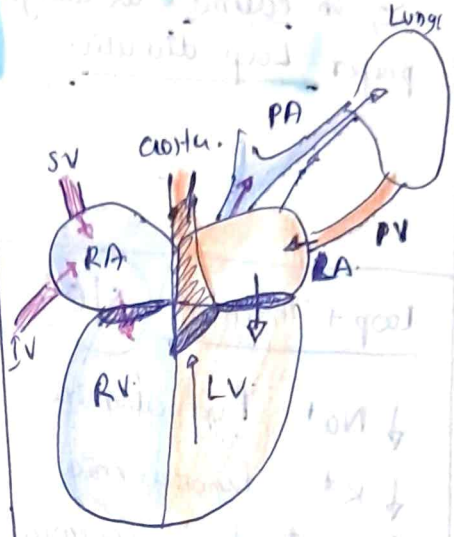
Congestive Heart failure

- what is the function of heart?
- It is to pump blood ✗
- actually It's function is to meet demands of body.
  - It does that through pumping
- If heart can't meet demands
  - Heart failure



- If left ventricular failure
  - ↑ blood in LV
  - ↑ Blood in LA
  - ↑ PV
  - ↑ Lungs
  - pulmonary edema

R ventricular failure

- ↑ RA
- SVC, IVC
  - Jugular vein ↑ → ↑ JVP
  - lower part of body, organs → Hepatomegaly (liver congestion)

R. ventricular failure

- * ↑ JVP ✓
- * Hepatomegaly ✓

In such failures, there is accumulation of blood.

- Congestion
  - called Congestive heart failure
    - CHF

This all is called as Acute congestive heart failure.

HF

- High output
  - thyrotoxicosis
  - Anemia
    - treat underlying disease ✓
    - no drugs ✗
  - High output HF ⇒ Blood is pumped normally but demand ↑ so heart can't meet demand even if it works normally.
    - High output HF
      - here, CO is Normal
      - So Rx is treat underlying condition ✓ not Drugs ✗
- Low output
  - ve drugs ✓
  - heart not pumping enough

Left ventricular failure

- easy fatigue
  - {can't pump blood effectively}
- dyspnoea {Lung} and
- pulmonary edema

Acute Congestive HF

problems

- heart is not pumping
- Blood is collecting.

Aim

- ↑ contractility
- remove fluid.

Rx

- Diuretics → ↓ fluid.
- Inotropics → ↑ contractility.

I Diuretics.

Loop diuretics

- high acting
- can remove litres of fluid
- short acting

Thiazides.

- removes less volume of fluid
- long acting.

So, we use.

↓

Loop diuretics.

↓

as it can remove litres of water due to edema

↓

edema ⇒ high volume alkalosis

So, in edema, we always prefer Loop diuretics.

Loop + Thiazides S/E

↓ Na^+	hyponatremia
↓ K^+	hypokalemia
↓ mg^+	hypomagnesemia.
↓ H^+	metabolic alkalosis.
↑ Glucose	hyperglycemia.
↑ uric acid	hyperuricemia.
↑ lipid	hyperlipidemia.

Loop looses Ca^{2+} : ↓ Ca^{2+}

Thiazide ↑ Ca^{2+}

L → ↓ Ca^{2+}

T → ↑ Ca^{2+}.

II Inotropics.

Stimulate β_1 : ↑ contractility

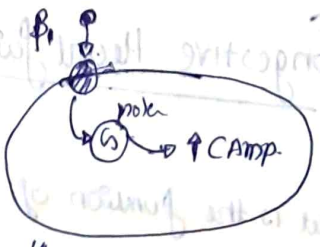
↓ sympathetic receptor on

↓

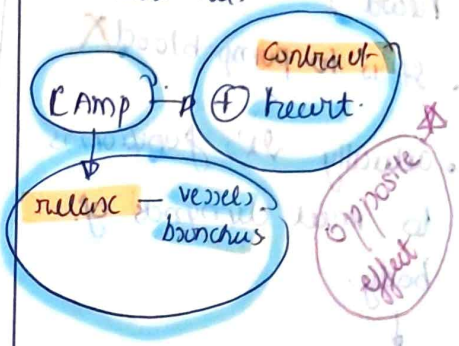
β_1 agonist

↓

- Dopamine : D_1 β_1 α_1
- dobutamine : β_1
- Isoprenaline : β_1, β_2.
- Noradrenaline : α_1, α_2 β_1



Heart cell.



- Since CAMP ↑ contraction, can't we use CAMP?
- CAMP is degraded by PDE

↓

phosphodiesterase.

- PDE ⊖ : ↑ CAMP.
- Inamrinone.
- Milrinone.

- when we give β agonist it only ↑ CAMP where β is there.
- But PDE ↑ CAMP in heart & blood vessels also.

So ↑ causes ↑ contraction of heart

- vasodilation.

ie Inotropic + vasodilator

Inodilators

Inotropic drugs

- β agonist
- PDE (−) → Inodilators.

Acute CHF.
↓
If not treated.
↓
Body Compensates.
↓
Here, there is ↓ C.O.
↓
Sympathetic activation.
↓
↑ Adrenaline / NA.
↓
act on β1
↓
↑ C.O. (2)

- Since ↑CO → why do we need drugs?
- by its own
- Cause symp also acts on α receptors → vasoconstriction.
- aldosterone release.

preload?

veins contract → SVC & IVC → ↑ blood in RA → ↑ in R ventricle → preload.

afterload.

after blood reaches LV. how much effort needed to pump blood through aorta.

- If aorta contracts
- effort needed ↑
- i.e., afterload ↑.

(1) act on α receptor also → vasoconstriction

- veins → ↑ preload
- arteries → ↑ afterload.

↑ work of heart

(3) β1 also on JG cells → Renin release

Angiotensinogen → Ag I → (ACE) → Ag II → AT_1 receptor

receptor of Ag II − AT_1 ✓ not AT_2 ✗.

AT_1 located on

(1) Blood vessel → Vasoconstriction.

(2) Adrenal Medulla → release of catecholamines.

(3) Adrenal cortex → aldosterone release → retain Na^+ & water.

- VC → ↑ preload & afterload. ↑ work
- Catechol → $β_1$ action, ↑ VC. ↑ work
- aldosterone → ↑ Na^+, H_2O → edema.

problems − work ↑, edema

But the most fatal thing is when aldosterone ↑↑↑ → very high / continuously → left ventricular hypertrophy or Cardiac remodelling → its size ↑ work, efficiency doesn't → needs more O_2 for it too.

- Lft ventricular hypertrophy.

Reason for death

- Occurs due to ↑, continuous aldosterone.

	reason	solution
↓ work	VC	VD.
↓ fluid	edema	loop diuretics
LVH	Aldosterone	⊖ RAAS.

The problems due to compensatory actions in acute CHF.

1. ↑ work load ↑. (VC).
2. edema
3. LV hypertrophy.

These are called Chronic CHF / ↑ Compensated CHF.

Acute CHF : decompensated CHF.

Aim of treatment of C°CHF

1. ↓ work
2. ↓ fluid
3. reverse LVH.
4. Inotropics - oral
   - ↳ due to regulations.
   - not priority / mech.
   - last impt
   - ↓ Sometime required when in some patients continuously is not enough.

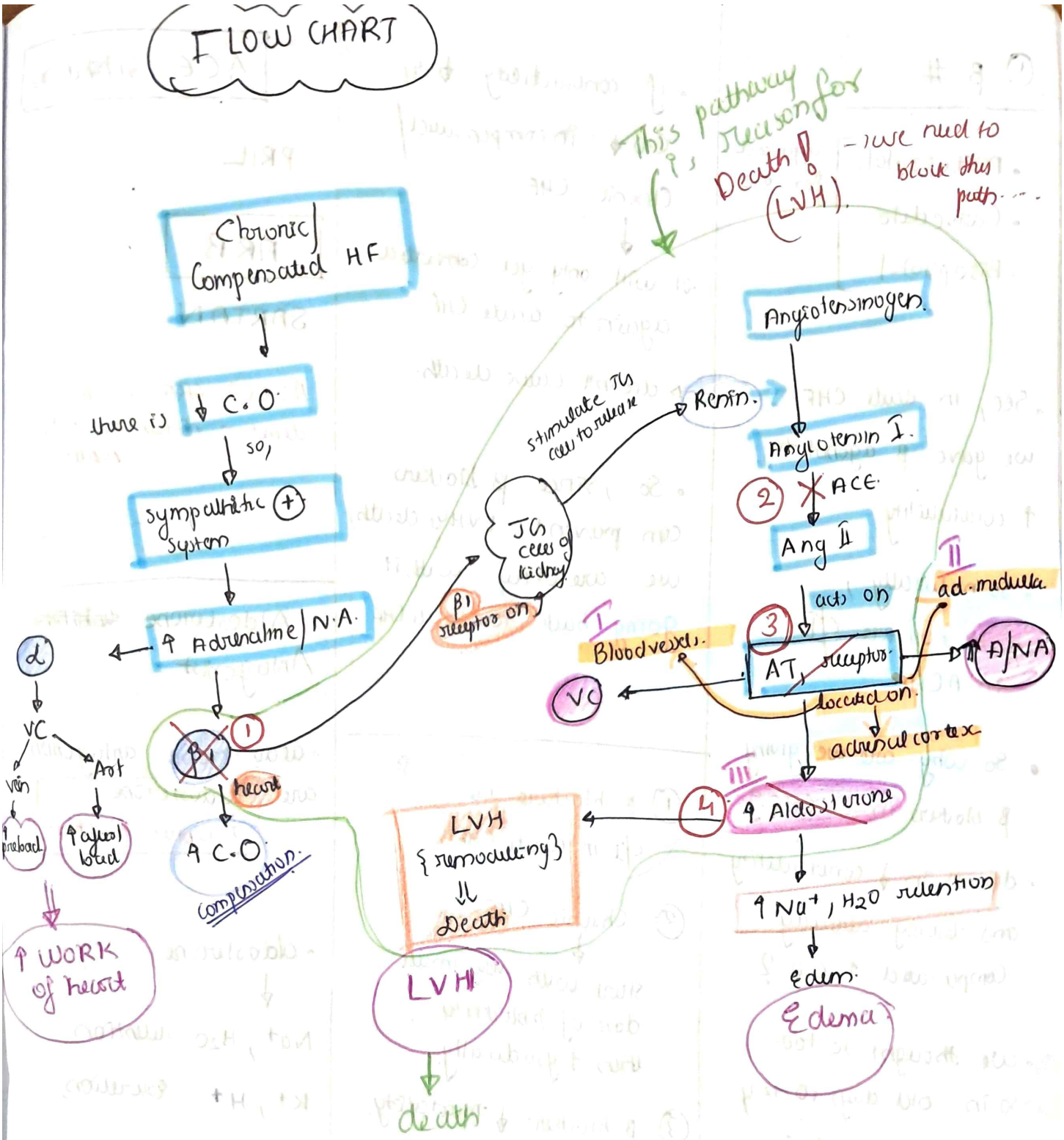
1. Vasodilators.
   - veins → ↓ preload
   - arteries → ↓ afterload.

- vasodilators (1) ↓ pre
  - Nitrates
- arteriodelators (2) ↓ after.
  - Hydralazine.
- (V + A) dilators (Both) (3). ↓ pre + after.
  - Nitroprusside.
  - ACE ⊖.
  - angiotensin receptor blocker (ARB).

2. Loop diuretics
   - ↓ fluid.

3. Reverse LVH.
   - LVH occurs

FLOW CHART



1. β blocker.
2. ACE inhibitors
3. AT1 receptor blocker.
4. Aldosterone antagonist.

prevent Death
LVH ✗.

Q: Drugs that ↑ survival / longevity.
↓ mortality ✓

① β

- metoprolol
- Carvedilo
- Bisoprolol

] approved for use.

- Sec, in acute CHF, we gave β agonist to ↑ contractility.
- so naturally, β blockers are C/I in ACHF.
- So why are we giving β blockers in C.CHF.?
- doesn't in ↓ contractility and destroy already Compensated ↑ C.O. ?
- We thought so too... so in old days 10-12 y β blockers were C/I in both A & C : CHF.
- But now we realised that β blockers can prevent ventricular remodelling
- It can prevent death

- if contractility ↓ & C.O ↓ in compensated/ Chronic CHF
  ↓
  it will only get converted again to acute CHF.
  → doesn't cause death.
- So, since β blockers can prevent LVHF death, we are okay with it going back to acute CHF

① β blockers are C/I in acute CHF ✱

② Chronic CHF.
  ↓
  start with very small dose of β blockers & then ↑ gradually.

③ β blockers ↓ mortality in C.CHF.

④ most commonly used β blocker in C.CHF is CARVEDILOL - y?

- α β #
- Cu^{2+} #
- antioxidant

due to these additional ppts, they are used.

ACE Inhibitors

PRIL

ARB

SARTAN

ACE⊖, ARB will be dealt in detail in HTN chapter.

Aldosterone Antagonist

- aldosterone antagonists are aldosterone receptor blockers

- aldosterone
  ↓
  Na^+, H_2O retention
  K^+, H^+ excretion

So, aldosterone antagonists are.
Na^+, H_2O excretors & K^+ retainers.

Na^+ ~~retention~~ = Diuretics
H_2O excretors
But
- K^+ retention = K^+ sparing diuretic.

- Aldosterone Antagonist
  ↓
  Aldosterone receptor blocker
  ↓
  K+ sparing diuretic
  ↓
  Spironolactone.

Sparing diuretics are K+ sparers. Not retainers.

- Aldosterone receptor & testosterone receptor are very close.
  ↓
  so it also block T_R
  ↓
  gynecomastia
  ↓

- D } digoxin
- S – spironolactone
- C – Cimetidine, ketoconazole.
- O – oestrogen.

Eplerenone
→ spironolactone's cousin.
→ doesn't act on T_R
→ no gynecomastia.

4) Inotropic

In some patients, we might need to use Inotropics in C. CHF

{ in C.CHF CO is already increased right? but some cases we might have to used Inotropics additionally }.

- We have to give on for long duration
  ↓ so need
  ORAL INOTROPICS
  ↓ major
  DIGOXIN.

Cardiac glycosides.
↓
Digitalis group.
↓ obtained from
Digetalis Purpurea.
↓
flowers that can be cupped on fingers, digets.

Initially, there were many drugs in digitalis group that were used. But now there are like 2 used cause of side effects.

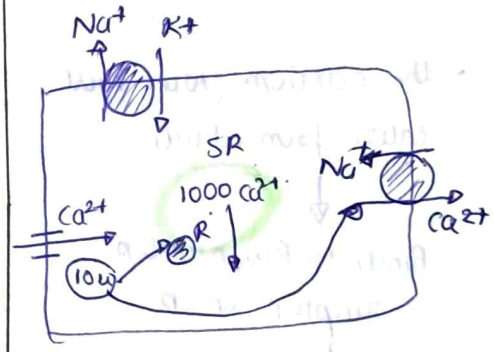
- DIGOXIN
- DIGITOXIN

DIGOXIN	DIGITOXIN
↓	↓
kidney metabolism	• metabolised in liver.
↓	↓
• avoided in kidney failure.	• avoid in liver failure

DIGOXN

• mechanism of action

ventricular fiber.



$Na^+ - K^+$ – atpase.
$Na^+ - Ca^{2+}$ Exchanger.
• Ca^{2+} channel.

Na^+ is being pumped out by Na-K+ ATPase

So,
Na^+ enters in &
Ca^{2+} leaves in
Na^+, Ca^{2+} Exchanger.

- Ca^{2+} is required for contraction of muscles

- through calcium channel, on small amount enters eg: 10 units

- for muscle contraction we need 1000 then...

- So its not enough. to compensate,

- Ca^{2+} is already stored in SR sufficiently so that during contraction, that much amount can be released,

- the calcium (ions) that enters from outside ↓ Binds to Ryanodin ↓ receptor on SR ↓ Causes release of Ca^{2+} from SR

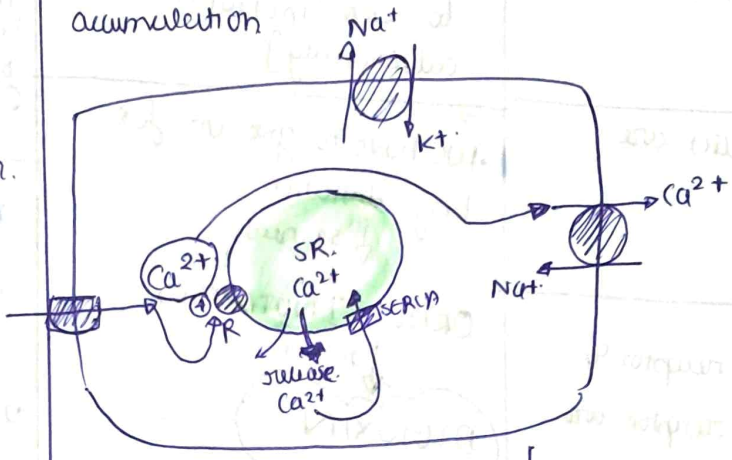
- then this Ca^{2+} binds to actin ... muscle contraction

- SERCA — sarcoplasmic ER Ca^{2+} ATPase. is the pump that is pumping Ca^{2+} back to SR.

The Ca^{2+} that is pumped out of SR is then pumped back in.

- calcium coming from outside goes out through Ca^{2+}-Na^{+} exchanger.

- so there is no net accumulation



Mechanism of action of DIGOXIN.

- DIGOXIN works by inhibiting $Na^{+}-K^{+}$ pump.

- $Na^{+}-K^{+}$ pump inhibited ↓ Na^{+} accumulates inside. ↓ so $Na^{2+}-Ca^{2+}$ exchanger can't bring in sodium ↓ Ca^{2+} can't be taken out too.

- due to $Na^{+}-K^{+}$ ATPase ⊖ ↓ $Na^{+}-Ca^{2+}$ exchanger also doesn't work ↓ Ca^{2+} starts accumulating ↓ each time SERCA pumps back accumulated calcium also ↓ next time released Ca^{2+} also increases. ↓ gradually Ca^{2+} release builds up and causes ↑ contractility.

Calcium (thereby contractility)

↓

only increases slowly slowly.

∴ DIGOXIN IS SLOW ACTING

DIGOXIN IS NOT SUITABLE FOR ACUTE CHF ✗

|Mechanism of action|.

$Na^+ - K^+$ ATPase ⊖

↓

↑ Na^+ in cells

↓

NCX ⊖

↓

↑ Ca^{2+} in cytoplasm

↓

↑ Ca^{2+} in SR

↓

↑ Contractility.

another mechanism of action

→ Vagomimetic effect

- this property is not useful in CHF
- Vagomimetic ppty is used in

Atrial fibrillation

- atrial rate is very high 400-500.

- What do you mean by fibrillation?

- we said rate is 400-500 right?

- Since it does that much.. it doesn't contract completely during each time

. ഒരുമാതിരി മിടിക്കും... not കൃത്യമായി

But full contract cheyyan pattula.

- Atria is not beating | contracting
- It is fibrillating.
- fibrillation means - ineffective Contraction.

if atria isn't contracting properly is it that much of a problem?

No!

Cause blood will enter ventricle automatically & only 30% is pumped by atria contracting.

- Since the atria is beating so fast

↓

conduction AV

↓

ventricle beats fast too

- if ventricle starts fibrillating then we are cooked.

- lot of times when we are treating AF... we are trying to prevent VF.

Drug Interaction ✓✓ Vimpt reason for toxicity

- which drugs increase digoxin toxicity?

① Electrolyte Imbalance.

- hypokalemia ($K^+ \downarrow$)
- hypomagnesemia. ($Mg^{2+} \downarrow$)
- hypercalcemia ($\uparrow Ca^{2+}$)

② Drugs.

- Quinidine.
- verapamil
- Amiodarone.
- Thiazides.
- clarithro, erythromycin

③ Diseases

- renal disease → digoxin tx
- liver ds → digitoxin - tx.

Toxicity

- Electrolyte imbalance.
- Drug
- Diseases.

How?

* how hypokalemia cause digoxin toxicity?

- digoxin ⊖ $Na^+ - K^+$ by binding to K^+ binding site.

→ there is competition btw them..

- when there is $\downarrow K^+$: no comp. that means digoxin action ↑ ⇒ toxicity

[redacted]

- when there is digoxin toxicity, potassium entry ↓ into cell.

↓

K^+ ↑ extracellular

↓

hyperkalemia

- hypokalemia causes digoxin toxicity

But

- Digoxin toxicity causes hyperkalemia.

Drug.

Q

V

A

T ✓

Thromycin

Clarithro & Erythromycin.

Inhibits p-glycoprotein which basically helps in digoxin excretion through kidneys.

↓

so their use causes toxicity

if we give digoxin
↓
Vagommetic action
↓
↓ AV conduction
↓
prevents VF.

• If say Atria beats 10 times, then out of 10 only 1 might reach V due to AV block.

Q) Mechanism of action of digoxin in AF
↓
• Vagommetic action. ✓
• Not $Na^{+}-K^{+}$ pump ⊖.

• DIGOXIN decreases conduction from Atria to ventricles
↓
Vagus like effect.

S/E

*most Common side effect (1)
→ Nausea, vomiting = toxicity indication.

(2) * Cardiac : arrhythmias

as digoxin sends mixed signals to ♡
• It says contract by $Na^{+}-K^{+}$ ⊖
• It says ↓ conduction by Vagommetic action.
↓ ♡ is confused
arrhythmia

• m.c arrhythmia :
• Ventricular bigemini.

most common overall s/e is GIT symptoms ✓

mc ♡ problem is Ventricular bigemini {it is not the m/c s/e}.

most specific arrhythmia.

Non paroxysmal atrial tachycardia with A-V block
↓
NPAT.

* if a person has Vent Bigemini we can't say it's digoxin 100%.

* But if there is NPAT with AV Block
↓
Digoxin 100%

• Tachy - stimulatory
• AV block - depression
the only drug that does both is digoxin ... so...

arrhythmias never seen in digoxin toxicity

• Atrial flutter — why?
• Mobitz type II heart block

---

(3) Gynaecomastia

(4) Colour vision defects
↓
yellow vision {xanthopsia}
↓
patient sees yellow everywhere.

• Management

① Correct Electrolyte/ metabolic Imbalance.

ie, give K+ in hypokalemia.

Q) which monovalent drug is used in Digoxin toxicity Rx?

↓

K+

② Stop drugs causing toxicity.

③ How to treat digoxin induced Arrhythmias

↓

DOC in Digoxin induced Arrhytmias (ventricular).

↓

LIGNOCAINE

or

PHENYTOIN alternative.

But if it is Brady arrhythmias?

Bradycardia & Brady arrhythmias

↓

Indicates

↓

Severe toxicity.

↓

Drug used

↓

DIGIBIND

↓

• ab against digoxin
• binds to & stops its action.

• DIGIBIND
↓ AKA
Digoxine Immune fab.

↓

used in SEVERE Toxicity

C. CHF

we use 3D's.

D — Dilators
D — Diuretics
D — Digoxin.

NEW DRUGS