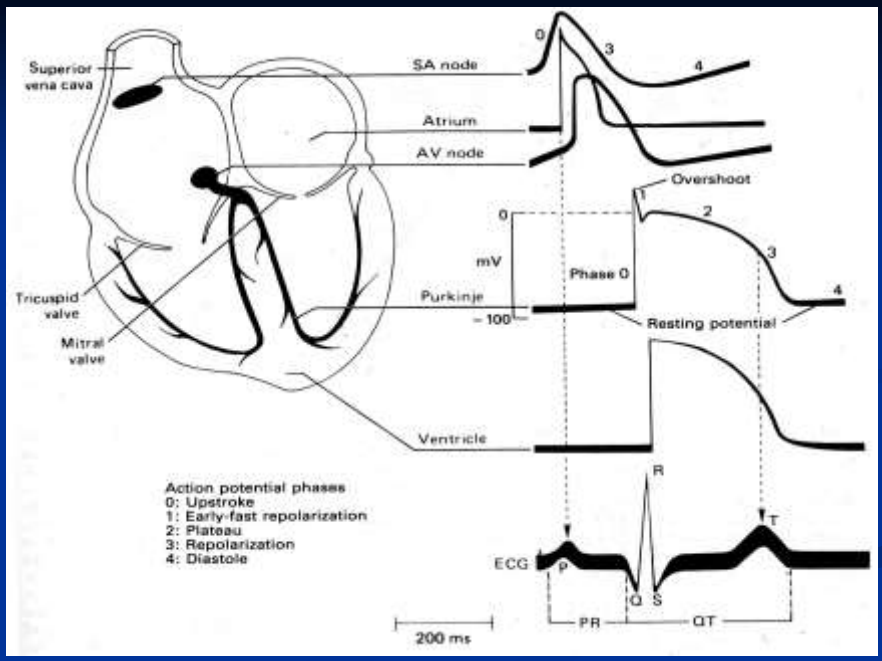
Early after-depolarization and arrythmias

presented by

Dr. Ayman Morttada
Ass.Prof.of cardiology- Ain Shams University

Mechanisms of arrhythmia

1. Re-entry.
2. Enhanced automaticity.
3. Triggered activity.



Triggered Activity

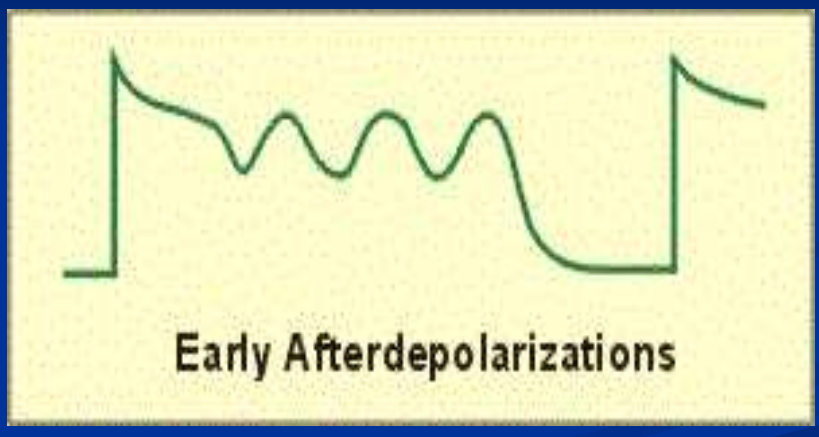
- Triggered activity occurs when abnormal action potentials are triggered by a preceding action potential, and can result in either atrial or ventricular tachyardia. The abnormal impulses are seen as spontaneous (yet triggered) depolarizations that occur during either phase 3 or 4 of an action potential (called "afterdepolarizations").

- Afterdepolarizations are oscillations of the transmembrane potential that depend on the preceding action potential (AP) for their generation and can give rise to new APs when they reach a critical threshold for activation of a depolarizing current. This form of abnormal impulse generation is called ‘triggered activity’

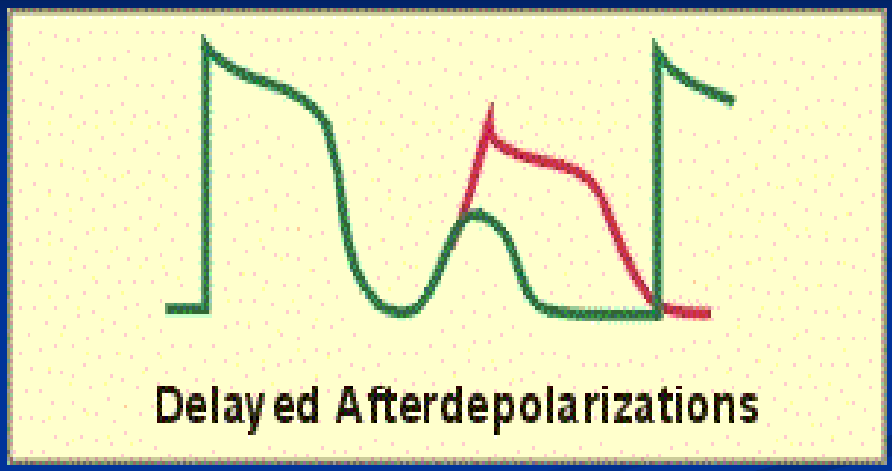
- Two types of afterdepolarizations have been distinguished: delayed (DADs) and early afterdepolarizations (EADs). DADs have been defined as "oscillations in membrane potential that occur after repolarization of an action potential"

- EADs are generated during the AP and have been defined as "oscillations at the plateau level of membrane potential or later during phase 3 of repolarization".
- Depending on the level of the membrane potential at which they are generated, EADs can trigger new APs that may appear as ectopic beats on the ECG.

- This form of triggered activity is more likely to occur when the action potential duration is increased. Therefore, drugs that decrease action potential duration (e.g., lidocaine) are often effective against tachyarrhythmias generated by this mechanism. Calcium channel blockers, by decreasing gCa^{++}, can also be effective in their treatment



- **Delayed afterdepolarizations** occur in late phase 3 or early phase 4 when the action potential is nearly or fully repolarized. The mechanism is poorly understood; however, this type of arrhythmia is found to be associated with high intracellular Ca^{++} concentrations as occurs with digitalis toxicity or excessive catecholamine stimulation. The triggered impulse can lead to a series of rapid depolarizations (i.e., a tachyarrhythmia).



- EADs can also augment electrical heterogeneity in regions of neighboring myocardium, which can lead to the formation of new APs via electrotonic interaction between areas that are still inexcitable and those that have already recovered from refractoriness.

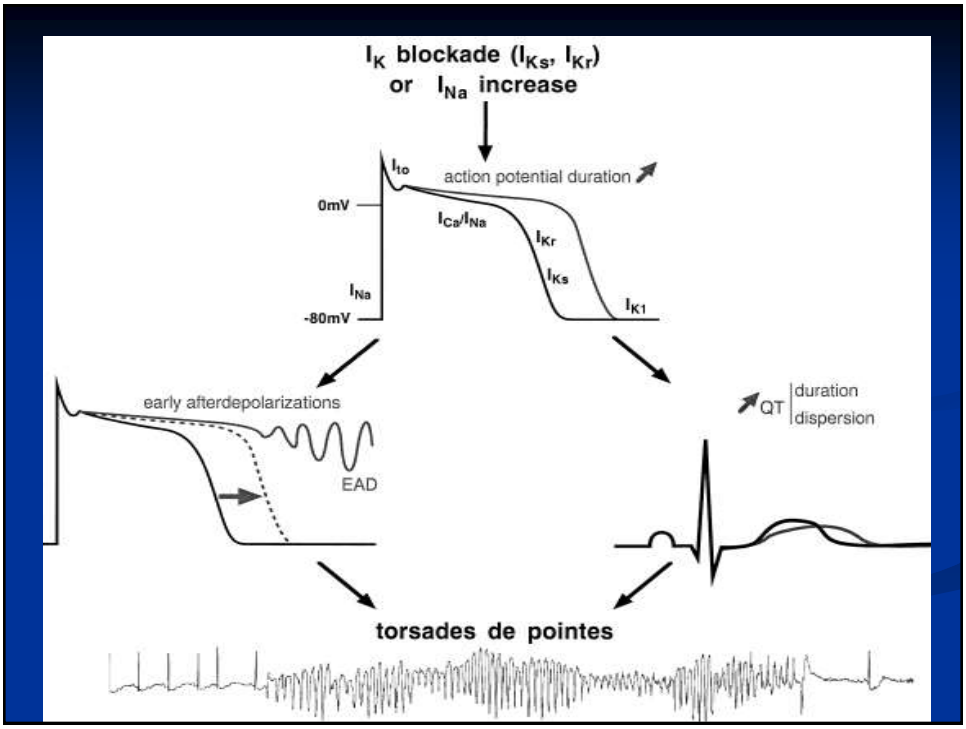
- The clinical significance of EADs lies in their capacity to provide both the trigger (premature ectopic beats) and the substrate (electrical heterogeneity with nonuniform repolarization and refractoriness) for the initiation and perpetuation of torsades de pointes.

- The appearance and mechanisms of EADs are diverse as they occur in various conditions. EADs present as transient retardations or reversals of the repolarization during phases 2 and 3 of the AP, often in the setting of AP prolongation

- Although the term 'early afterdepolarization' per se would not comprise a mere retardation of the repolarization, this is actually the priming event of the EAD formation, and must be incorporated into any theoretical mechanistic framework on EADs.

- At the ionic level, a decrease in outward current(s), an increase in inward current(s), or combinations of the two can unbalance the repolarization such that EADs arise.

- Due to the very complex dynamics and overlapping of transsarcolemmal ionic fluxes during the AP, the impact of individual current alterations on repolarization characteristics cannot easily be estimated. In the congenital long-QT syndromes, one can pinpoint single current defects as the primary event.



- **Mechanism: Increased intracellular Ca++ stimulates:**

1. Oscillatory release of Ca++ from the SR.
2. Na+Ca++ exchanger creates an inward cation current that contributes to DADs.

Long QT syndrome

- Definition: disorder in which the QT interval of the ECG is longer than normal.
- Correspond mainly to the plateau period of the ventricular action potential.

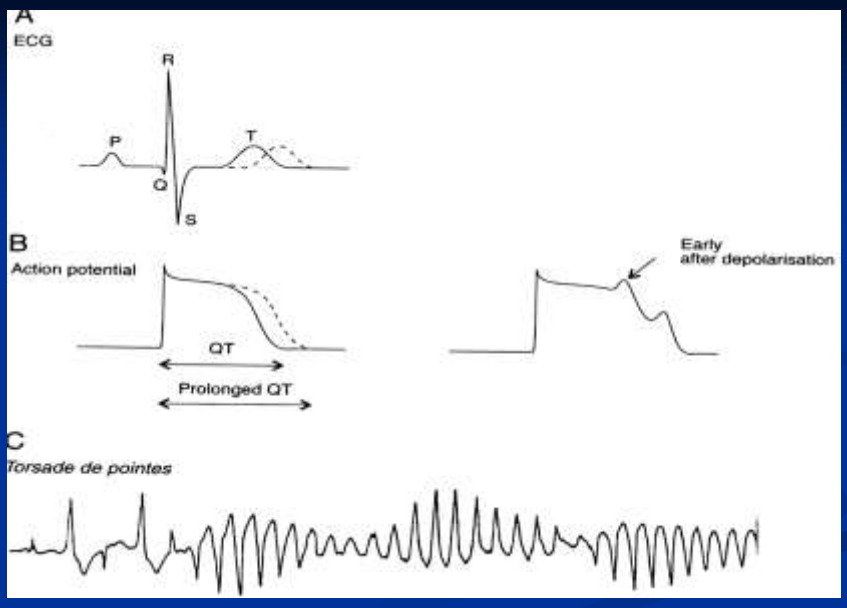
Long QT Syndrome

- Caused by:

1.Congenital:mutations that produce either a gain of function on sodium current (LQT3) : or calcium currents (LQT4) , or a loss of function on potassium (LQT1, LQT2, LQT5, LQT6 &LQT7)

2. Acquired: induced by some antiarrhythmic drugs, etc.

- longQTsyndrome: prolongation of the myocyte refractory period extends the vulnerable period during which extrastimuli can evoke tachycardia or fibrillation
- So,Patients with long Qt syndrome are predisposed to ventricular tachycardia called torsades de pointes.



Management

- All patients with long QT syndrome (LQTS) should avoid drugs that prolong the QT interval or that reduce their serum potassium or magnesium level. Potassium and magnesium deficiency should be corrected.

Management

- No participation in competitive sports for patients with the diagnosis established by means of genetic testing only
- Beta-blockers should be given to patients who have QTc-interval prolongation (>460 ms in women and >440 ms in men) and are recommended (class IIa) for patients with a normal QTc interval

- An implantable cardioverter-defibrillator (ICD) should be used in survivors of cardiac arrest and is recommended (class IIa) for patients with syncope while receiving beta-blockers; ICD therapy can be considered (class IIb) for primary prevention in patients with characteristics that suggest high risk (including LQT2, LQT3, and QTc interval >500 ms)

Questions


Thank You