ANTI ARRHYTHEMIC DRUGS

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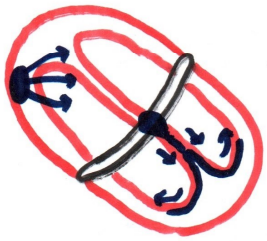
From: Dr. NAJEED Lectures

ARRYTHMIA:
Abnormal rythm of the heart.

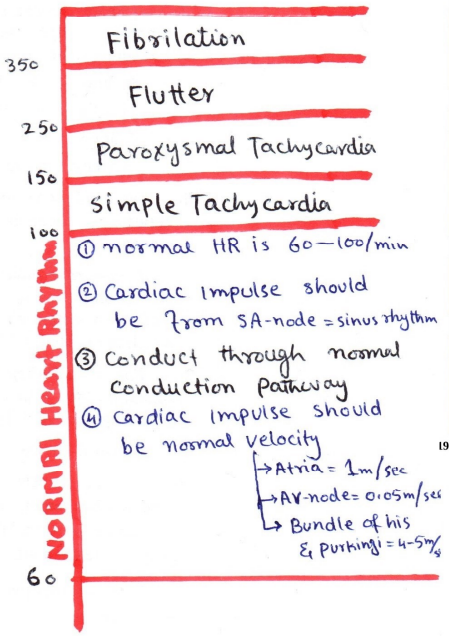
Normal rhythm of Heart.

Normal Rhythm of heart is some where B/w 60–100 b/min



If HR is originated from somewhere else than SA-node, it is called as Abnormal rhythm.

Normally cardiac impulse pass from atria through moderate velocity (1m/sec), from AV-node very slowely (0.05 meter/sec) & from Bundle of his + purkinji fibers with high velocity (4–5 meter/sec).



CLASS I (Na^+-channel blockers)
Disopyramide (IA) NORPACE
Flecainide (IC) TAMBOCOR
Lidocaine (IB) XYLOCAINE
Mexiletine (IB) GENERIC ONLY
Procainamide (IA) GENERIC ONLY
Propafenone (IC) RYTHMOL
Quinidine (IA) GENERIC ONLY
CLASS II (β-adrenoreceptor blockers)
Atenolol TENORMIN
Esmolol BREVIBLOC
Metoprolol LOPRESSOR, TOPROL-XL
CLASS III (K^+ channel blockers)
Amiodarone CORDARONE, PACERONE
Dofetilide TIKOSYN
Dronedarone MULTAQ
Ibutilide CORVERT
Sotalol BETAPACE, SORINE
CLASS IV (Ca^{2+} channel blockers)
Diltiazem CARDIZEM, CARTIA, TIAZAC
Verapamil CALAN, VERELAN
OTHER ANTIARRHYTHMIC DRUGS
Adenosine ADENOCARD
Digoxin LANOXIN
Magnesium sulfate GENERIC ONLY
Ranolazine RANEXA

19.1 Summary of antiarrhythmic drugs.

CARDIAC IMPULSE

- Normal generation
  - Sinus origin
  - 6–100 b/min
- Normal Conduction
  - Normal Pathway
  - Normal Velocity

Rhythm: Any activity which is occuring again & again & with almost same (normal interval.

* Heart is having cyclic electrical activity & cyclic Mechanical activity & both them activity have to be normal to produce normal cardiac output.

Syncope

Transiet loss of consciousness due to decreased Cardiac output, which cause decreased cerebral Metabolism.

patient with arrhythmias may come with syncope, palpitation, hypotention, precipation of cardiac failure, abnormal puise, Ischemic heart disease.

* Cardiac arrhythmias is an important cause of sudden cardiac death.
* Arrhythmias may be due to abnormal generation of impulse or problem in conduction of impulse

Anti arrhythmic drugs either alter generation or conduction of impulse.

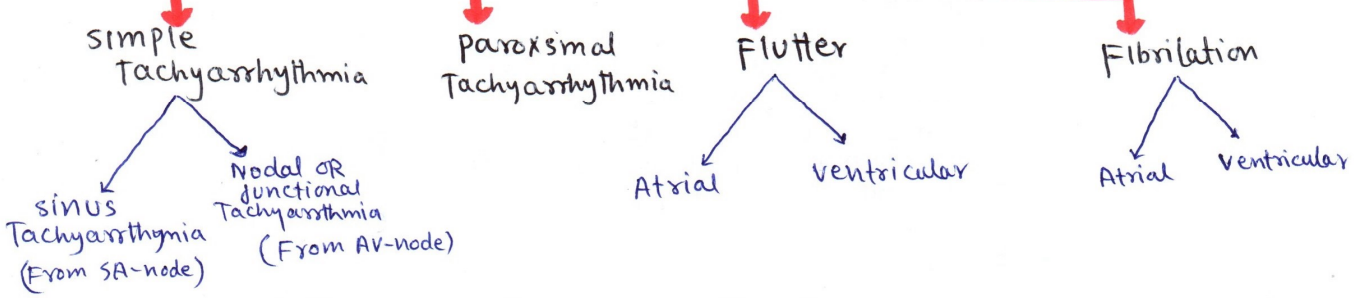
Simple Tachycardia:
which heart rate keep on increasing somewher B/w 100–150b/min

Paroxysmal Tachycardia:
Sometime Tachycardia appears B/w 150–250 & than disappear.

FLUTTER:
Sometim heart Rate appears B/w 250 – 350 b/min

Fibrilation
Heart rat greater than 350 b/min

Tachyarrythmias



Paroxysmal Junctional Tachyarrthmia: If Junctional Tachycardia appear & than disappear.

Automaticity: Capibility of cell to undergo depolarization sponteneously without external stimuli.

ARRYthmia pathogenesis

- abnormal Cardiac impulse generation
  - Rate of impulse generation
  - site of impulse generation
    - SA-node
    - AV-node
    - His+Purkinji
- Abnormal Cardiac Impulse Conduction

Myocardial cells

Pacemaker's

Cells with inherent automaticity

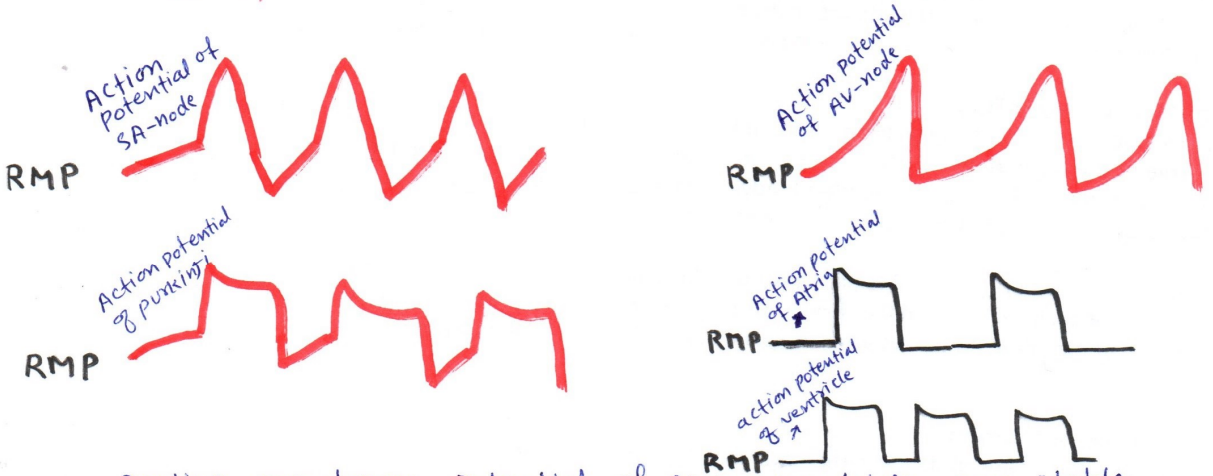
e.g SA-node, AV-node, Purkinji system

Non-Pacemakers

Cells without inherent automaticity.

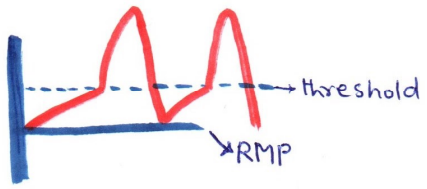
e.g
* Atrial Myocardial cells
* Ventricular Myocardial cells

Arrhythmias Can be produced by Abnormal alltomaticity ie by SA-node, AV-node & Purkinji system.

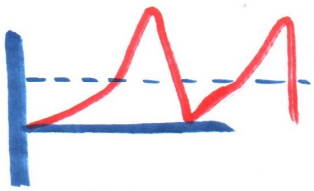


* Resting membrane Potential of Atria+ Ventricle are stable.
* Resting membrane of SA, AV-node & Purkinji are slope.
  ie RMP of healthy atria+ ventricle normally does not reach to threshold.

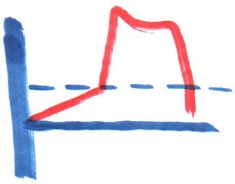
RMP of SA + AV + Purkinji easily reach to threshold.



SA-node

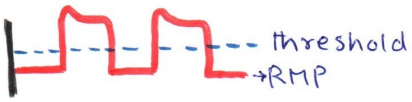


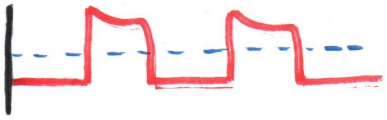
AV-node



Purkinji

Their RMP directly reach to threshold & depolarization occur spontaneously.

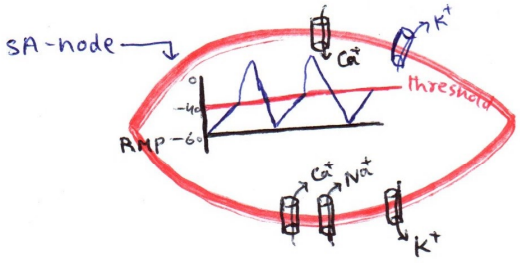




In atria + ventricle RMP does not reach to threshold, so no action potential occurs.

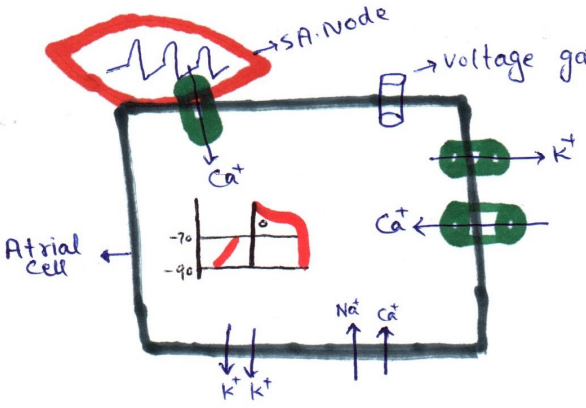
* The slope is given many names, so called "phase-4", the slope is also called as pre-potential.

Why this slope is present in SA-node, AV-node, & Purkinji system i.e. their RMP is not resting, From where this restlessness Comes.



In SA-node Ca^+ & Na^+ move in by leacky channel, while small amount of K^+ Come out.

Due to this inward movement of Ca^+ & Na^+ Ions, RMP move toward threshold. As this Ca^+ & Na^+ move in voltage gated Ca^+ channel opens & Ca^+ move in, this Cause action Potential to move toward zero(0), & depolarized, than Voltage Gated K^+-Channel opens & large amount of K^+ goes out; & Cell again become hyperpolarized, this process repeat every 0.8 sec & in each minute 72 b/min is produced.



In atrial myocardium RMP doesn't move to threshold B/c whatever Na^+, Ca^+ move in by leacky channel, same amount of K^+ come out. $Ca^+ + Na^+$ influx = K^+ efflux. If atrial myocardium is connected to depolarizing SA-node, some of Ca^+ move from SA-node to atria.

This Cations which Jump by gap junction from SA-node to atria move atrial Curve from RMP to threshold. than voltage gatted Na^+-channel opens & Na^+ move into cell and bring Actional potential toward depolarization this is Called as zero phase of Actional potential of atrial cell.

After that Na^+ Channel is off & K^+ channel opens K^+ goes out at a same time Ca^+ channel open & Ca^+ move in so gain of Cation is equal to loss of Cation, so No change in Action potential Platue is formed.

Than time sensitive Ca^+-channel is off, while K^+ channel is opened, so more K^+ comes out, while no Ca^+ move in so cell again become Repolarized.

SA-node depolarization is dependant on Ca^+.

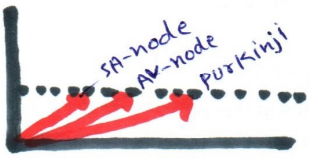
Atrial depolarization is dependant on Na^+.

* This atrial cell throws Na^+ to next cell & pass next cell potential to threshold.

* SA-node have capability of auto excitment (Automaticity)
B/c they have slope which cause this automaticity.
(sam from AV+ purkinji)

Healthy atria + ventricle RMP is stable.
Cation efflux = cation influx
* when atria + ventricle is injured than gap junction appear and conduction pass to every cell.
SA → Atrial cell → next atrial cell

In normal person SA-node is pacemaker.
When SA-node, AV-node & purkinji are pacemaker cell than why only SA-node is cause automaticity.
B/c normally SA-node Automaticity is fast than AV-node & purkinji cells
e.g SA-node RMP is more slope than AV-node & purkinji



=> SA-node First reach to threshold.

So SA-node slope is more leaky to cations than AV-node & purkinji
SA-node impulse pass to AV-node before AV-node produce its own automaticity, and from AV-node impulse pass to purkinji before purkinji produce its own automaticity.
SA-node fire First & its impulses pass to next latent pacemaker, they behave as conductor for impulse.
when SA-node is destroyed than AV-node & than purkinji become pacemaker.

If we remove heart & take one one tissue from SA-node, AV-node & purkinji & put in a tissue culture have normal electrolyte balance, Than SA-node fired at 100 AV-node=50 & purkinji at the rate of 40 b/min

Law of loius

As we go downward from SA-node ~~of~~ automaticity decreses

overdrive suppression

In the prescence of normal SA-node electrical activity of AV-node & purkinji is suppressed.
(physiologic Concept)

Abnormal automaticity

How arrhythmias are produced by alteration in Rate?

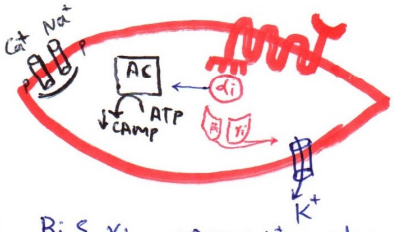
Normal rate = 60 — 100 b/min

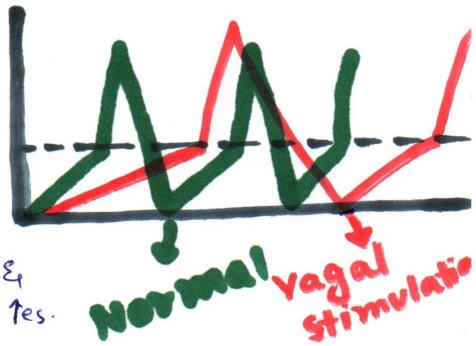
when rate is less than 60 it is called as bradyarrthmias.

* why SA-node produce ↓ impulses?

One reason is strong vagal stimulation, as vagal nerve endings release Acetyl Choline

Mechanisms of action of Ach on SA-node.





As Ach act on Gi, βi & γi opens K^+ — channel & alot of K^+ goes out, so cell electronegativity ↑es.

αi bind with A.C, so CAMP level decreases, ↓ phosphorelation of channels, & ↓ influx of Ca^+ & Na^+, so SA-produce less depolarization in given time, this is called as sinus Brady arrythmias, so Rate is less than 60 b/min.

Tachyarrhythmias:

e.g: * Sometime in Exercise heart rate goes up physiologically.

* In Fever ⟶ Heart rate goes up.
* in Hyperthyroidism ⟶ Heart rate goes up.

b/c in all these conditions SA-node is overloaded with cations.

B/c in these conditions sympathetic overflow occurs, & HR ↑es, so this is sinus Tachyarrhythmia.

* when Cation loading increases ⟹ Tachyarrythmia
* If Cation loading decreases ⟹ Bradyarrythmia

* Vagal influence ⟹ Bradyarrythmia
* If sympathetic influence ⟹ Tachyarrythmia

Arrythmia also occur by disturbe in site of impulse generation If by any reason SA-node is not fired for few second, sinus arrest occur, at that time AV-node escape from overdrive suppression, so AV-node have a chance to displayed its own automaticity, than it start Nodal rythm; this type of Rhythm is called **Escap Rhythm.**

Sometime SA-node stop working & one escap rhythm occurs, sometime SA-node is arrested for long time & full escap rhythm comes, this is another arrythmia due to SA-node fail.

Sometime AV-node is also destroyed "nodal arrest" than Purkinji escap from overdrive suppression, & now new pacemaker is purkinji system, but now heart is beating at a rate of 30 — 40 b/min. " purkinji escap rhythm.

People who developed inferior wall myocardial infarction, have more chance to develop ischemia (↳ AV-node), B/c of same arterial supply.

* Than atria contract at a rate of 80b/min e.g ⇒ SA-node
* The ventricle contract at a rate of 40b/min,

ie in ECG there is 80 P wave & 40 QRS-complexes.

Pulse is produced by ventricle activity so it will also be 40.

Abnormal impulse generation

- Altered Normal automaticity
- Triggered Automaticity.

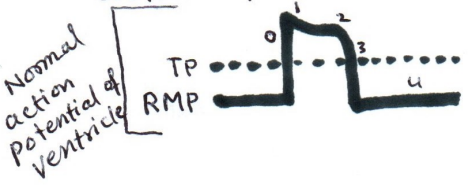
Mechanism of Arrhythmias

- **Abnormality of Impulse generation**
  - abnormality of sponteneous automaticity
  - Triggered automaticity
    - EAD
    - DAD
- **Abnormality of impulse conduction**

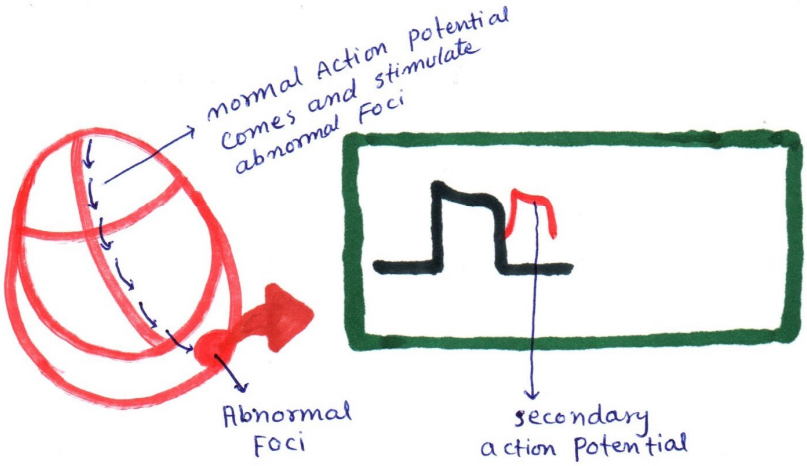
* TRIGGERED AUTOMATICITY

It is an abnormal situation in which some normal Action Potential Triggers Automaticity.

e.g: There is an abnormal area in myocardium & firing when normal action potential reach to it.



* "0" phase → Na^+ move in (depolarization)
* "1, 2" phases → platue phase (Ca^{++} move in & K^+ out)
* "3" phase → repolarization (K^+ goes out)
* "4" phase → is nol slope



In this cell secondary upstroke (depolarization) occur before primary upstroke (normal) undergo repolarization.

* Some RMP fluctuate and reach to threshold automatically and secondary upstroke appears.

Secondary action potential May be:

① Early after depolarization (EAD)
② Delayed after depolarization (DAD)

These upstrokes are called after depolarization, b/c these are occuring after normal depolarization (These are abnormal electrical activity).

* These EAD & DAD are the cause of arrhythmias.

Cause of EAD

EAD = depolarization which occur before normal repolarization.

Na^+-channel consist in 3 confirmation stages. (has)
- M-gate
- h-gate

① No, Na^+ move in b/c M is closed & only h is open.

② Na^+ move in b/c M-gate is open. (h-gate is going to close)

③ NO Na^+ move in b/c h-is closed

Than channel again going to Rest

* M-gate is also called activation gate.
* h-gate is Called Inactivation gate.

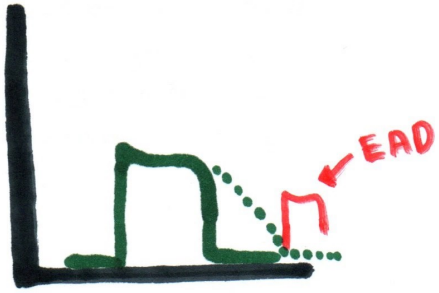
Restin channel
* It is not active now, but can be activated

It slip to Inactive state & Canit activated until ~~be~~ donit go to rest.

Canit be Stimulated (Refractory)

Normally when channel are inactive, whatever stimulus is bring no activation occur, this is called "Absolut Refractory Period."
If some of repolarization occurs, some Na^+- channel move to ~~refractory~~ resting phase, even strong stimulus is bring than some of them depolarized, this is called "Relative refractory Period".

* why no 2nd upstroke occur in normal action potential during Repolarization?
Because most of Na^+ channels are Trapped in inactive Phase.



If due to any reason Action potential is prolonged, than repolarization occur a time when most of Na^+ channels recover from inactive to resting phase, so of action potential occur and premature beat occur, this is called EAD

Conditions which Prolong Repolarization

① If K^+-channel is congenitaly defective, & efflux of K^+ is slower than normal, so most of Na^+-channel recovered from inactive phase to resting phase.
This type of action potential Trigger another depolarization wave before repolarization occurs. this develop tachyarrhythmia.

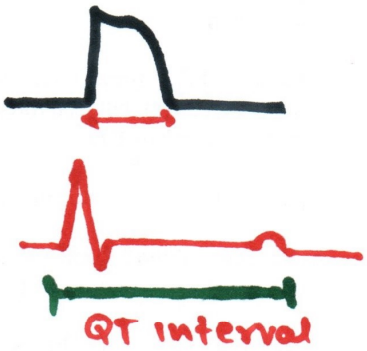
② If Na^+-channel is Mutant, it will decrease depolarization (action potential) time, so the cell Na^+-channels early goes from inactive to resting phase & refractory period is shortened & Premature beat occurs. (EAD). they develop Tachyarrhythmia

③ Long QT-interval syndrome:

in early days, Dr. does not know why people of long QT-interval die

later on Drs. Know that such patient with long QT-interval develop tachyarrhythmia, these QRS-complexes change its Morphology, some are pointing upward & some pointing downward.

They called such arrhythmia as "poly morphic Tachyarrhythmias"



when french look these patients they called them "Torsa-De-Pontes" (T·D·P) → (twisted points)

But at that time they do not knew why long QT interval or T·D·P occur.

Now they know that why QT-interval are long (B/c their K^+-channel is not working well)

later on they discovered that in such a patient when repolarization is going to occur, large number of Na^+-channel recover from inactive to resting phase & they trigger action potential.

similar type of problem also occurs when Na^+-channels are mutant, they develop T·D·P.

T·D·P are associated with long QT-interval.

These days we are using many drugs which make these K^+-channels slows & produce complications like T·D·P.

Many drugs which block K^+-channel, prolong QT-interval and produce risk of T·D·P

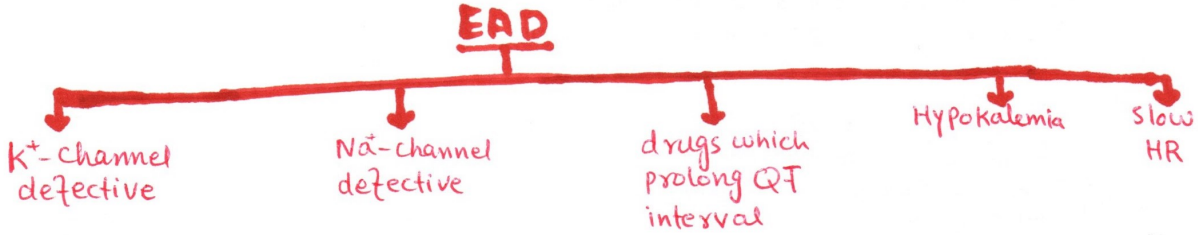
④ Hypokalemia: Can also produce trouble like this.

K^+ wasting diuretics also cause hypokalemia.

Normally cells are bag of K^+.

when person have svear hypokalemia, not only K^+ is less in circulation But K^+ is also less in the cells. so in these patients during repolarization K^+- comes out slowely. in these patients EAD occurs & this will ↑es Tachyarrhythemia.

⑤ Low HR also Lead to EAD, (when HR↓es whole process of A·P ↓es)

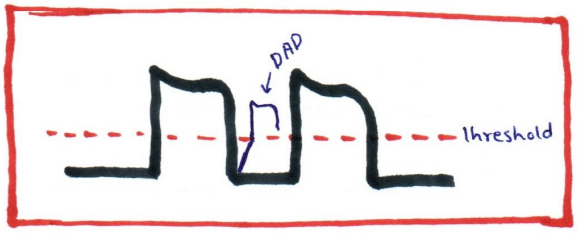


On of way to prevent T·D·P is to make HR fast.

DELAYED AFTER DEPolarization (DAD)

DAD which occur after normal repolarization occurs.

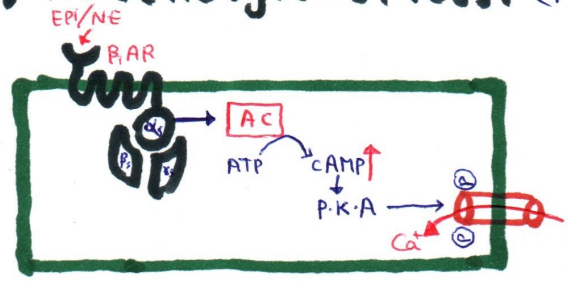
when Ca^+ move into cell, It overload cell with cations. This overloading of Ca^+ does not allow the cell to remain at rest.



This Extra Ca^+ will move the Action potential toward threshold, this will produce DAD; & Increase risk of Tachyarrhythmia.

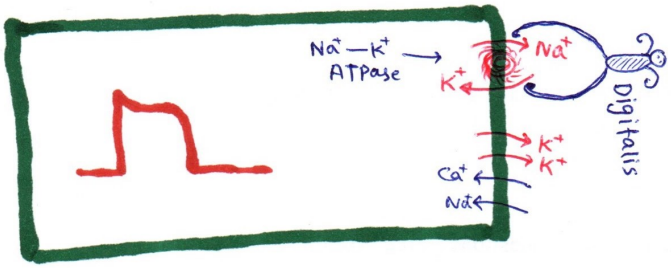
Cause of DAD

(1) Adrenergic stress: (↑Epi or N.E)



when β_1 AR are stimulated, it stimulate α_s unit of G_s protein, which activate A.C which convert ATP → into cAMP, the cAMP activate P.K.A → which phosphorelate Ca^+-channel, so alot of Ca^+ influx occur. So cell will loaded with Extra Ca^+.

(2) Digitalis Toxicity: also increase cation overloading of cell.



Digitalis block Na^+—K^+ ATPase, so Na^+ move in but not come out, so Na^+ will find another way to escape so, Na^+ come out by Na^+—Ca^+ exchanger by this way Ca^+ ↑es in the cell which cause Tachyarrhythmias.

(3) Ischemic cells

All ischemic Cells have low O_2, so low ATP, will produced → Less activation of Na^+—K^+ ATPase, so Na^+ come out by Na^+—Ca^+ exchanger, more Ca^+ move in which cause Tachyarrhythmia.

This problem is solved by Ca^+-channel blocker "VERAPAMIL"

But ↑ To ischemic patient we can't give VERAPAMIL B/c such tissues are already contracting weakly & Ca^+-channel blocker further inhibit the cell activity.

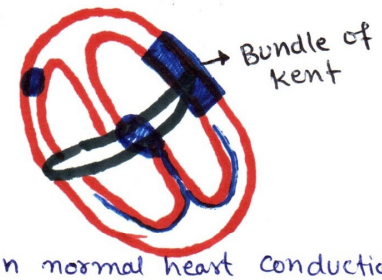
Another way is to give Na^+-channel blocker to patient than inspite of fluctuating No depolarization occur. Na^+-channel blockers Trap the cell in inactive phase.

Abnormalities of Impulse conduction

Re-entry

Anatomical defined Re-entry

e.g WPWS
(wolf parkinson white syndrome)



In normal heart conduction pathway is from:
SA → Atria → AV → Bundle of his → purkinji → ventricles

In WPWS abnormal pathway is developed B/w atria & ventricles this is called "Bundle of kent" actually these patients have normal rhythm but sometime these develope svear Tachyarrhythmia

How Tachyarrhythmia are produced in WPWS?
These Tachyarrhythmia are produced when some abnormal focus in atria will fire.

Functionally defined Re-entry

This type is seen in patient with ischemic hart disease who have develop fibrillation, B/c multiple areas in ventricle is ischemic and multiple pathways are produced impulse pass through some pathways & fail in other pathways & one impulse produce many doughter impulses.

* Patient with after myocardial infarction ie post MI patient, have multiple areas of ischemia, they have high risk to develop Tachyarrhythmias.

patients with ischemic heart disease eventually die of Tachyarrhythmia

* If patient have multiple areas of ischemia heart become electrically & Mechanically abnormal.

→ This electrical abnormal myocardium will produce ↓ S.V → ↓HR so → ↓ CO → ↓ filling of root of aorta → so further is chemia.

Impulse Block

In this condition AV-node is unable to pass impulses from atria to ventricles.

- AV- may be ischemic
- AV- may be suppressed

AV-node suppressors:
1. β-blocker
2. Ca^{+}-channel blocker
3. Digitalis (stimulate vagal outflow)
4. Adenosine

Bundle of Kent have Na^+ dependant depolarization, so it is fast responce accessory pathway.

electrical property of bundle of kent is somewhat like atrial cells.

ie: in this patient there are two connections B/w Atria + ventricles

① Slow responce pathway which is due to "Ca^+ influx"
- → SA-node
- → AV-node
- → Purkinji

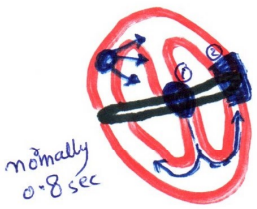
② Fast responce pathway which is due to "Na^+ influx"
- → Atria
- → ventricle

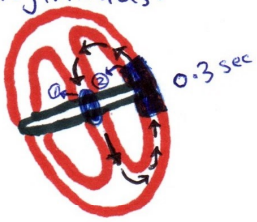
In These patients impulse from SA-node → Atria → AV-node, Bundle of Kent

from both of them impulse pass downward

* Normally there is no refractory
* They are refractory to each other (ie a patient which is depolarized by AV-pathway should not be depolarized by bundle of Kent.

most of patient with WPWS does not have Tachyarrhythmia, but they have increase chance of Tachyarrhythmias.





Further development of multiple areas in myocardium with different mechanical and electrical activity cause further Tachyarrhythmia, leading to further failure of mechanical activity of heart.

further reduction in Cardiac output decrease filling of Coronary system, further increase of ischemic spots

* some conducting Normaly
* some conducting Not at all.
* some conducting through one pathway but not on other

so multiple Re-entry Mechanisms will start, & in ventricle there are 100 to 1000 of areas with such cycling moving.

When and How these patients develop Tachyarrhythmia?

They develop Tachyarrhythmia when atria have some ectopic foci.

Let us consider from ectopic foci impulse generated and able to pass through only

(1) one pathway as impulse move downward these impulses move upward in bundle of Kent, which is already depolarized by SA-node, impulse is again ready for Conduction, so impulse pass throug bundle of Kent to atria, and again come down through AV-node, this whole cycle take 0·3sec

this cycle occurs every 0·3 sec so Rate of ventricular Contraction increase, leading to tachyarrhythmia, B/c there is much of Re-entry.

ie: Ectopic foci in atria → AV — ventricle →
Bundle of Kent → Atria → AV → → →

Sometime AV-node is not able to Conduct, while bundle of Kent is able to conduct, so impulse move from

ectopic focci in atria → Bundle of Kent → ventricle → AV-node →
bundle of Kent in atria → ventricle → →

B/c by that time AV-is recovered from refractory period this reverse cycle again Takes up 0·3 sec, so there are 200 cycles in 60 sec.

1 cycle	= 0·3 sec
10 "	= 3 sec
100 "	= 30 sec
200 "	= 60 sec

If there is a problem B/w Atria & ventricle, this is called Junctional Tachyarrhythmia

such conditions are blocked by →
- Ca^+-channel blocker (block AV-node)
- Na^+-channel blocker (block bundle of Kent)
- any drug which suppress Ectopic foci

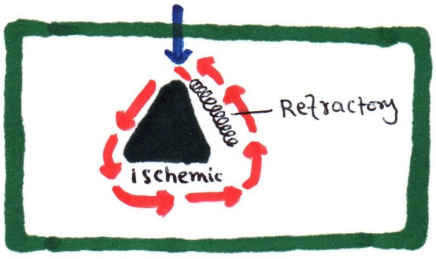
If any patient of MI recover from Na^+ inactive to Na^+ Resting phase, it is stimulating by any nearby circle movement, & it undergoes abnormal depolarization.

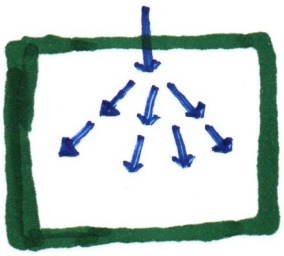
* on this way patient with svear ventricular Tachyarrhythmia goes to Mechanical failure & progressive further decrease in coronary supply → further ischemia → further electrical abnormalities & patient goes into ventricular fibrilation
* similarly if patient with ventricular flutter not treated invariably goes into Fibrillation.

There are 2 pathways to discus Re-entry.

① WPWS → Anatomical Re-entry

② Any abnormal piece of Myocardium which has two conduction pathways, both of which have different electrical property → Functional Re-entry





NORMAL

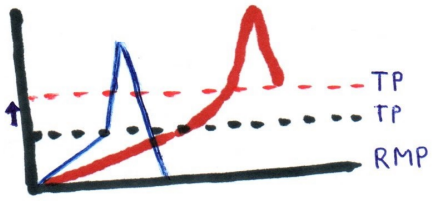
If impulse enter into myocardium, & myocardium have Ischemic area than such impulse divided into two, but if one conduction pathway is normal and other is refractory. Than impulse pass forward from normal pathway so whatever, impulse pass from normal pathway. It pass all way round untill refractory tissue become recover, so it also pass from this area and Continue as a cycle which occur again & again this lead to Tachyarrhythmia.

ie This pathway does not allow antigrade impulse Conduction but allow retrograde impulse conduction.

* Arrhythmias are produced by Electrical, & Mechanical abnormalities in Myocardium.

ARRhythmia

- Abnormality in Impulse Generation
  - **Abnormality in Sponteneous Automaticity**
    - ✱ This tachycardia is treated by Ca^+ & Na^+-channel blocker
      So, influx of Na^+, & Ca^+ decreases.



This Na^+ & Ca^+ channel blocker:

① reduce slope of phase 4 (diastolic current)

② increasing threshold Potential

  - **TRiggered Automaticity**
    - EAD
    - DAD

- Abnormality in Impulse Conduction

Abnormality in sponteneous Automaticity we can treat such tachyarrhythmia by:

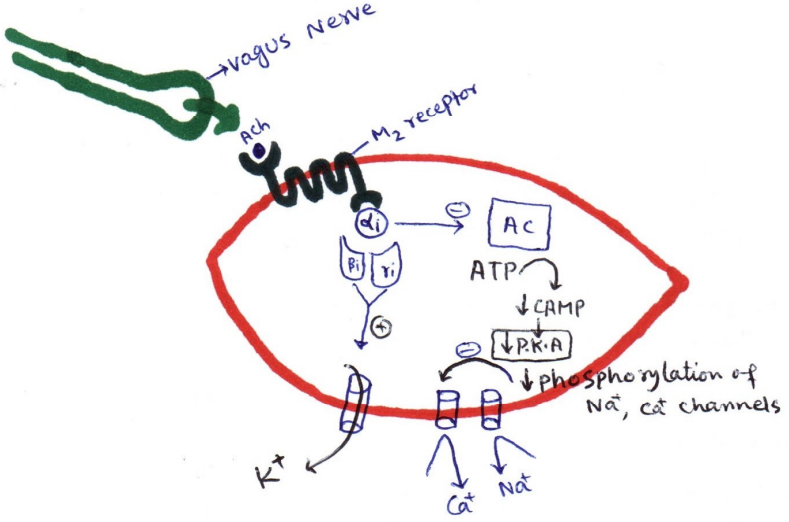
① ↓ the slope

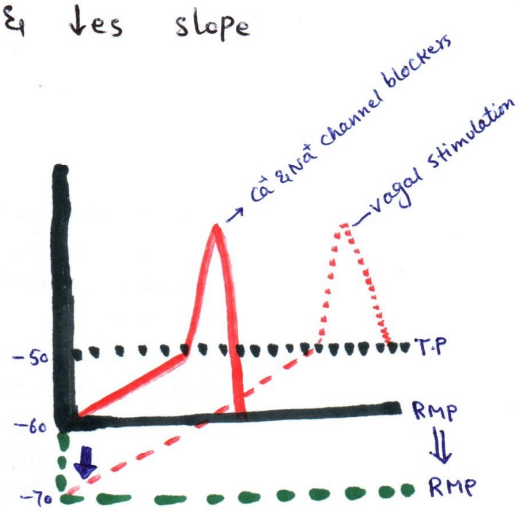
② down RMP (hyperpolarize the cell)

③ ↑es T.P

④ ↑ duration of Action potential

⊛ Vagal stimulation decreasin RMP & ↓es slope



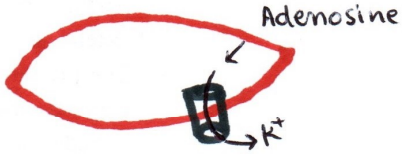


So the cell become more electronegative (Hyperpolarized OR ↓ diastolic potential). b/c RMP goes from -60 ⟶ -70.

* **Adenosine** (IV)

Adenosine work on Purinergic receptor & lead to loss of K^+, by activation of K^+-channel.

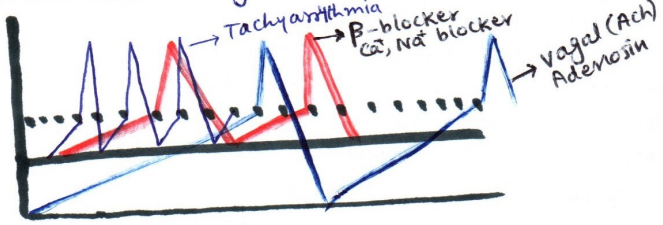
Adenosine work like Ach, block the phosphorylation of Ca^+ & Na^+ channel & open K^+ channel

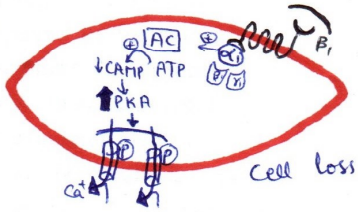


Adenosine ⇒ * ↓es slope
* ↓es RMP
So Tachyarrhthmia will disappear.

Adenosine work more on AV-node, but also work on SA + Purkinji.

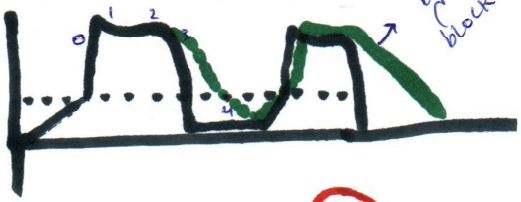
* **β-Blockers** only decrease the slope





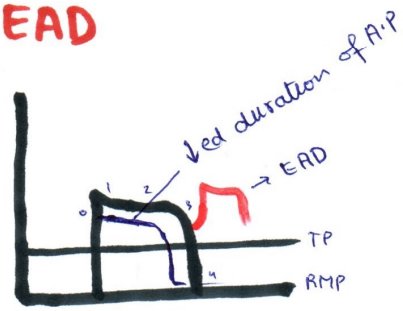
* **K^+-channel blocker** ⇒ ↑ duration of action Potential

K^+-channel blockers ↓ing efflux of K^+, so ↓ing Repolarization, so duration of action potential ↑es. These drugs ↑ Risk of T.D.P



Triggered Automaticity

EAD



Stratigies to treat these patients:

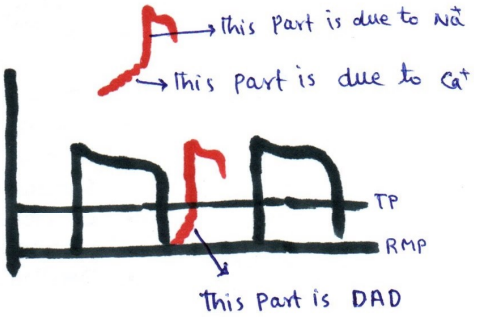
① ↓es Duration of action Potential

one way is to slightly ↑ HR

- Intravenous infusion of Isoproterenol
- Pacing of Heart

② give Mg^+:
It interfere with recovery of Na^+ from inactive to Resting phase

DAD



Stratigies to treat these patients

① Ca^+-channel blocker

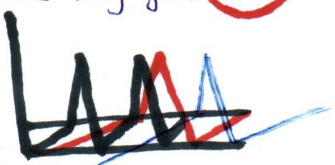
② Na^+-Channel blocker

Abnormality in impulse conduction

Anatomically defined Re-entry

e.g: WPWS

- ① Ca^+-channel blocker are very good in these patients b/c
  - ⓐ ↓ slope
  - ⓑ ↑ threshold
  - ⓒ ↑ duration of action potential



- ② Digitalis (stimulate vagus) → ↓ slope, ↓ RMP
- ③ β-blocker

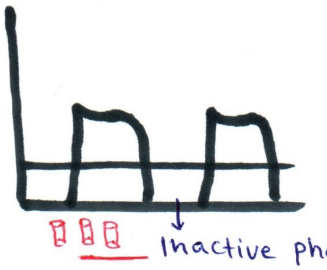
All these drugs inhibit AV-node

Functionally defined Re-entry

Fast response tissue	slow response tissue
* Atrial Myocytes	* SA-node
* Purkinji fiber	* AV-node
* ventricular Myocytes	
Na^+ dependant depolarization	Ca^+ dependant depolarization

① ↑ ERP (Effective refractory period)

Fast Responce Tissue



ERP Can be increased by
* Na^+ - channel blocker OR
* K^+ - channel blocker

what bring the inactive Na^+ channel to Resting Na^+ channel.

① As repolarization end most of Na^+-channels automatically move from inactive to resting phase.

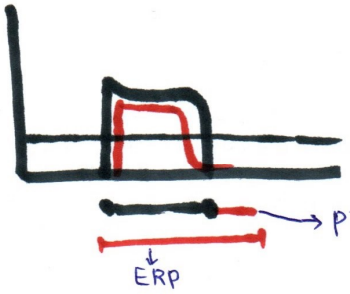
② ↑ed inactive phase
* May be by K^+-channel blocker (which increase repolarization) that will help to prolong ERP (& keep most of Na^+ channel in inactive phase

ERP Is the time duration for which myocardium is resistance to produce next stimulation
ie from active → inactive Na^+ Channel

③ Na^+- channel blocker
ⓐ decrese the slope of UPstroke
ⓑ decrese the Conduction velocity

initially there is only antegrade block.
By increasing ERP we also ↑es Retrograde block

so ∫active Na^+ channel takes more time to move to resting phase.

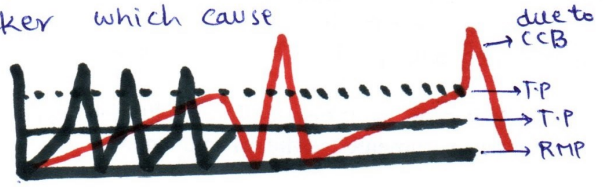


→ prolonged inactive phase of Na^+ so, ↑ERP

Slow Responce Tissue

These are Ca^+ dependant depolarization so we give:

Ⓐ Ca^+- channel blocker which cause
① ↓ slope
② ↑ threshold



End of ANTIARRHYTHMIC Drugs

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