Electrophysiology of cardiac muscle and origin of the heart beat

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ILOs

1. Define excitability and know action potentials in the cardiac muscle, the cause of long action potential and plateau and describe the ionic basis of each phase of the action potential, and the characteristics of the action potential in different regions of the heart, including the pacemaker potential. Describe the extrasystole and its mechanism.

2. Define rhythmicity and know the rhythmicity in different parts of the cardiac muscles and factors affecting it.

Properties of cardiac cells

- Excitability
- Auto rhythmicity
- Conduction
- Contractility

The cardiac action potentials (AP):

1- slow(pace maker action potential) recorded from the S-A node and A-V node (poor in gap junction)

2- fast (non-pace maker)response cardiac action potentials recorded from the atria, ventricles and His - Purkinje system which are rich in gap junctions (so the cardiac fibers in these regions are called fast response fibers and contracted as one syncytium).

Electrical potentials in cardiac muscle cells:

Resting Membrane Potential: At rest, the ventricular cell membrane is most permeable to K+ and the resting membrane potential (RMP) is therefore close to the K+ equilibrium potential (EK); – 90 mV.

Resting membrane potential in:

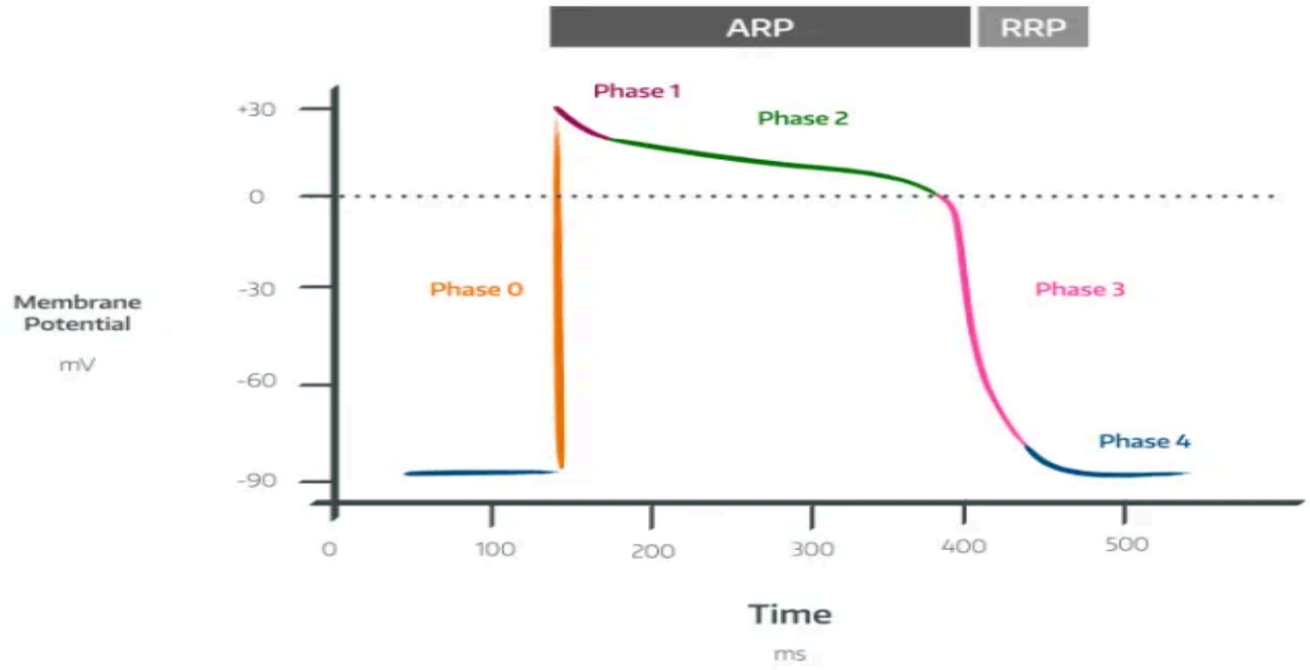
Sinoatrial (SA) node – 55 to – 60 mV.

Single cardiac muscle fiber – 85 to – 95 mV.

Purkinje fibers – 90 to – 100 mV.

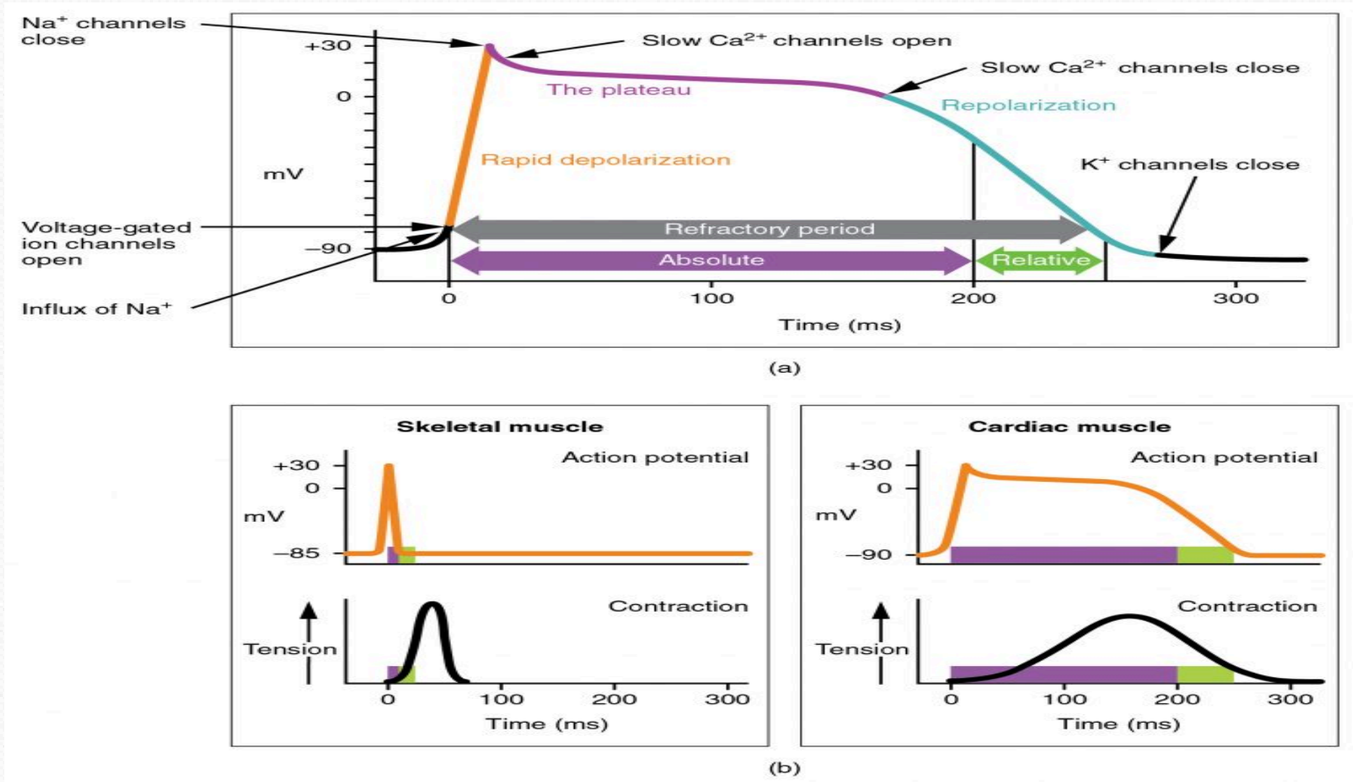
Phases of cardiac muscle action potential (fast response in none-pacemaker cells)

CARDIAC ACTION POTENTIAL



Fast response cardiac action potentials (non-pacemaker action potential):

The atria and ventricles as well as the His - Purkinje system which are rich in **gap junctions**.



Phases of myocardial action potential

Action potential in a single cardiac muscle fiber occurs in the following phases:

1. Initial depolarization (Phase 0).
2. Initial repolarization (Phase 1).
3. A plateau or final depolarization (Phase 2).
4. Final repolarization (Phase 3).
5. Complete repolarization and Restoration of Resting Membrane Potential (Phase 4)

1.Phase 0: Initial Depolarization (up to+20 mv)):

- Initial depolarization is very rapid and it lasts for about 2 msec.
- Amplitude of depolarization is about + 20 mV.
- It is because of rapid opening of fast sodium channels**(voltage gated Na channel).**

2. Phase 1:Initial Repolarization (+20 -+10 mv):

- opening of potassium channels and efflux of a small quantity of potassium ions via **transient K+ channels** from the muscle fiber.
- Closure (inactivation) the fast sodium channels . Phase 1 lasts for 2-3 msec.

NB Inactivated Na+ channels cannot be reactivated until the potential returns to less than −60 mV. So, another AP cannot be initiated until the cell repolarizes (refractory period).

NB Cardiac muscle has long refractory period and long contraction so, cardiac muscle cannot be tetanized unlike skeletal muscle.

3.Phase 3: Plateau or Final Depolarization (+10- 0 mv):

- The muscle fiber remains in depolarized state (prolonged depolarization) for sometime before further repolarization.
- It forms the plateau (stable period) . Plateau is due to the **balance between ca influx and K efflux** .

-Ca in flux via L-calcium channels (L-type) causing influx of large number of calcium ions.

-K+ efflux via delayed out ward rectifier K+ channel , producing prolonged depolarization, i.e. plateau.

Importance of plateau

NB Importance of plateau: **Due to long plateau (200-300 msec) in action potential:**

1- the contraction time is also longer in cardiac muscle by 5to 15 times than in skeletal muscle.

2- Cardiac muscle not tetanized→ long ARP.

NB Ca2+ entry during the plateau is vital for cardiac muscle contraction

4. Phase 3 :Final Repolarization (0- -90 mv)):

- Final repolarization is due to

1. **closure of L-type Ca channels**
2. **efflux of potassium** ions via delayed out ward rectifier K+ channel.

- Number of potassium ions moving out of the muscle fiber exceeds the number of calcium ions moving in. It makes negativity inside, resulting in final repolarization. it lasts for about 50 to 80 msec .

5. Phase 4: Complete repolarization and Restoration of Resting Membrane Potential :

Complete repolarization occur due to K+ efflux via **inward rectifier K+ channel** .

For restoration of resting membrane potential

1- all sodium ions, which had entered the cell throughout the process of action potential move out of the cell and potassium ions move into the cell, by activation of **sodium-potassium pump**.

2- ***Simultaneously, excess of calcium ions, which had entered the muscle fiber also move out through*** **sodium-calcium exchanger.**

Thus, the resting membrane potential is restored.

Spread of action potential through cardiac muscle

- Action potential spreads through cardiac muscle very rapidly because of the presence of gap junctions between the cardiac muscle fibers.
- Both atria and both ventricles contract as one syncytium and obey All or none law.
- Gap junctions are permeable junctions and allow free movement of ions and so the action potential spreads rapidly from one muscle fiber to another fiber.

Relation between AP and mechanical response

- Contraction (mechanical response) starts just after beginning of depolarization & reaches its maximum by end of plateau (phase 2).
- Repolarization **coincides with** first half of relaxation (diastole). (diastolic time double repolarization time).

Relation between AP and mechanical change

1. **Systole**: coincides with depolarization phase till the end of plateau.

2. **Diastole:** coincides with final repolarization and resting membrane potential.

Relation between AP & excitability change

1- Absolute Refractory period **coincides with** period of depolarization till end of plateau (the excitability is lost)

2- Relative refractory period **coincides with** the period of rapid Repolarization phase (the excitability is weak)

Relation between AP & ECG

- QRS	**Coincide with** depolarization
- S-T segment	**Coincide with** plateau
- T wave	**Coincide with** rapid repolarization

Autorhythmicity of cardiac muscle

It is the ability of heart to beat regular impulses independent of any nervous connection				
Rhythmic cels are:	Rhythmic cell	**① SAN**	**② AVN**	**③ Purkinje**
	Rate of Discharge	90 /min	60 /min	30 /min

The pacemaker of the heart

- Pacemaker is the part of the heart that initiates and controls the heart beat.
- **SA-node is the pacemaker of the heart as it has the highest rhythm.**
- SA-node have the highest rhythm as it has a rapid recovery from action potential, than other parts

Rhythmic or pacemaker cells

Rhythmic cells are characterized by:

① Discharge spontaneously

② Membrane potential is unstable no RMP

③ It has no plateau

④ Membrane more permeable to Na^{+} & Ca^{++}

⑤ Firing level = -40 mV

⑥ Peak of AP = + 10 mV

The prepotential (or pacemaker potential or Slow response fibers):

- **The pacemaker cells in the nodal tissue (SA node and AV node) have**

a resting membrane potential of *-55 to - 60 mV.*

- **Resting membrane potential is unstable →the membrane is more permeable to Na than K→ continuous Na leak (funny current)→** gradual depolarization occurs spontaneously till a threshold (the firing level) is reached **(- 40** mV) at which an action potential is initiated.

pacemaker prepotential (slow response)

1- Phase 4: resting membrane potential (-60- - 40 mv) :

a) **(from -60 - -50 mv)→ Increased inward Na+ →Na leak channel → (the funny current)**

b) **(from -50 - -40 mv)→ opening 0f inward Ca2+ current via T (transient) type Ca++channels → firing level -40 mv**

3- Phase 0 :Rapid depolarization (-40 -+10 mv)due to: Rapid influx of Ca+ → **L-type ca channels at -40 mv** it opens.

Mechanism of gradual depolarization in pacemaker potential

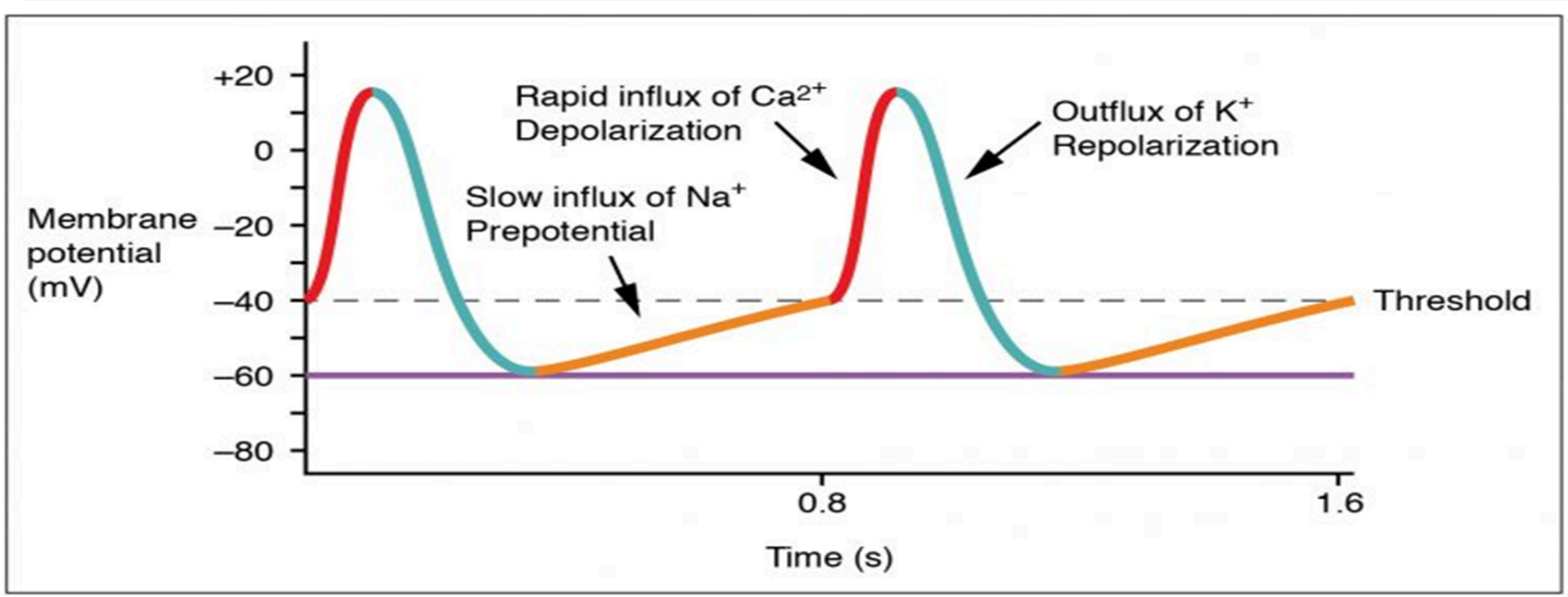
4- Phase 1 &2 are absent.

5- Phase 3 :Repolarization (+10- -60 mv) : 1- closure of L-calcium channels

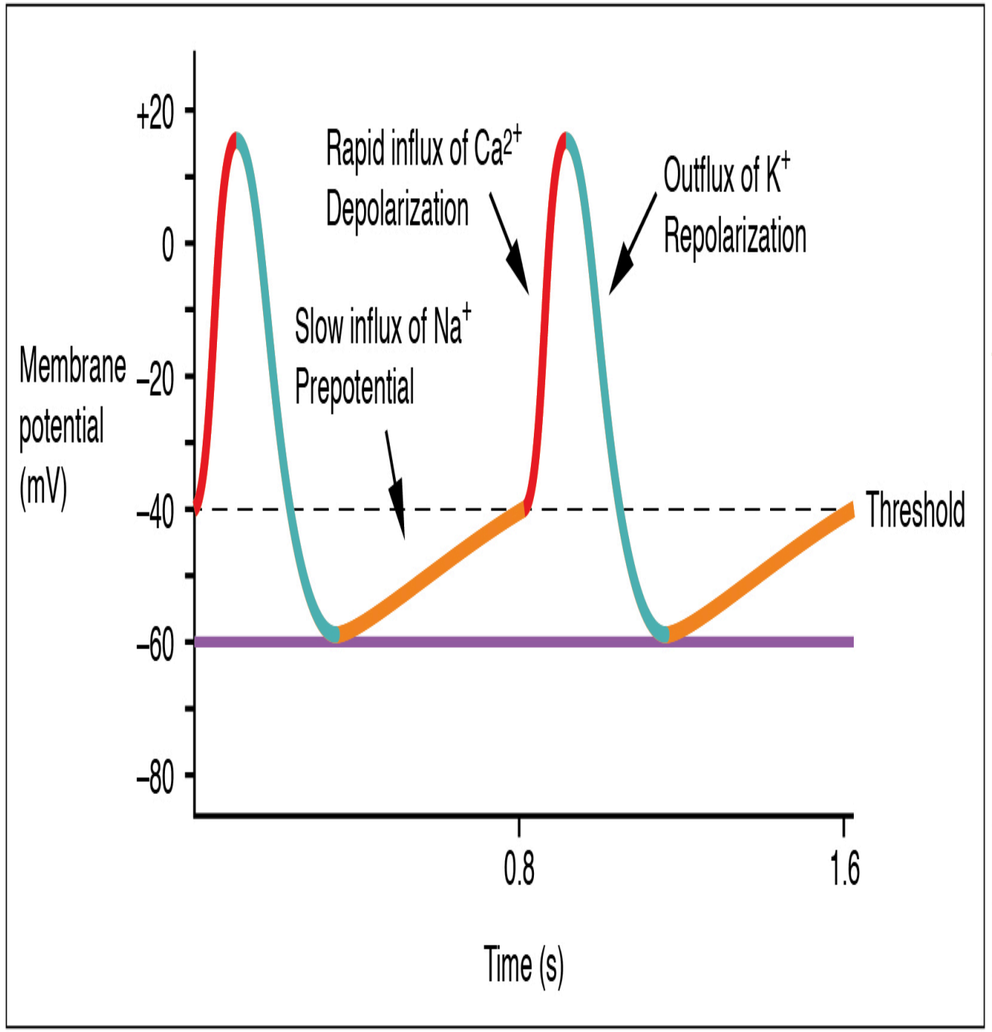
2- opening of K channels **(delayed out ward rectifier K+ channel)**

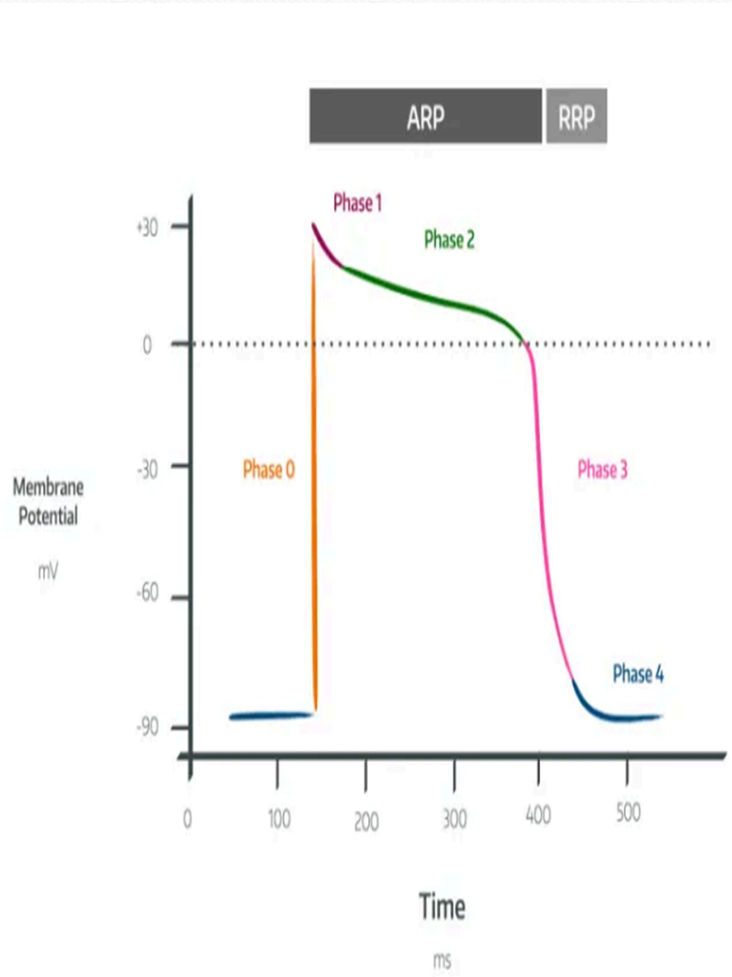
6- **At -60 mv: Inactivation of K+ channels (so K+ efflux stops)**

Prepotential in pacemaker cells



Cardiac Action Potential





Excitability changes during cardiac action potentials:

1. **Absolute refractory period (ARP)**
2. **Relative refractory period (RRP)**
3. **Supernormal phase**

(1) Absolute refractory period (ARP):

- This is a period during which the **excitability level is zero. no stimulus whatever its strength can initiate a propagated action potential)**.
- It extends from the start of **phase 0 ,1,2 to the middle of phase 3.**
- **It correspond to all systole and 1st third of diastole**
- **The membrane completely depolarized→ all fast Na channels are inactivated.**

(2) Relative refractory period (RRP):

- **This is a period during which the excitability is improved but still below normal and only stimuli that exceed the normal threshold (suprathreshold) can produceaction potentials**.
- It occupies **the remainder of phase 3**.
- It corresponds to **the 2nd third of the diastole**
- **Some not all Na+ channels are now activated (closed by outer gates).**

(3)supernormal phase

during it the excitability is more than normal so weak stimuli can produce action potentials.(may cause ventricular fibrillation which is fatal) vulnerable period.

occurs only in the fast response fibers.

This phase occupies phase 4 of the action potential.

It correspond to last third of diastole.

All Na+channels are activated (closed by inner gates) & ready, and the membrane potential is close to the firing level

NB

In spite of the SA node rhythm is 100 beats/min ,our radial pulse is only about 70 beats /min .

why??

Factors that affect autorhythmicity & excitability:

(1) **Nervous factors**: Parasympathetic -Sympathetic stimulation

(2) **Physical factors**: body temperature

(3) **Chemical factors:** Hormones - Blood gases

Nervous factors

Parasympathetic stimulation Stimulation of the parasympathetic nerves to the heart (the vagi)

1- **decreases the rate of rhythm of the sinus node.**

2- decreases the excitability.

Nervous factors

Sympathetic stimulation

1- increases auto rhythmicity of the pacemaker cells resulting in tachycardia. **+ve chronotropic**

2- **increase excitability.**

(2) Physical factors:

Rise of the body temperature (e.g. in muscular exercise and fevers)increases the heart rate by about 10-20beats /minute for each 1 ° C rise.→ increase the metabolic activity of the pacemaker cells in the SAN

Hypothermia the auto rhythmicity and heart rate are decreased.→ decrease the metabolic activity of the pacemaker cells in the SAN.

(3) Chemical factors:

a) **Hormones**: Catecholamines and thyroxine increase the Auto rhythmicity by a mechanism similar to that of sympathetic stimulation.

b) Blood gases: Mild hypoxia increases the auto rhythmicity (by stimulating the pacemaker cells both directly and by increasing sympathetic activity), while severe hypoxia & hypercapnia inhibit it and may cause cardiac arrest.

Thank you

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