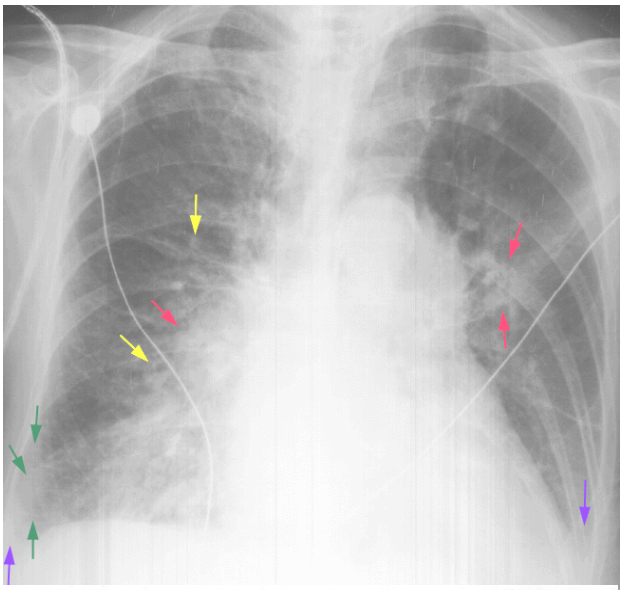
Liver Function Tests Looking for liver failure, to exclude a non-cardiac reason for hepatomegaly

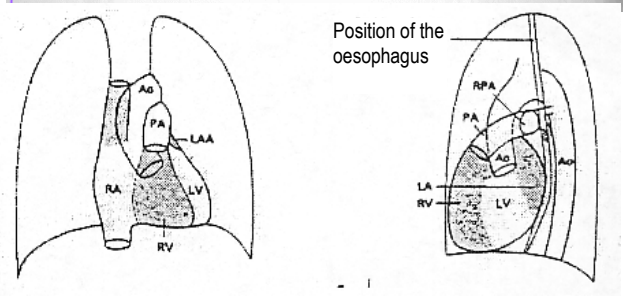
ABGs

Looking for O2; to see if more is needed.
If there is hypercapnea, hypoxemia, and the pt. is acidotic
- consider doing something RIGHT AWAY

Remember the
Kerley lines!!
= signs of oedema; = fluid in the interlobular septum

CHEST X-RAY

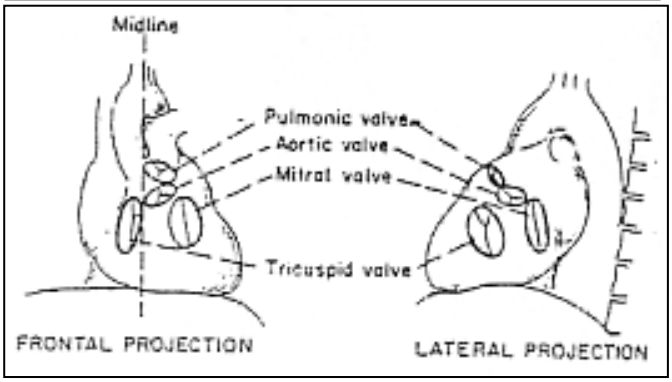




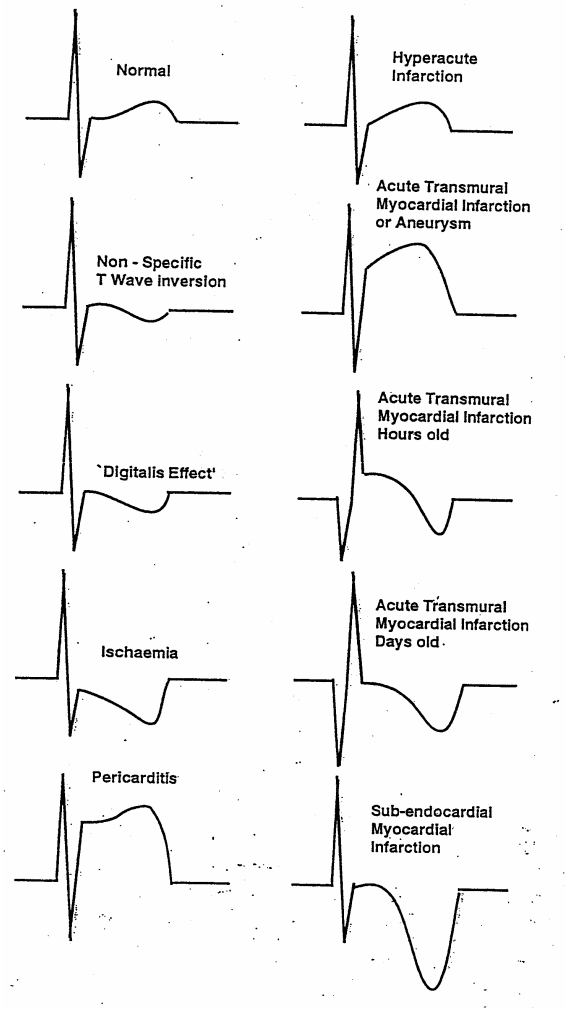
KEY WORDS FOR RADIOLOGICAL ABNORMALITIES OF HEART FAILURE:

- **Enlarged cardiac silhouette**
- **Spread fan of "batwings" around heart: opaque distended vessels**
- **cuffing of the bronchial walls (OEDEMA)**
- **pleural effusions at the costodiaphragmatic recesses**
- **Kerley Lines**

CARDIO-RADIOLOGY: *ALWAYS MEASURE* ***PA FILM*** *to get the right magnification, else the heart seems too big*
1st thing: HEART SHOULD OCCUPY NO MORE THAN HALF OF THE THORACIC DIAMETER
2nd thing: look for effusion (blunt angles)
3rd thing: look for pulmonary congestion (batwings)

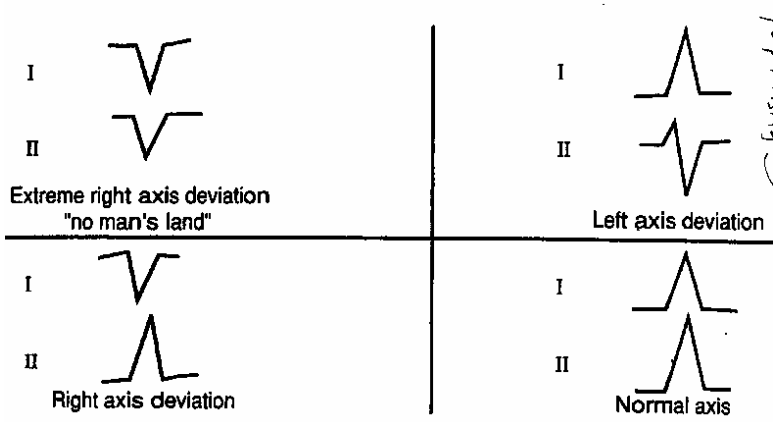


ECG



THERE IS NO DIAGNOSTIC "HEART FAILURE" ECG!
Instead, youre LOOKING FOR:

- **ARRHYTHMIA**
  - *atrial fibrillation is present in 25 percent of patients with cardiomyopathy, especially elderly patients with advanced heart failure.[23] The prognosis is worse for patients with atrial fibrillation, atrial or ventricular tachycardia, or left bundle branch block*
  - ***IF THEY ARE IN ATRIAL FIBRILATION, GIVE THEM ANTICOAGULANTS RIGHT AWAY!! Don't wait for the thrombus to break off and sail to the brain***
- **LV ENLARGEMENT: left axis deviation**



- **ST SEGMENT CHANGES to indicate infarct; see left**

ECHOCARDIOGRAM

Shows everything! → EASIEST + LEAST EXPENSIVE

- **Function of valves**
- **Whether anything regurgitates through the valves**
- **Thickness of LV wall**
- **Presence of pericardial disease**
- **Regional wall motion abnormalities**

In general, patients with an ejection fraction below 25% have *severe heart failure.*

Disease Definition

Heart failure: when cardiac output is less than what the tissues demand; i.e the HEART IS NOT DOING ITS JOB

Management: DRUGS to either live longer or feel better (and rarely both)

!! Most effective drugs are those that modify harmful neurohormonal adaptation !!

THERE IS AN ESTABLISHED PATHWAY OF TREATMENT according to patients condition:

Patients' condition: BAD → WORSE

0. **non-glycoside inotropes @ ACUTE PRESENTATION =** use for short-term circulation support
1. **NITRO VASODILATORS:** reperfuse the myocardium, reduce **TPR**
2. **Beta Blockers.** Start right away
3. **ACE Inhibitors** while LV dysfunction is asymptomatic
4. **Mild Diuretics + Digoxin** when it becomes symptomatic
5. **Loop diuretics**
6. **Spironolactone (aldosterone inhibitor)** when theres dyspnoea at rest
7. **Specialised therapies, angioplasty transplant, multi-agent diuresis**

AND ALL THE WHILE:

- **Education: QUIT SMOKING !! STOP DRINKING !!**
- **Exercise**
- **Salt and Fat reduced diet**

estimated 5-year mortality rate of 50%.

Prognosis

HEART FAILURE ALONE: you have a 5-20% chance of dying in the hospital
WITH MYOCARDIAL INFARCTION, 20-40% mortality

Epidemiology

- Nearly 1 million hospital admissions for acute decompensated CHF occur in the United States yearly,
- Affects 2% of the USA population
- Nearly 2% of all hospital admissions in the United States are for decompensated CHF,
- An estimated $23 billion are spent on inpatient management of CHF every year
- Another $40 billion are spent in the outpatient setting on patients with compensated or mildly decompensated heart failure every year
- incidence and prevalence of CHF are higher in the underprivileged proletariat
- Men and women have equivalent incidence and prevalence of CHF
- most common in individuals older than 65 years

Behavioural science: HOW TO DETECT AN ALCOHOLIC

Historical assessment:

Ask about

- **amount, (men = 28 /wk, women = 14)**
- **regularity (need alcohol-free days)**
- **favourite drink (spirits more dangerous)**
- **"eye-openers" (= sign of addiction)**
- **withdrawal effects**
- **depression, anxiety**
- **social problems, psychological problems**
- **relationship, family, work-related or legal problems**

Physical assessment:

Look for:

- **liver edge:**
    - **swollen (steatosis, early)**
    - **or shrunken (cirrhosis, late)**
- **abdomen: distended with ascites?**
- **Jaundice?**
- **Cardiomegaly?**
- **Neuro exam: encephalopathy?**

Laboratory assessment:

- **LIVER FUNCTION TESTS are all-powerful; look to GGT and ALT**
- **BLOOD FILM AND COUNT: looking for megaloblastic anaemia of alcoholism**

Aetiology / Pathophysiology: mechanism of HEART FAILURE

CHRONIC ALCOHOL CONSUMPTION > 90 g/day

Genetic defect of the SARCOMERE

→ **DILATION CARDIOMYOPATHY**
myocardium remodels in series in response to distending stimulus

MITRAL or AORTIC REGURGITATION → **Chronic VOLUME OVERLOAD** = INCREASED PRELOAD

INFARCTION

ISCHAEMIA → **Myocyte death And FIBROSIS**

→ **IMPAIRED CONTRACTILITY**
- Too few myocytes
- Reduced force per unit area (inefficient dilated anatomy)
- Too much preload (heart muscle stretched by influx of blood- too much blood filling it to contract effectively

→ **SYSTOLIC DYSFUNCTION**
i.e diminished ejection fraction

AORTIC STENOSIS

HYPERTENSION

→ RESISTANCE TO BLOOD FLOW: INCREASED AFTERLOAD

→ **Myocardiocytes remodel in parallel**
i.e wall thickness increases; =
= CONCENTRIC CARDIOMYOPATHY

Left Ventricular HYPERTROPHY

FIBROSIS

Genetic defect of the SARCOMERE

RESTRICTIVE cardiomyopathy eg. pericardial adhesions, etc

→ CHRONICALLY STIFFENED LEFT VENTRICLE

ISCHAEMIA → Transiently impaired relaxation – due to ion pump starvation

→ **IMPAIRED RELAXATION**
Thus DIMINISHED FILLING

LV filling obstruction: mitral stenosis, cardiac tamponade etc.

→ **DIASTOLIC DYSFUNCTION**

→ **REDUCED CARDIAC OUTPUT**

→ REDUCED CARDIAC NUTRITION

INCREASED HEART RATE
Thus INCREASED METABOLIC DEMAND @ MYOCARDIUM

Decreased perfusion pressure sensed by carotid sinus and aortic arch baroreceptors

REDUCED RENAL ARTERY PERFUSION

@ MEDULLA:
decreased parasympathetic outflow
increased sympathetic outflow

VIA CRANIAL NERVES 9 and 10

Some return to NORMAL CARDIAC OUPUT

Reduced delivery of salt to the macula densa of the kidney

VASOCONSTRICTION → Increased VENOUS RETURN

INCREASED AFTERLOAD

REDUCED STROKE VOLUME

!!! REDUCED CARDIAC OUTPUT !!!

RENIN IS SECRETED
→ converts circulating angiotensionogen into
ANGIOTENSIN 1
→ converted by endothelial ACE into
ANGIOTENSIN-2
= **arterioconstrictor**
= **thirst stimulator** via hypothalamus
= **ADH secretion stimulator** @ant. pituitary (thus reducing Na+ excretion)
= **ALDOSTERONE secretion stimulator** (thus further reducing Na+ excretion)
NO Na+ EXCRETION = WATER RETENTION

Increased blood pressure

→ **INCREASED BLOOD !! VOLUME !!**

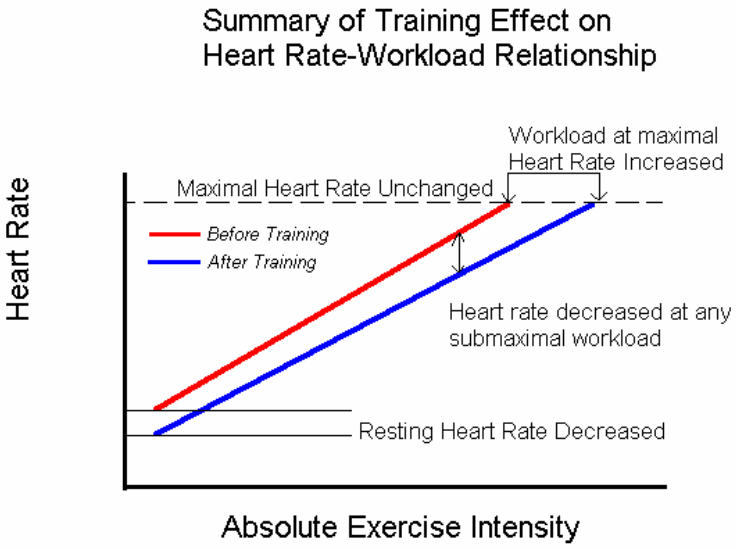
INCREASED LOAD ON CHAMBERS:
= ATRIA DISTENDED
→ Atrial Natriuretic Peptide released
= INHIBITS RENIN SECRETION
= REDUCES EFFECT OF Angiotensin 2 on ALDOSTERONE secretion
= INCREASED EXCRETION OF SODIUM;
→ thus REDUCED BLOOD VOLUME

The Heart and Exercise

Cardiac Output increases in response to increased oxygen demand.

MAXIMAL EXERCISE:

Maximal heart rate does not increase **after training. It stays the same** (or might even decrease just slightly). However,
maximal stroke volume increases.



MAXIMUM HEART RATE:

The rate beyond which the heart will not have time to fill
DECREASES WITH AGE
= 220 minus age in years

- useful max = ~180 bpm

EXERCISE:

- **As you begin to exercise, the oxygen demand increases.**
- **THUS cardiac output increases:**
  BY INCREASING BOTH HEART RATE AND STROKE VOLUME
- **HOWEVER** one would expect mean arterial pressure to increase from all this extra blood being pumped in –
- **MAP** does not increase – because the blood vessels also dilate,
  redirecting blood flow TO THE STARVING MUSCLES
- **The blood flow can increase 35-fold!!**
- **THUS the blood pressure doesn't increase nearly as much as the heart rate**

PRELOAD:
end-diastolic pressure just before contraction

AFTERLOAD
= pressure required to open the aortic valve

Physiology of heart function:

DIASTOLE:

Relaxed ventricles fill with atrial blood
The ventricle wall distends

SYSTOLE:

Ventricular wall contracts in response to pacemaker signal
Rising ventricular pressure forces the "in" valve shut
NO VALVES ARE OPEN AT THIS STAGE!!
= ISOVOLEMIC CONTRACTION (volume does not change)
Ventricles continue to contract
Pressure rises
Eventually the "out" valve (eg. aortic) is forced open
THUS: A jet of blood is squirted into the systemic circulation
THIS JET IS THE STROKE VOLUME
Now, the ventricle begins to relax
Pressure inside it falls
The back-pressure from the systemic circulation
(eg. pressure inside the aorta)
forces the "out" valve closed.
Ventricle continues to relax until the pressure falls so far that the "in" valve is open again
THUS, FILLING FROM THE ATRIA COMMENCES AGAIN.

→ DIASTOLE

The cardiac output = (Stroke volume) times (Heart Rate)

End-diastolic LV volume:
(before pumping)=
$= 70 \pm 20$ ml/m^2 s

End-systolic LV volume:
(after pumping) =
25 ± 10 ml/m^2 s

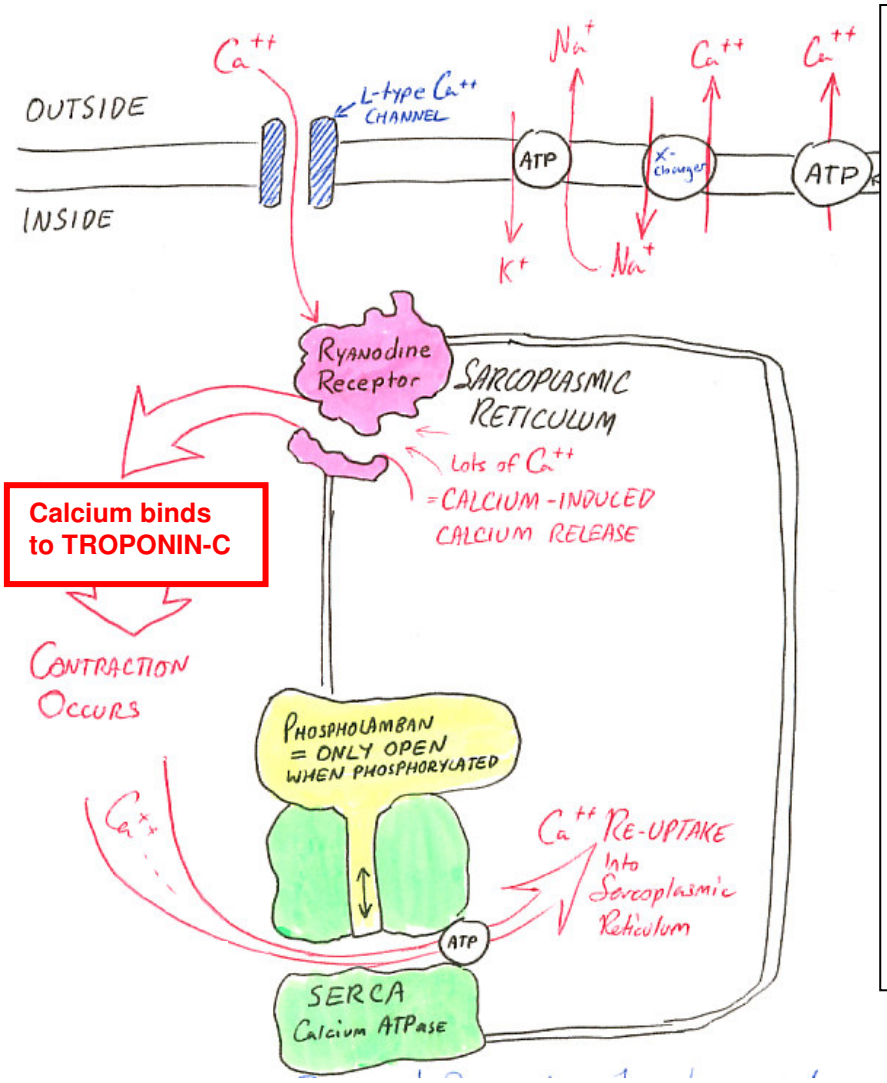
Ejection Fraction:
50%-70%

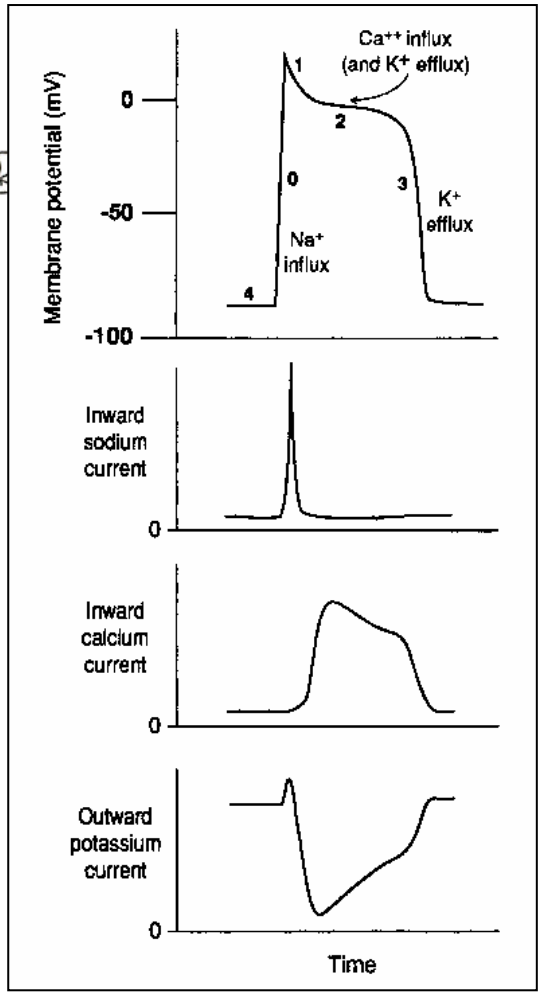
Normal atrial pressure:
RA= 3-5 mmHg
LA = 5-10mmHg
Ventricles in diastole: 1-3mmHg
Up to 8-10mmHg at the end of filling up

NORMAL SYSTOLIC VENTRICLES:
RV =20-25mmHg
LV = 110-130 mmHg

NORMAL pulmonary artery pressure:
=25/12 mmHg
Normal Aortic Pressure:
=120/80 mmHg,
all because the resistance is higher in the systemic circuit

Molecular Biochemistry and Physiology of Myocardiocytes





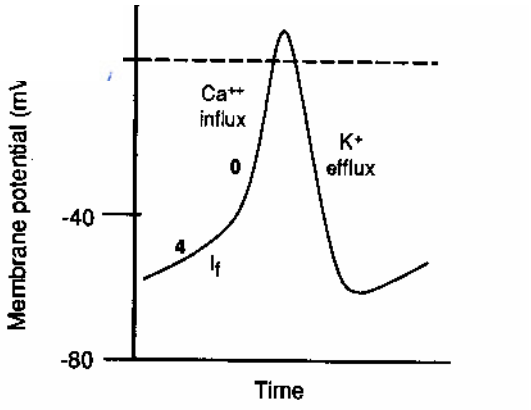


Figure 1.15. Action potential of a pacemaker cell. Phase 4 is characterized by gradual, spontaneous depolarization owing to the pacemaker current (I_f). When the threshold potential is reached, at about −40 mV, the upstroke of the action potential follows. The upstroke of phase 0 is less rapid than in non-pacemaker cells, because the current represents Ca^{++} influx through the relatively slow calcium channels.

The steps:

The fast sodium channel waits for the arrival of an action potential
@ rest the voltage is –90 mV;
DEPOLARISES THE CELL (by allowing lots of Na+ into the cell)
The fast Na+ channel is ONLY ACTIVE FOR MILLISECONDS!
will not open again until the cell has reached –90 mV again
THIS DEPOLARISATION is the FAST UPSTROKE PHASE
Voltage activates the POTASSIUM CHANNEL
→ potassium rushes out of the cell
→ THUS: transient repolarisation
BUT: voltage opens L-type VOLTAGE GATED CALCIUM CHANNELS
→ CALCIUM RUSHES IN along concentration gradient
this (K+ out, Ca++ in) current maintains the flat PLATEAU
!! calcium influc opens Calcium-gated Calcium Channels !!
@ sarcoplasmic reticulum
THUS → MASSIVE INFLUX OF CALCIUM from the reticulum)
THUS → CONTRACTION OCCURS
The calcium is then pumped out:
→ to the reticulum (SERCA ATPase)
→ to the outside (Na+/Ca++ exchanger)
(which means the Na+ ends up in the cell)
(thus → Na+ pumped out by Na+/K+ ATPase)

thus, the positive charge is removed from the inside of the cell, and it is ready to depolarise again when the fast NA channels re-activate and sit ready, waiting for an action potential

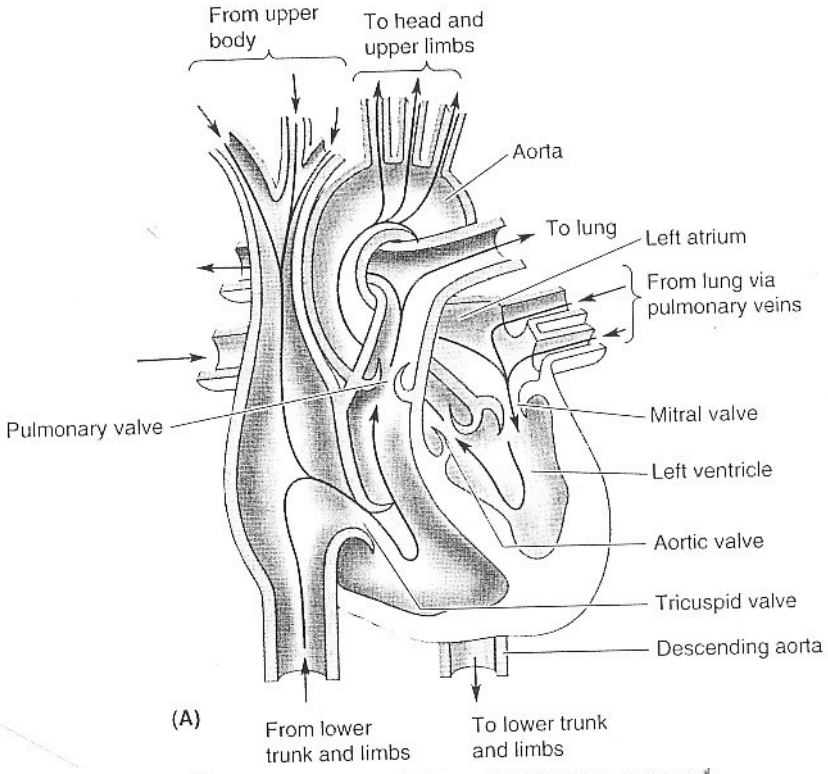
FRANK-STERLING PRINCIPLE:
The more you stretch the sarcomeres, the more they will contract.
i.e. the more the heart fills, the more it will contract
If the sarcomere is overstretched, contractile force declines.

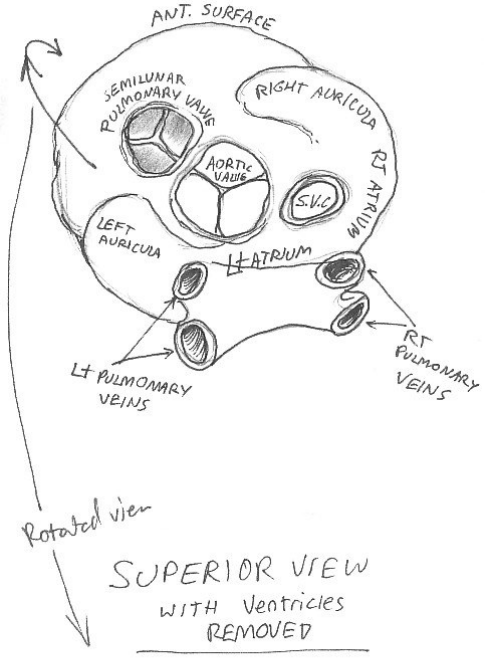
!! PACEMAKER CELLS DEPOLARISE SPONTANEOUSLY !!

= are much less negative (only –60mV) and thus THE FAST Na+ CHANNELS ARE PERMENENTLY CLOSED
THUS: no rapid upstroke! Relatively gentle upstroke instead, via Ca+ channels

***PACEMAKER CHANNEL** slowly depolarises the cell by slowly sucking Na+ back into it

Relevant cardiac anatomy

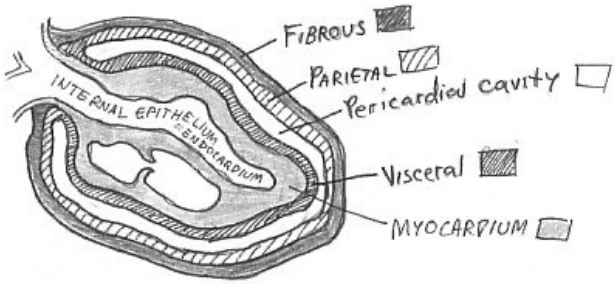


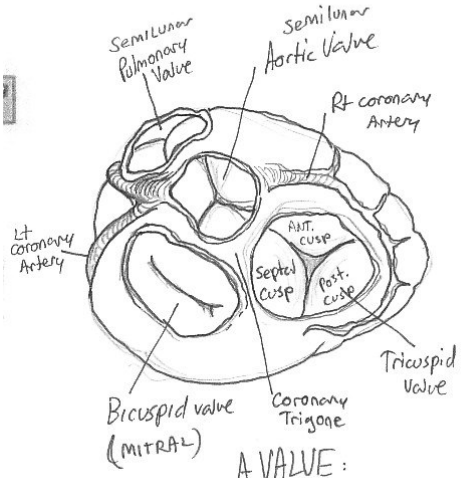


The Pericardium: "A DOUBLE-WALLED FIBROUS SACK"

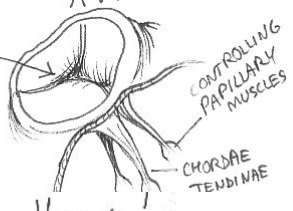
EXTERNAL LAYER: tough AND FIBROUS

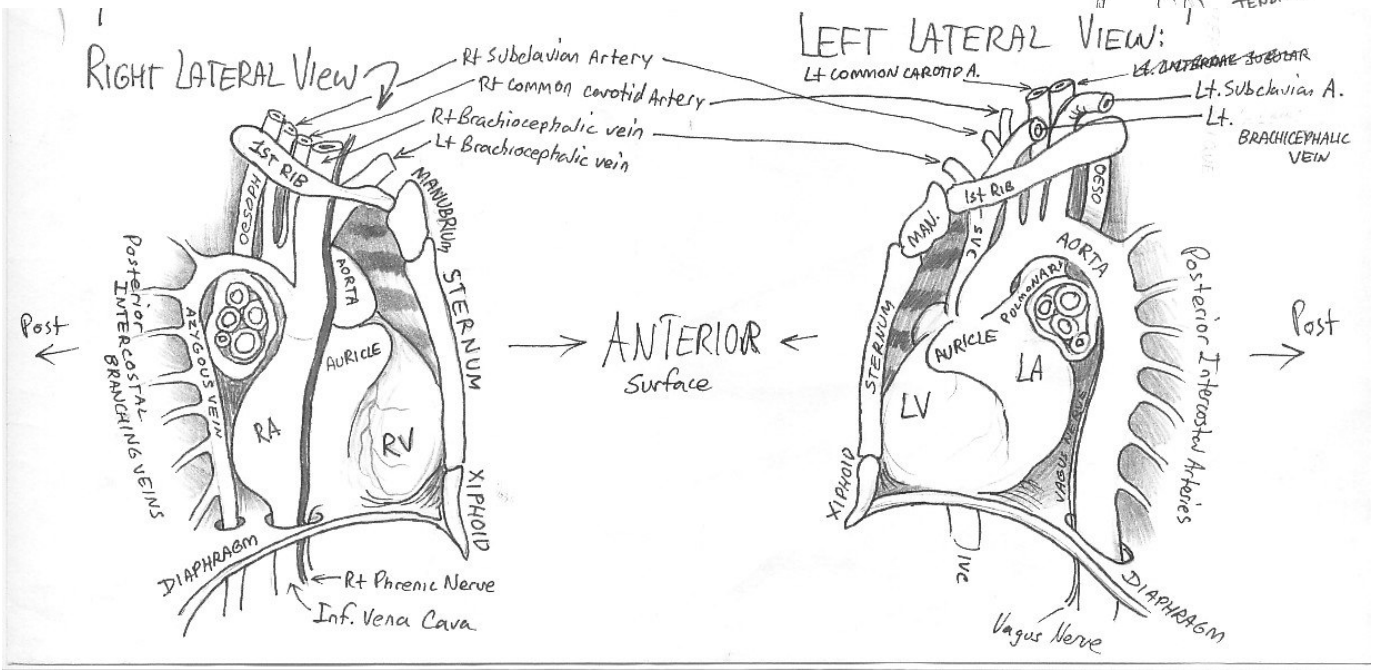
INTERNAL LAYER: slippery, "Serous" PERICARDIUM



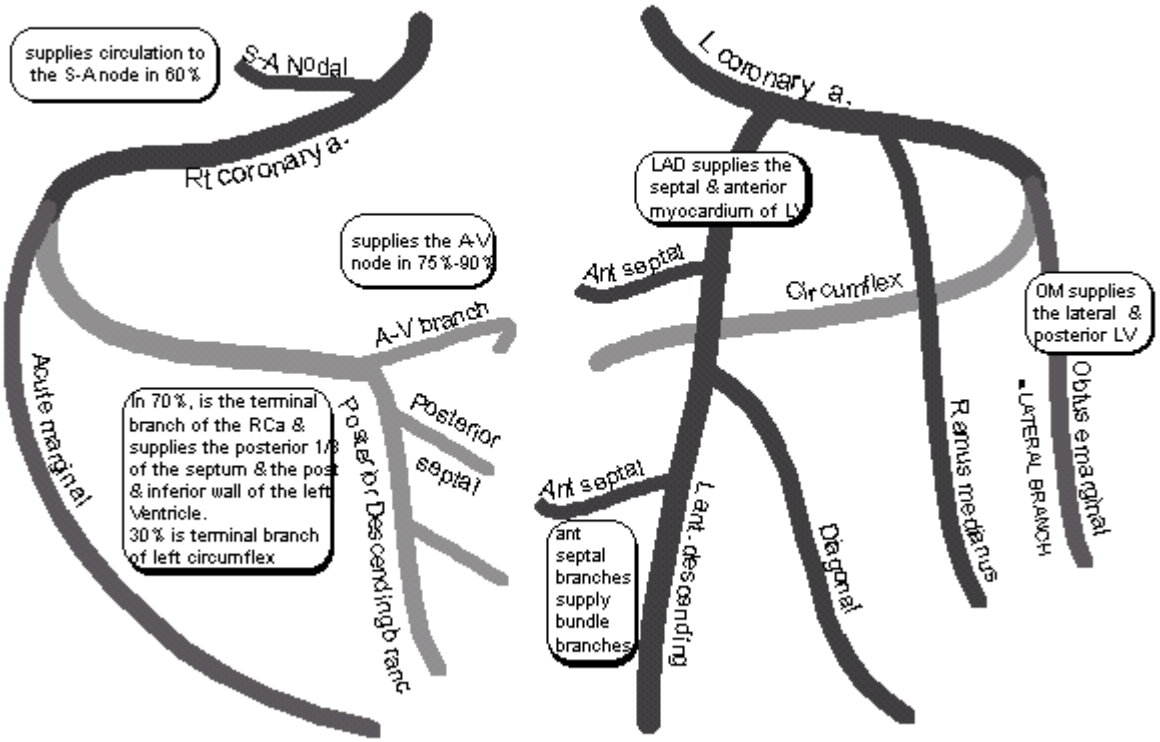


A VALVE:

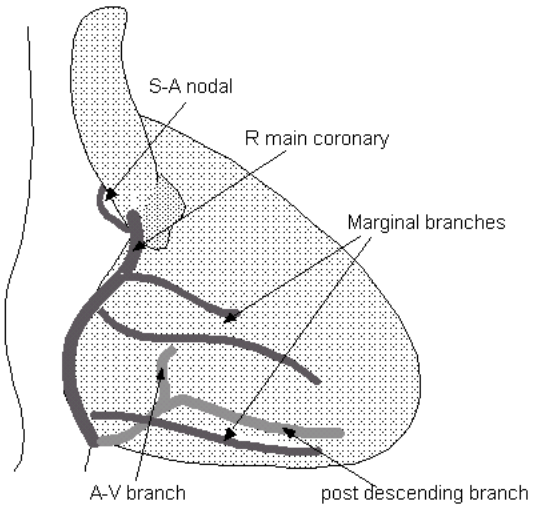


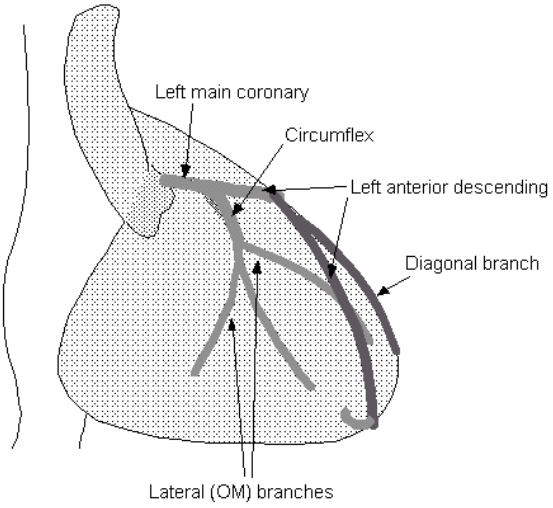


CORONARY CIRCULATION



Coronary arteries — Right Anterior-Oblique view





Cell biology: contractile properties of the MYOCARDIUM

Myocardium myocytes are quite small cells→
They have to be, to let the oxygen diffuse more easily.

MAJOR DIFFERENCE from muscle cells: these myocytes can transfer their action potential to one another (and skeletal muscle cannot)- this is done via **intercalated disks**

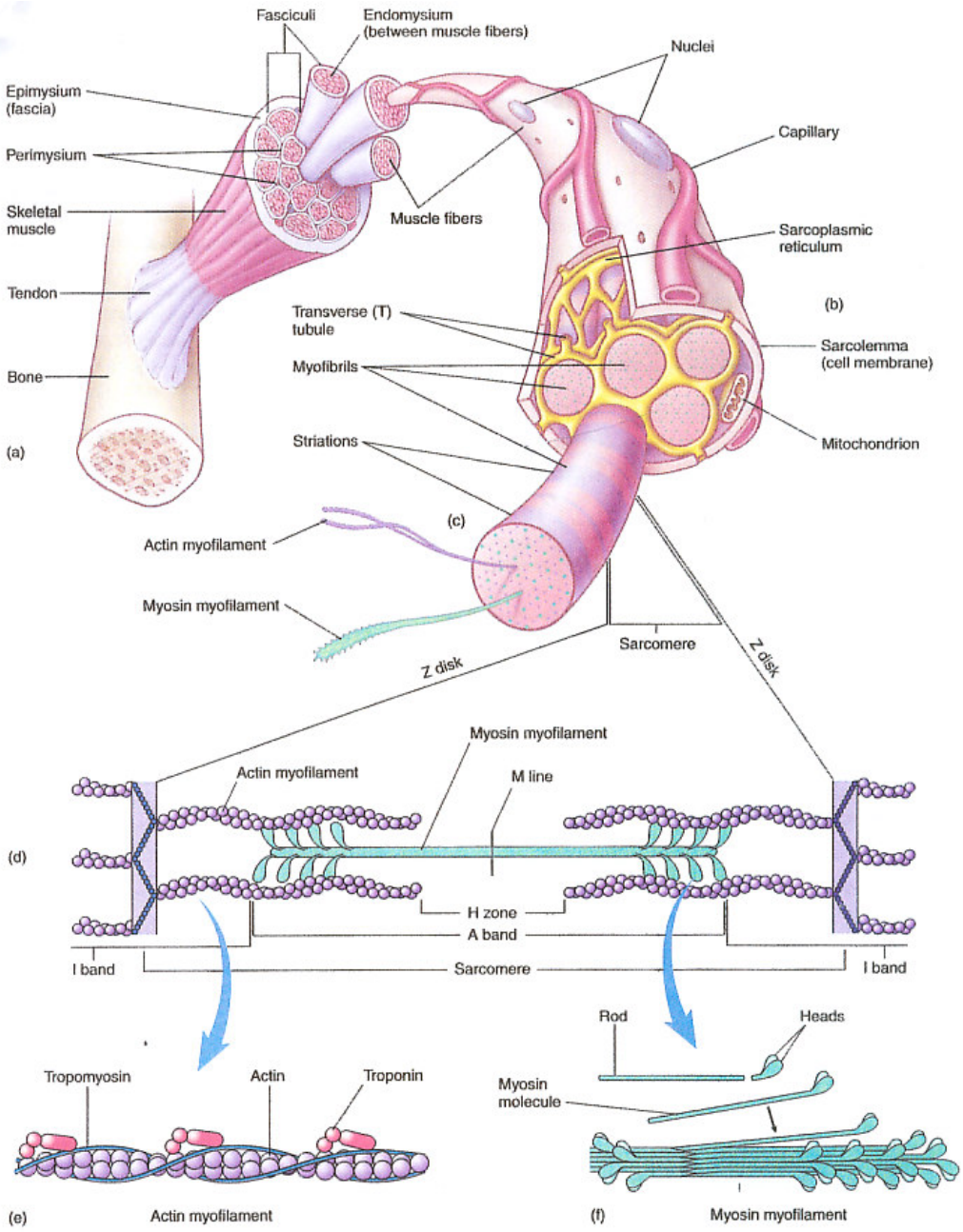
Intercalated Discs:

- contain anchoring desmosomes and gap junctions
- **Desmosome**: sites of attached between adjacent cardiac cells
- **Gap Junction: essentially tiny holes in the disk**

About 25-30% of the human heart cell volume consists of mitochondria.
THAT'S 30% of the crossection!
In contrast, mitochondrial make up less than 5% of the untrained skeletal muscle cell volume
THUS: whereas skeletal muscle can survive for hours in hypoxia, the heart muscle RELIES ON OXYGEN TOO MUCH and thus will die rather quickly.

METABOLISM OF MUSCLE
4 chief sources of energy in order of importance:
- **ATP: = 3-4 seconds of max contraction**
- **Phosphocreatine (PCr)**- PCr + ADP → ATP + Creatine = **10-15 seconds of max. contraction**
- **Glycogen (AEROBIC):** Glycogen → lactic acid producing 3 ATP per glucose unit **= 1-2 minutes**

PHYSIOLOGY OF MUSCLE:



The interaction of the myosin head with an exposed actin binding site is central to the contractile process. After binding to actin and myosin, the myosin molecule bends at the head-rod junction and this protein deformation shortens the myofilament (power stroke). Repetition of the power stroke shortens the muscle. This process requires hydrolysis of ATP at the rate of 1 ATP molecule per power stroke per myosin molecule.

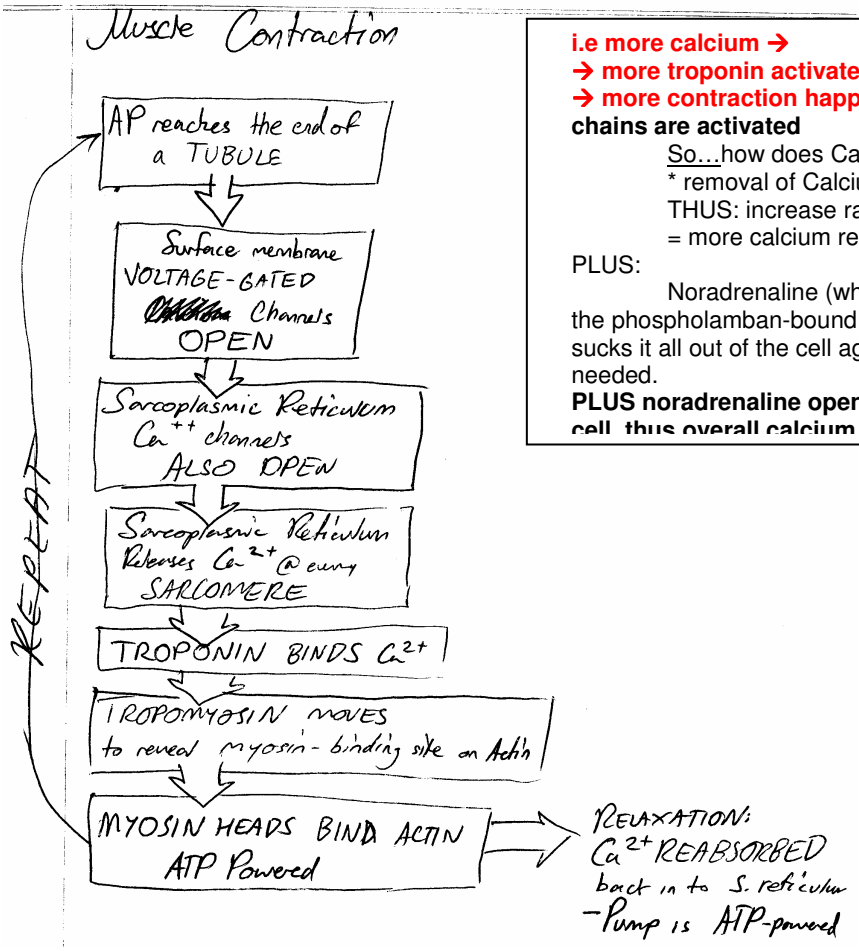
→Myosin heads bind to actin (ATP-powered)
→ this is ONE CYCLE; repeated cycles result in MUSCULAR CONTRACTION;
from rest it is a 50-fold increase in ATP consumption.

RELAXATION: *Ca++ reabsorbed into sarcoplasmic reticulum (SERCA calcium pump is ATP-powered)*

Skeletal muscle: composed from fibres of similar length
Muscle Fibres are composed of multinucleated muscle cells-
Nuclei are on the outside while the inside is filled with *myofibrils*
Myofibrils are composed of 2 proteins:
-Actin (thin)
-also **Troponin**
-also **Tropomyosin**
-Myosin (fat)
each actin/myosin unit is a SARCOMERE
Sarcoplasmic reticulum is a folded membrane which surrounds the areas of sarcomeres where actin and myosin overlap; it has a high concentration of Ca++ ions
-***T Tubules*** penetrate into the sarcolemma to convey the travelling Action Potential (AP)
CONTRACTION:
- when AP reaches the end of the tubule the *surface membrane voltage-gated channels* open,
→ sarcoplasmic reticulum Ca++ channles (ryanadine receptors) also open
→ sarcoplasmic reticulum releases Ca++ ions at every sarcomere-
→**troponin** binds the Ca++
→ **tropomyosin** moves to reveal the myosin-binding site on actin
(which is normally hidden)

Structure of the Myocardium
myocardium
= syncytium of myocytes
Myocytes
: contain contractile yofilaments.
Myofilaments:
contain contractile proteins (actin and myosin) + regulatory proteins (such as troponin and tropomyosin).
These proteins are assembled into **sarcomeres**, which are the contractile units of the myocardium.

Control of contractility is achieved via the **Calcium concentration**



i.e more calcium →
→ more troponin activated →
→ more contraction happens because more actin/myosin chains are activated

So…how does Calcium increase in the cells?
* removal of Calcium occurs only during diastole*
THUS: increase rate = decrease diastole
= more calcium remains inside

PLUS:
Noradrenaline (which increases heart rate) activates the phospholamban-bound SERCA calcium pump which sucks it all out of the cell again, meaning shorter relaxation is needed.
PLUS noradrenaline opens calcium channels into the cell, thus overall calcium increases

CAUSES OF HEART FAILURE

The underlying cause is the pathological process affecting the heart and leading to impaired myocardial pump function.

A precipitating cause is a factor or event which results in decompensation of the heart and symptoms.

Typical precipitating causes are factors placing an additional load upon the heart such as

- **fever,**
- **anaemia**
- **systemic infection.**
- **arrhythmias** such as atrial fibrillation

potential underlying causes of heart failure:

- **coronary artery disease,** thus impaired blood supply
- **myocardial infarction,**
- **valve disease,** (thus increased haemodynamic load on the heart)
- **cardiomyopathy**,

Causes of dilated cardiomyopathy include

- alcohol abuse,
- previous myocarditis,
- hereditary defects in myocardial metabolism
- metabolic abnormalities such as hyper/hypo-thyroidism, or haemochromatosis.
- Occasionally drugs or heavy metal poisoning can cause cardiomyopathy.
- An important drug cause is the anti-cancer drug, adriamycin.

restrictive cardiomyopathy.

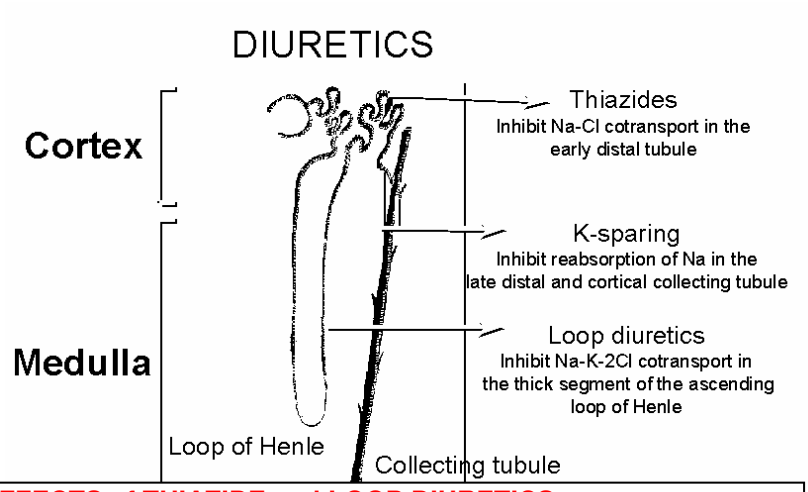
These patients typically **have thickened and stiff ventricular myocardium**,

- due to fibrous infiltration or deposition of abnormal glycoproteins.

The most common cause in Australia is **amyloidosis** which is manifest mostly in older women.

Pharmacology, from the glorious mouth of the DEAN OF MEDICINE

Diuretics:



= good in combination!
Thus, mix and match at will.
BUT: 1 + 1 equals 50. So be careful.
DO NOT OVERDO IT

GOOD COMBINATION:
a loop diuretic + K sparing diuretic

EFFECTS: none on cardiac output, but certainly improves preload

THIAZIDES:
mild but powerful in combination
cause increased excretion of
Na, K, Ca, uric acid, HCO3

K-sparing:
Weak, but spare potassium which is good if you want to avoid arrhythmia

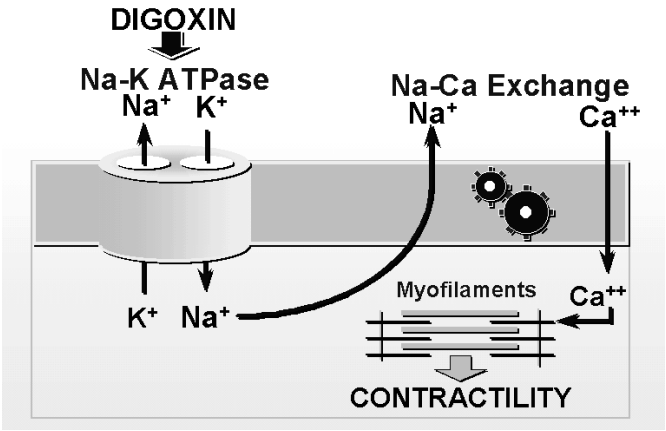
LOOP diuretics
POWERFUL alone, beware;
May excrete 15-20% of filtered Na+

SIDE EFFECTS of THIAZIDE and LOOP DIURETICS:
Reduce volume, reduce NA+, K+, Ca++, Mg++ →THUS: Confusion!!
INCREASED SERUM LDL, UREMIA, GOUT, DELIRIUM, alcalosis!!
Must titrate dose: no standard; observe patients condition and judge:
try to hover between prune and blob

K-sparing diuretics will instead cause Acidosis and rash/pruritis

!! OBSESS !!
over
!! POTASSIUM !!

Digoxin : oldest drug in the cardiology book.



BEST EVER for atrial fibrillation;
!! NARROW THERAPEUTIC RANGE !!
may cause visual disturbance + arrhythmia (??)

Effects:
Reduced serum noradrenaline
(thus less sympathetic vasoconstriction)
Reduced RAAS activity
Reduced peripheral nervous activity
INCREASED vagal tone

LONG TERM: SURVIVAL SIMILAR TO PLACEBO
FEWER hospital admissions, but…
MORE serious arrhythmias
MORE myocardial infarctions

SIDE EFFECTS of DIGOXIN:
Heart block, nausea, vomiting, diarrhoea, depression, disorientation, paraesthesia, blurred vision, scotomae, "yellow-green vision", gynaecomastia.

BIOCHEMISTRY
Increases intracellular calcium and allows more calcium to enter the myocardial cell during depolarization via a sodium-potassium pump mechanism; this increases force of contraction (positive inotropic effect), increases renal perfusion (seen as diuretic effect in patients with CHF), decreases heart rate (negative chronotropic effect), and decreases AV node conduction velocity.

Non-Glycoside Positive Inotropic Agents

→Adrenaline and beta-adrenoceptor agonists
→ phosphodiesterase inhibitors (sympathomimicry)
INCREASE FORCE + RATE !!
great for resurrecting a massive acute MI: BUT NEVER FOR LONGER THAN 3 DAYS!!

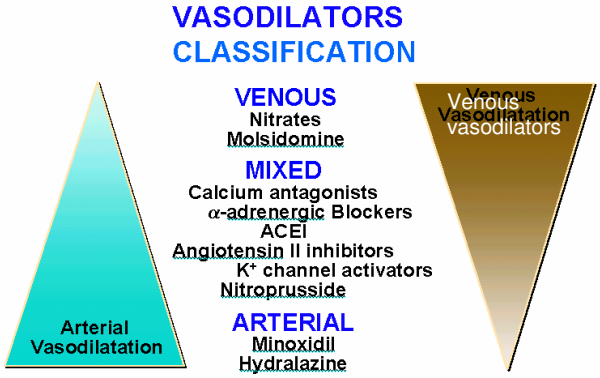
ONLY FOR
SHORT TERM
!! CIRCULATORY SUPPORT !!
you can kill the patient with these

Aldosterone Inhibitors, namely the great SPIROLACTONE

SIDE EFFECTS: gynaecomastia, renal failure

= a competitive antagonist of the aldosterone receptor
= DO NOT USE if the pt. has bad kidneys, hyperkalemia or metabolic acidosis

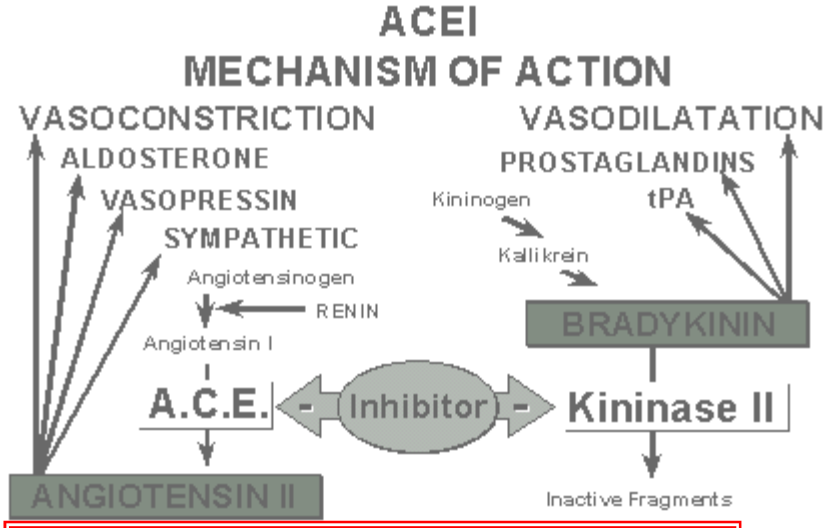
VASODILATORS:



These aren't bad as the heart will require less effort to pump through a circulatory system which has less RESISTANCE:
BUT:You build up a resistance to them

NITRATES:
Not very important;
only for acute MI with congestive failure
TOLERANCE DEVELOPS!
→ must abstain for 24hrs
DO NOT GIVE in hypotension

Angiotensin Converting Enzyme Inhibitors (These also vasodilate)



→ ACE-Inhibitors IMPROVE SURVIVAL
- they inhibit post-MI remodelling of the myocardium,
- they modify the progression of congestive heart failure
- they reduce the number of hospitalisations

ACEI
UNDESIRABLE EFFECTS

- **Inherent in their mechanism of action**
  - Hypotension
  - Hyperkalemia
  - Angioneurotic oedema
  - Dry cough
  - Renal Insuff.
- **Due to their chemical structure**
  - Cutaneous eruptions
  - Neutropaenia, thrombocytopenia
  - Digestive upset
  - Dysgeusia
  - Proteinuria

DO NOT GIVE ACE-Inhibitors in:
- Renal artery stenosis,
- renal insufficiency,
- hyperkalemia,
- severe hypotension

Angiotensin II receptor antagonists are also available

Beta Blockers →OVERWHELMING BENEFITS!! Criminal not to use them

Beneficial actions:
- increased density of beta radrenoceptors
- reduced nurohormonal activation
- reduced heart rate
- antiarrhythmic, antianginal, antioxidant

Harmful actions
- reduced Cardiac Output
- Bronchospasm
- Risk of heart block
- Risk of decompensated HF

ß-ADRENERGIC BLOCKERS
CONTRAINDICATIONS
- **Hypotension: BP < 90 mmHg**
- **Bradycardia: HR < 50 bpm**
- **Clinical instability**
- **Chronic bronchitis, ASTHMA**
- **? Severe chronic renal insufficiency**

START CAREFULLY, ON LOW DOSES; WITHDRAW SLOWLY, TITRATE CAREFULLY

Calcium Channel Blockers

Counter-ischaemic, and vasodilatory; reduce inotropy

Anticoagulants (for Atrial fibrillation, or previous Cerebrovascular accidents)

Antiarrhythmics eg. amiodarone if about to die from ventricular fibrillation

ALL ELSE FAILS: Implanted pacemaker