Conduction System of the Heart

-Conduction system is very important; without it we will not have impulses or action potentials and there will be NO contraction of the heart muscle.

-It consists of modified cardiac muscle cells which are able to produce **automatic** and **rhythmic** impulses.

- Functional modification → by leakiness to Na+ (these cells are leaky to Na+)
- Structural modification → by presence of actin and myosin (contractile cells)

-Leakiness differs from one part to another:

- SA-node is the most leaky one to Na+
- AV-node is less leaky
- Purkinje fibers are the least leaky to Na+

That's why they have different rates (highest rate in SA-node, lowest rate in Purkinje)

SA-node >AV-node > Purkinje

↓ Leakage to Na+/ rate decreases

-SA-node produces impulses, they spread through the atrial muscle to the AV-node (which is emerged in the atrial muscle), so AV-node picks the impulse and conducts it to the AV-bundle (bundle of His), then through right & left bundle branches, to Purkinje fibers to the ventricular muscle cells.

- There is NO direct connection between SA-node & AV-node; AV-node receives the impulses from the atrial muscle (since it is part of it).

-Approximately 1% of cardiac muscle cells are autorhythmic rather than contractile, despite that, they are very important; because they are able to produce intrinsic impulses that spread all through the heart and cause contraction.

- SA-node : 70-80 (highest rate)
- AV-node : 40-60
- Purkinje : 15-40 (lowest rate)

-Normally, the SA-node produces (70-80) action potential/min, which is conducted through AV-node to AV-bundle to Purkinje, so the heart is working with that rate also (70-80) beats per minute.

-As a result, **intrinsic** rates of AV-node and Purkinje fibers have been suppressed by the higher intrinsic rate from SA-node (they are not working with their own rates), this is called **Overdrived suppression**.

- By removing SA-node → working by the rate of AV-node (40-60)
- If AV-node is blocked → no direct connection between the atrium and the ventricle, therefore, ventricles beat by the rate of Purkinje (15-40), whereas atria beat by the rate of SA-node (70-80), this is called **AV block** or Heart block.

Conduction speed

(how fast they conduct the impulse or action potential)

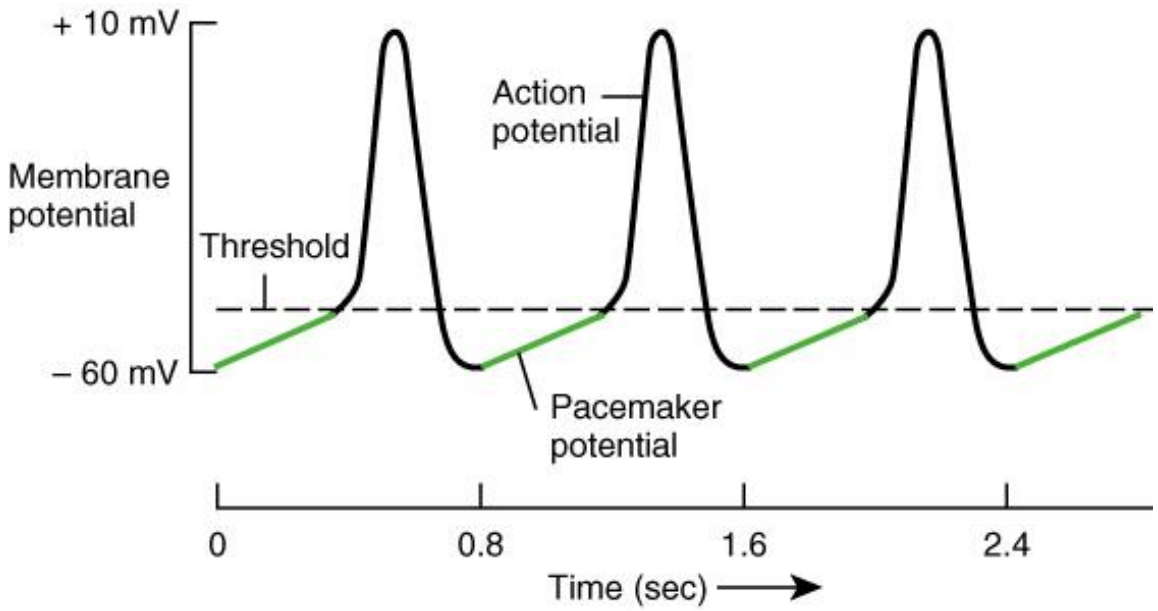
- AV-node has the slowest conduction speed
- Purkinje fibers have the fastest conduction speed (4-5 m/sec)
- Ventricular & atrial muscle cells have moderate speeds

-As we took before, conducting rate of nerve fiber depends on the myelination and diameter.

- **The AV-node conducts the impulse very slowly, why?**
  Normally, the atria and the ventricles should NOT contract together (the atria should contract and finish their contraction then the ventricles start to contract), to assure this, there should be a **delay** in the impulse so they will not overlap.
- **Purkinje fiber conducts with the highest rate, why?**
  In order to conduct the impulses to all ventricular muscle cells almost at the same time, so that they can contract simultaneously as one unit. (Purkinje is wider)

Slow Response Action Potential (pacemaker potential)

- Because these cells are leaky to Na^+ , the resting membrane potential will *never* reach -90mV (it reaches -60mV)
- Slow depolarization due to Na^+ influx (because it is slowly depolarized, the inactivation gate of Na^+ channels close before the activation gate opens → so Na^+ gated channels are closed), and then Ca^{++} channels open causing Ca^{++} influx (depolarization)→ phase zero
- Slow Depolarization due to Na^+ influx through leakage channels → phase 4
- Repolarization due to K^+ efflux → phase 3
- There is <u>NO</u> (1 or 2) phases → no Plateau

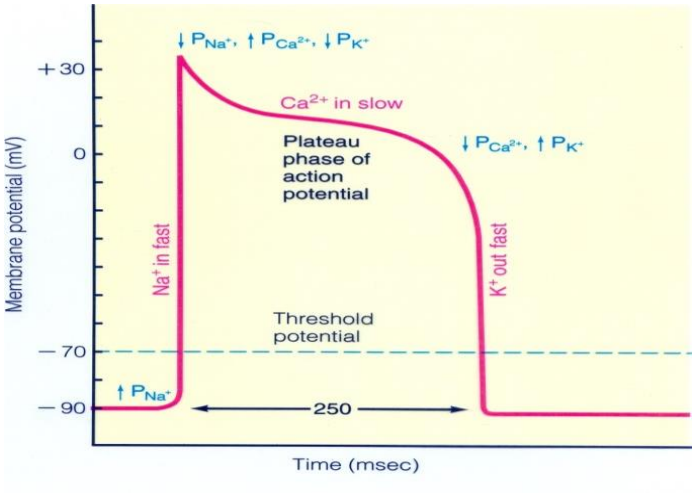


(b) Pacemaker potentials and action potentials in autorhythmic fibers of SA node

20.10b

Fast Response Action Potential

- Resting membrane potential is much more negative
- Fast depolarization due to Na+ influx → phase zero
- There are phases 1 & 2 (Plateau)



-Ectopic pacemaker: abnormal site of pacemaker (ex: AV-node).

Extrinsic Innervation of the Heart

-The heart is supplied by *Autonomic nerves* (sympathetic & parasympathetic)

-They are working for ***regulation*** of the impulse not initiation

-Chronotropic effect: change in the *rate*

-Inotropic effect: change in *force of contraction* in atria and ventricles (*contractility*)

-Dromotropic effect: change in *rate (speed) of conduction*

❖ Sympathetic Extrinsic Innervation of the Heart

- From the cardiac plexus
- Supplies all parts of the heart (atria, ventricles, SA & AV nodes, AV bundle and Purkinje)
- Affects either directly or indirectly through its neurotransmitters which are epinephrine and norepinephrine (AKA: adrenaline and noradrenaline)
- Causes *increase* in permeability of cardiac cells to **Na+** & **Ca++**
- Positive Chronotropic , positive Inotropic , positive Dromotropic

- *Increasing permeability to Na+*
  -The resting membrane potential will not reach (-60mV) → less negative (ex. -55mV) due to Na+ influx (more positive charges enter these cells)
  -Faster depolarization → we reach the threshold earlier, so that we have higher rate
  -Positive Chronotropic effect (increase in the rate)

- *Increasing permeability to Ca++*
  -This will affect the contractile cells _especially the ventricles_ (Ca^{++} does not affect conductor cells)
  -Increasing in the force of contracting (due to Ca^{++} influx, so more Ca^{++} would be inside) →more contractility
  -Positive Inotropic effect (increasing contractility)
  -Positive Dromotropic effect (faster rate (speed) of conduction of the impulse)

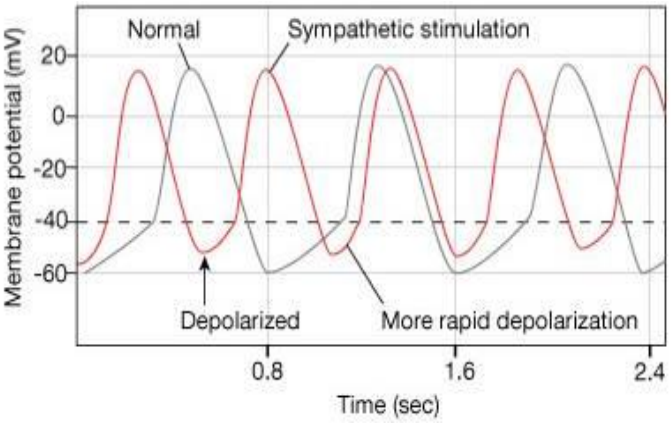
❖ Parasympathetic Extrinsic Innervation of the Heart

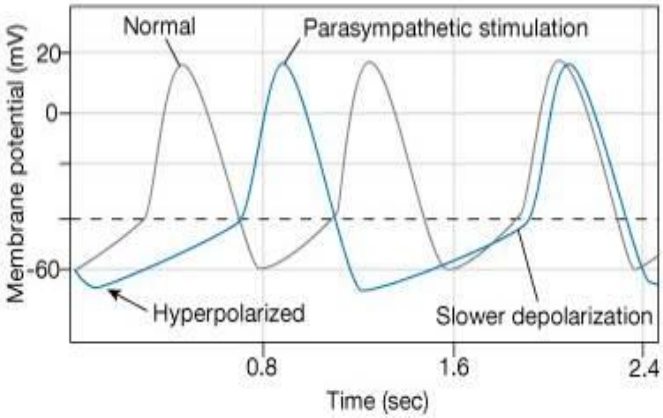
- From Vagus nerves
- Supplies only the SA & AV nodes and the atria (does not supply the ventricles)
- Affects either directly or indirectly through its neurotransmitter which is acetylcholine
- Causes *increase* in permeability of these cells to **K+** and *decrease* of permeability to **Na+** & **Ca++**
- Negative Chronotropic , negative Drpmotropic , NO Inotropic effect

- *Increasing permeability to K+*
  -The resting membrane potential will be more negative due to K+ outflux

- Decreasing permeability to Na+
  -Slower depolarization → longer time to reach the threshold, so that we have slower rate
  -Negative Chronotropic effect (decrease in the rate)

- Decreasing permeability to Ca++
  -Has almost NO effect on contractility; because the ventricles are not supplied by parasympathetic Vagus nerve
  -Almost NO Inotropic effect





To summarize:

**sympathetic → increase in rate, resting membrane potential is less negative

**parasympathetic → decrease in rate, resting membrane potential is more negative (hyperpolarization)

**the maximum rate is not affected

**the heart rate we measure is the ventricular rate NOT the atrial rate

- If you stimulate the vagal nerves, the heart will stop for a while (not forever), and the patient falls down, after a while (15-30 sec) the heart pumps again but with a slower rate ,which is ***Purkinje rate (15-40)*** , this is called **Ventricular escape.** (Firstly, Purkinje was suppressed by Overdrive suppression from SA-node. However, the ventricles are not supplied by the vagus nerve ,so when the vagus nerve is stimulated , the ventricles won't be affected ,and thus escape from the parasympathetic effect.)

Receptors functions and Signal Transduction

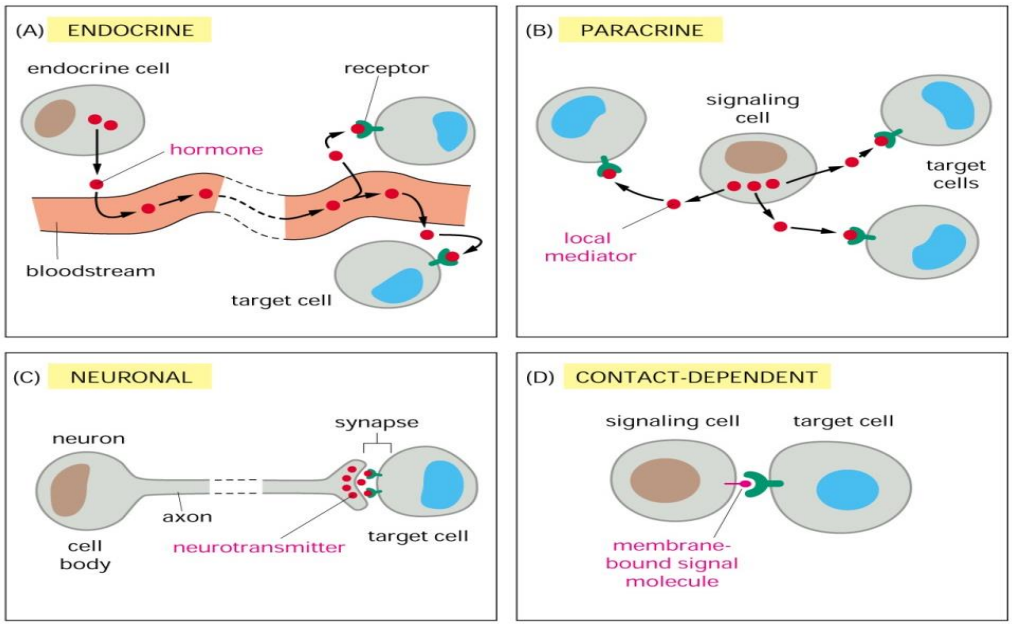
- **Transduction**: conversion of one type of energy into another
- Signal molecules (**hormones**) need specific receptors on their **target cells** (without receptors, hormones do not act and there will be NO response)
- First messenger is the signal molecule which is the hormone. Second messenger is something inside the cell
- Hormones act on the cell, specifically the cell membrane (which consists of phospholipid bilayer ,and has a lot of proteins which work as receptors)

- **Intercellular Communication**
- Hormones are secreted by glands or cells then they diffuse into the blood for circulation and bind to specific receptors on target cells elsewhere in the body
- If the target cell (which has the receptors) is far from hormone-secreting cell → **Endocrine**
- When the receptors are on cells nearby (very close) to the hormone-secreting cells→ **Paracrine**
- When the receptors are on the secreting cell itself → **Autocrine**
- When specialized neurons secrete chemicals (*neurohormones*) into the blood to a distant target cell → **Neuroendocrine**

**Sometimes the signal molecule is gas (ex- nitric oxide); it will permeate to all cells around; passing through the membrane; because membranes are highly permeable to gases.

**Cells that do not have receptors to a specific hormone cannot respond

- Hormones of the **endocrine system** usually affect the metabolism, growth and reproduction of the cell. On the other hand, **neurohormones** of the nervous system affect the contraction and relaxation of the muscle.



➢ To see the importance of the receptors ....

- A person with a (44 + XY) chromosome should be a male
- When we come on a female -at age of 18-20 years- with (44 + XY) chromosome, she looks like a lady from all aspects. Her parents thought that she is a girl from the start, they discover that there is abnormality after puberty because she does not have menstrual cycle (menstruation), by taking the genotype cells they discover the (44 + XY), this is called **Testicular Feminizing syndrome**.
- Reason: genetic *absence* of testosterone **receptor**, so there will be NO action for testosterone. Therefore, there will be no development for male sexual characteristics and this leads to a female. (phenotype=female , genotype=male) The hormone can be substituted, but we can`t substitute the receptors

- **Classes of Hormones:**

1) **Peptide and protein hormones**

- They differ in the amino acid chain (<100 amino acids → peptide , >100 amino acids →protein)
- They are water soluble hormones

2) **Steroid hormones**

- Derived from cholesterol
- They are lipid soluble hormone
- Examples: estrogen, progesterone, testosterone, cortisone and aldosterone

3) **Amine hormones**

- Derived from amino acids
- Could be lipid or water soluble
- Two kinds:

  → Thyroid hormones T3,T4 (tri-iodothyronine , tetra-iodothyronine, respectively.) and they are lipid soluble

  →Catechol hormones (ex. Epinephrine and norepinephrine) and they are water soluble

4) **Gas (ex. Nitric oxide NO)**

*** The difference between lipid soluble and water soluble hormones is in their receptors. Receptors for lipid soluble hormones are found inside the cell; either in the cytoplasm or in the nucleus. Whereas receptors for water soluble hormones are found on the target cell membrane.

Good luck :)

Done by: Bushra Maaqbeh