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CARDIAC ACTION POTENTIAL AND ELECTROLYTE DISTURBANCES : A JOURNEY INTO IONIC INTELLIGENCE

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OUTLINE

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Cardiac Action Potential and Electrolyte Disturbances : A Journey into ionic intelligence

A Narrative Review

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Intelligence is not measured by how much the brain knows, but in what way it tackles the situation to let the life run smoothly. An efficient intelligent approach dealing with the alarming situations makes the life to shine like a rainbow and one may exclaim with joy - WAH!.

The way the cardiac action potential writes the story of different electrolyte disturbances with reorientation of ionic choreography on its curve , one is amazed to see its intrinsic intelligence. There are two phases of cardiac action potential : depolarization and repolarization.

- ☐ **Depolarization primes the heart to be active for its ownward journey and it is dependent upon the availability of fast acting Na^+ channels (phase 0).**
- ☐ **The repolarization phase is concerned mainly with cardiac contractibility (plateau phase 2) and to bring the cardiac action potential again to its resting phase , passing through phases 3 and 4.**

The intelligent display of cardiac action potential with different electrolyte disturbances paves the way of understanding – how the situation is tackled as per ionic perturbances.

1. Introduction (Keypoints)

- Ionic chorography is the inner voice of heart , reflected as cardiac action potential with its different phases as sequential pauses. There are two main phases of cardiac action potential : depolarization and repolarization.
- The rhythmic beating of the human heart is sustained to life by the disciplined ionic display across the cardiac cellular membrane.
- Understanding how the cardiac action potential normally functions and how it becomes disorganized by ionic disturbances is essential to know. This is worthwhile to mention here that such disturbances in ionic choreography may be reflected on ECG as the earliest indicators of its coherence breaking.
- In nutshell , it would be wiser to keep in memory the concerned fundamental rule : **Electrolyte disturbances first determine whether the RMP (resting membrane potential , phase 0) is destablished (mainly K^+ impact) or not. Then the further journey in relation to ECG changes depends on which action potential phase 2 or 3 is primarily involved by the particular electrolyte ionic handling. Potassium disturbances affect phase 3 (potassium dependent) and calcium disturbances affect phase 2 (calcium dependent).**

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2. Electrophysiology of cardiac action potential under normal condition

The Cardiac Action Potential is a series of brief changes in voltage across the cardiac cell membrane, brought about by fluxes of ions through ion channels.

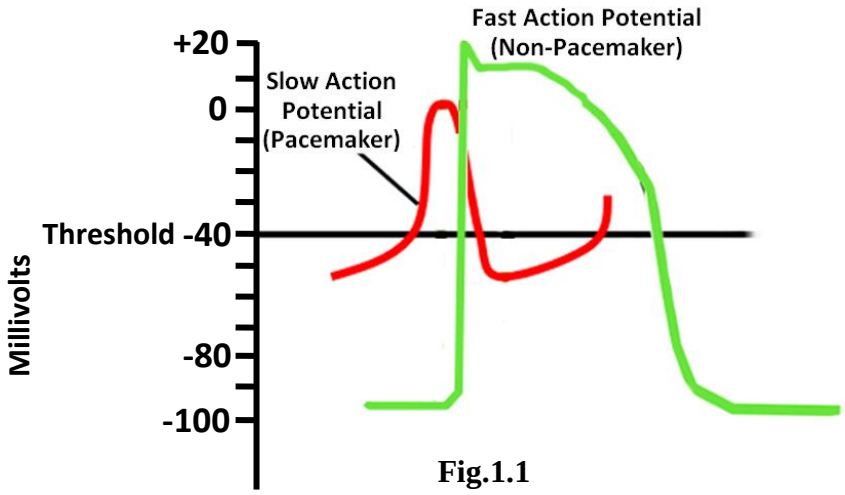

Fig.1.1

There are two sets of action potential :

- **Fast Action Potential** : This potential is seen in contractile cells (atria and ventricles) that are backed up by rapid depolarization due to the opening of fast **Na^+**channels. Since HIS bundle - purkinje system is connected to the ventricular myocytes , it also shares the fast action potential to allow the impulses to pass rapidly through it.

- **Slow Action Potential** : The SA and AV nodes , being rich in slow **Ca^{2+}** channels cause different ion channel kinetics. The initial potential of this nodal system is less negative compared to the RMP of the contractile units of myocytes. This lesser negativity allows the action potential to be automatically activated in a slowly rising semi-curve manner (SA node activation automatically) → AV node via atrial tissue with transient delay – 0.10 sec therein to facilitate the atrial empty into the ventricles.

The cardiac action potential gets operated through SA node with the spread of its impulses through intermediate steps to the ventricular myocytes, as stated below :

SA node → passing through atrial tissue → AV nodal delay (0.10 sec to empty the atrial contents into the ventricles) → HIS bundle-purkinje system →ventricular myocytes (in a well synchronized way).

It would be quite reasonable to mention first some facts related to slow action potential :

- The spontaneous depolarization of the slow pacemaker potential during its phase 4 imparts the SA node its auto-rhythmicity through Na^+ + K^+ channel , mainly Na^+ (through funny current – details here is not mentioned).
- The depolarization of SA/AV node is governed by increase in Ca^{++} conduction and the repolarization is caused by increase in K+ conductance
  (the details of this slow action potential is illustrated on the next page)

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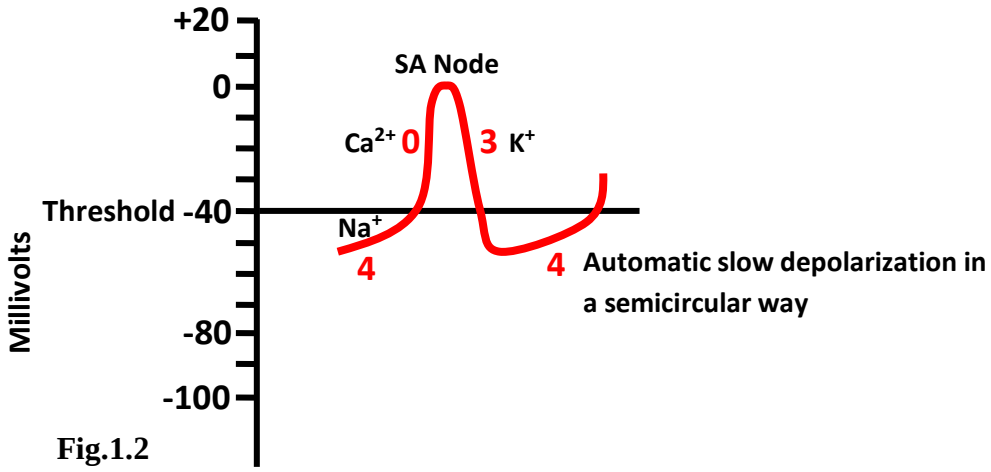
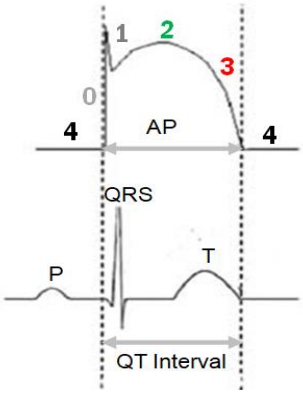


Fig.1.2

The next important consideration is to understand relevant steps in relation to fast action potential.

The phases of normal cardiac action potential are illustrated by the following sketch :



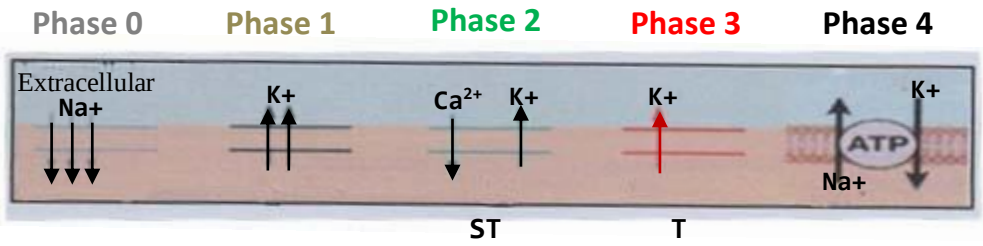


Fig.1.3

- ☐ The rapid inward flow of Na^+ during **Phase 0** , governed by negative resting potential at about -90 mV
- ☐ A brief outward flow of K^+ during **Phase 1**
- ☐ The inflow of Ca^{2+} with simultaneous outflow of K^+ during **Phase 2** (Plateau Phase) – concerned with ventricular contraction.
- ☐ Cessation of Ca^{2+} inflow followed by outflow of K^+ during **Phase 3**

And at the end there is restoration of resting phase (**Phase 4**) brought about mostly by Na^+-K^+ ATPase pump.

NB :

SA and AV Nodes operate at negative action potential (-60 to -70) while fast action potential curve operates through further more negative potential (-80 to -90). Atrial myocytes - HIS bundle-purkinje system – Ventricular myocytes complex constitutes the group of Fast Action potential.

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3. Ionic choreography perturbances dependent on resting membrane potential (RMP) : destabilised or stablished

- **Destablished RMP**
  With potassium ionic disturbances , potassium is the main determinant of RMP. Better to say it is the presence of K^+ions in extracellular compartment , which determines the status of RMP polarity. This RMP polarity is destablished in either hyperkalemia or hypokalemia.
  - **Hyperkalemia** : RMP becomes less negative (depolarized) →
    Na+ channels partially inactivated → slowed conduction (phase 0) with accelerated phase 3.
  - **Hypokalemia** : RMP becomes more negative (hyperpolarized) → conduction disturbed a bit , but repolarization delayed (phase 3).
- **Stablished RMP**
  Calcium does not significantly change the polarity of RMP
  - **Hypercalcaemia** : Shortens plateau phase (early inactivation of L-type calcium channels). In addition with severe hypercalcemia adaptive K^+ efflux may lead to heterogeneous prolongation of phase 3 → arrhythmias.
  - **Hypocalcaemia** : Prolongs plateau phase (sustained Ca^{++} influx)

4. Hyperkalemia and the corresponding ECG changes

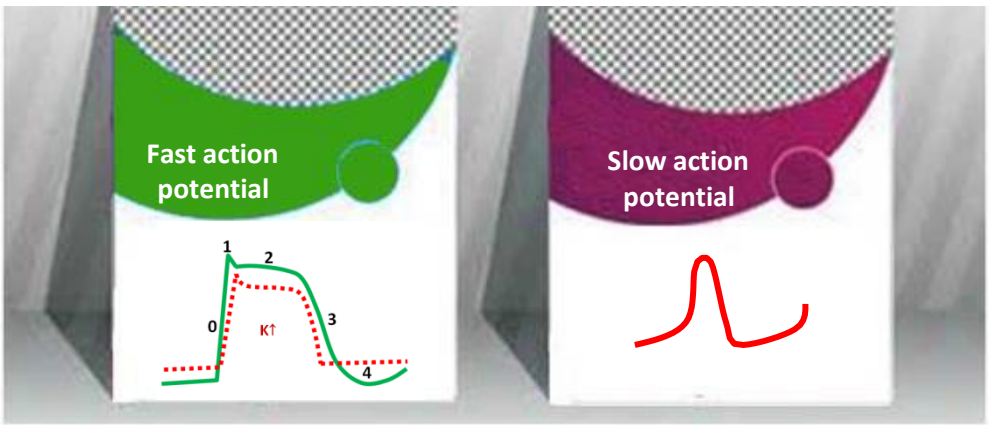

Fig.1.4

- Fast action potential is affected first
  RMP becomes less negative (depolarized) → Na^+ channels partially inactivated → slowed conduction (phase 0) with accelerated phase 3.
- SA and AV nodes are relatively spared in the initial stage :
  They use slow Ca^{++} channels which are less sensitive to early K^+ rise but they may be affected later , initially protected by their self-automaticity. Later on , excess K^+ in extracellular fluid reduces the initial automatic drive induced by Na^+ ions , that's why it causes impairment of these nodes either partially or completely.

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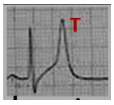
Fast Action Potential	Slow Action Potential
• In hyperkalemia → resting potential is less negative , with Na+ channels partly inactivated → the overall effect is smaller upstroke, shortened plateau, faster repolarization • Speeding up repolarization phase 2 and 3 → tall , peaked T-wave with shorter ST segment and QT interval.	• SA and AV nodes are less affected initially They use slow Ca^{++} channel , which are less sensitive to early K^{+} rise but they may be affected later , initially protected by their self automaticity • The overall effect is its flattened phase 4 slope , concerned with automaticity

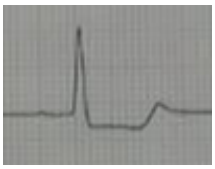
Sequential steps may be summarized as below :

❒ **T-Wave Changes & QT Shortening**

Extra potassium outside cells speeds up repolarization phase 2 and 3. This causes tall, peaked T-waves and shorter ST segment and QT interval 

❒ **Slowed Atrial Conduction**

Hyperkalemia makes atrial cells less negative, affecting fast Na+ channels first . Atrial myocytes depolarize earlier, but with slower and weaker conduction , ultimtately sweeping to atrial paralysis (flattened or low-amplitude P-wave with prolonged PR interval).



Flattened P-wave→Atrial standstill

❒ **Internodal Tracts Stay Functional Longer**

Though they use Na+ channels, they don't have automaticity , so they resist early effects of hyperkalemia.

❒ **SA & AV Nodes Are Less Affected Initially**

They use slow Ca++ channels, which are less sensitive to early K+ rise but they may be affected later , initially protected by their self automaticity.

❒ **Blockade**

Bundle branch block , AV block

❒ **Ventricular Conduction**

His–Purkinje and ventricles use fast Na+ channels

✓As extracellular potassium rises, it lays its heaviest hand on the most distal segments—be it the Purkinje arborization or the terminal ventricular myocytes.

This descending suppression paints a different electrophysiological spectrum , as illustrated below :

Secondary pacemaker capability of Purkinje fibres is suppressed → infranodal escape pacemaker is unreliable due to its downregulated conduction (either of bundle branches) → associated diffuse intraventricular conduction delay → sine wave → asystole (the pattern of sine wave is illustrated on the next page)

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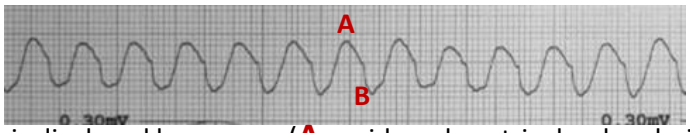

Classical sine wave is displayed here as up (**A** – widened ventricular depolarization phase) and down (**B** – widened ventricular repolarization phase) oscillation

5. Hypokalemia and the concerned ECG changes

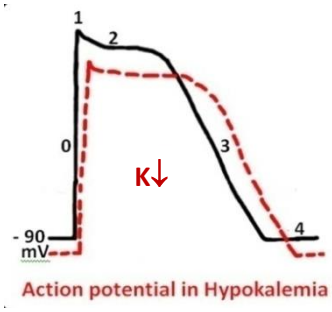

Fig.1.5

- RMP becomes more negative (hyperpolarized) → this increases the threshold for depolarization , it tends to slow its conduction a bit.
- Repolarization phase 3 is delayed

ECG changes are mainly attributed to delayed repolarization phase 3

Firstly the decreased T-wave amplitude , with the corresponding increase in U-wave amplitude (a progressive inverse relationship in between T and U wave morphology) , all these lead to a fusion of T with U resulting in pseudo prolongation of QT (QU) interval. The next immediate signature is ST segment depression.

NB :

U wave reflects delayed repolarization of the HIS-Purkinje system or mid-myocardial M-cells

Illustration of inverse relationship in between the T and U waves :

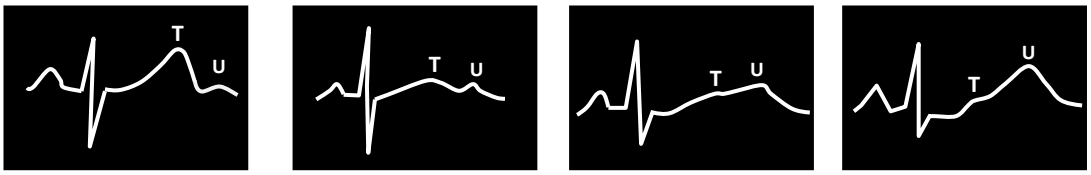

Fig.1.6

- The ECGs may show a characteristic "dip (T) and rise (U) pattern" reflecting these waveform perturbations.
  Hypomagnesaemia is often associated with hypokalemia , which may increase the risk of malignant ventricular arrhythmia.

6. Hypercalcaemia and related ECG changes

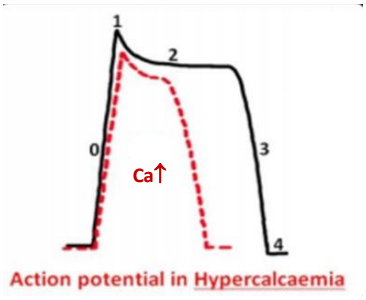

Fig.1.7

- Shortens plateau phase (early inactivation of L-type calcium channels).
- In addition with severe hypercalcemia adaptive K^+ efflux which may lead to heterogeneous prolongation of phase 3 → arrhythmias.

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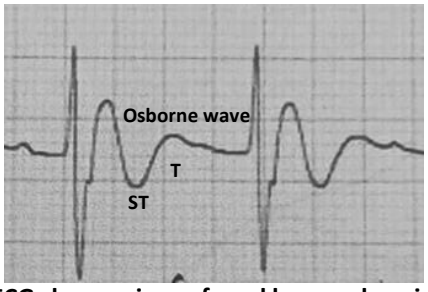
Corresponding ECG changes

It is worth mentioning at the outset that in hypercalcemia elevated calcium serum level accelerates the closure of the L-type calcium channels, effectively shortening the plateau phase (phase 2) of the cardiac action potential. Due to the adapted repolarization kinetics there is a potassium efflux during phase 3 resulting in changes in T-wave configuration. But in more profound cases there is more exaggerated J-point , witnessed as J-wave (Osborne wave) at the junction in between QRS and abbreviated ST segment.
Shortening of the plateau phase (phase 2) is reflected on ECG as abbreviated ST segment with shortening of the QT interval (shortening of ST segment may be to the extent that ST segment at times is hardly discernible),

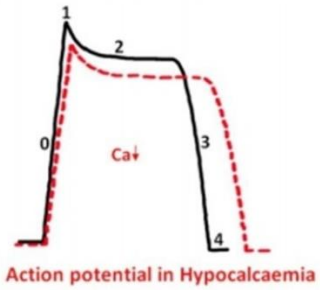


ECG changes in profound hypercalcemia

- Abbreviated ST segment
- Superimposed Osborne wave (at the junction between QRS and abbreviated ST segment)
- Widening of T-wave

Fig.1.8

7. Hypocalcalcemia and the corresponding ECG changes



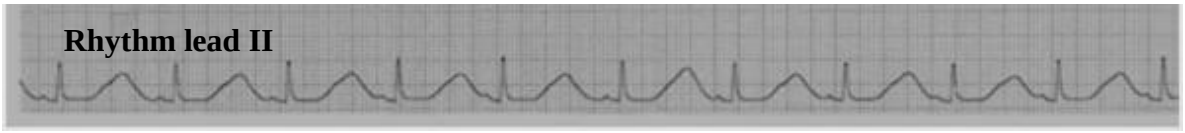
Action potential in Hypocalcaemia

- Prolongation of plateau phase (sustained Ca^{++} influx)
- With extended plateau phase there is no repolarization hetereogeneity during phase 3→ usually normal configuration of T-wave.
- The smooth run of plateau phase is having a stablizing anti-arrhythmic effect

Fig.1.9

Corresponding ECG changes

In collaboration with extended phase 3 , there is prolongation of ST segment , accompanied with QT prolongation.



This ECG tracing reveals marked QT prolongation with T-wave extending beyond the mid of corresponding RR interval , with smooth running of prolonged ST segment.

8. Take Home Message

- ☐ Ionic chorography is the inner voice of heart , reflected as cardiac action potential with its different phases as sequential pauses. There are two main phases of cardiac action potential : depolarization and repolarization.

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- Understanding how the cardiac action potential normally functions and how it becomes disorganized by ionic disturbances is essential to know. This is worthwhile to mention here that such disturbances in ionic choreography may be reflected on ECG as the earliest indicators of its coherence breaking.

- **Fundamental rule concerned with electrolyte disturbances**
  Electrolyte disturbances first determine whether the RMP (resting membrane potential , phase 0) is destablished (mainly K^+ impact) or not. Then the further journey in relation to ECG changes depends on which action potential phase 2 or 3 is primarily involved by the particular electrolyte ionic handling. Potassium disturbances affects phase 3 (potassium dependent) and calcium disturbances affect phase 2 (calcium dependent).

- **Ionic choreography perturbances dependent on resting membrane potential (RMP) : destablished or stablished**

  - **Destablished RMP**
    With potassium ionic disturbances , potassium is the main determinant of RMP. Better to say it is the presence of K^+ions in extracellular compartment , which determines the status of RMP polarity. This RMP polarity is destablished in either hyperkalemia or hypokalemia.
    - **Hyperkalemia** : RMP becomes less negative (depolarized) → Na+ channels partially inactivated → slowed conduction (phase 0) with accelerated phase 3.
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    - **Hypercalcaemia** : Shortens plateau phase (early inactivation of L-type calcium channels). In addition with severe hypercalcemia adaptive K^+ efflux may lead to heterogeneous prolongation of phase 3 → arrhythmias.
    - **Hypocalcaemia** : Prolongs plateau phase (sustained Ca^{++} influx)

- Some points with special reference to hyperkalemia
  - Fast action potential governed by fast Na+ channels is affected first
  - SA and AV nodes are relatively spared in initial stage :
    They use slow Ca^{++} channels which are less sensitive to early K^+ rise but they may be affected later , initially protected by their self-automaticity. Later on , excess K^+ in extracellular fluid reduces the initial automatic drive induced by Na^+ ions , that's why it causes impairment of these nodes either partially or completely.

- Concerned ECG changes have been well described with the corresponding ionic disturbances (see the preceding pages for details).

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