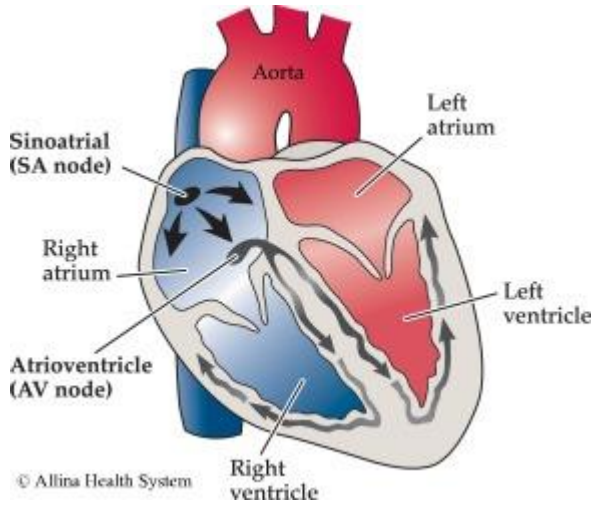
Arrhythmias

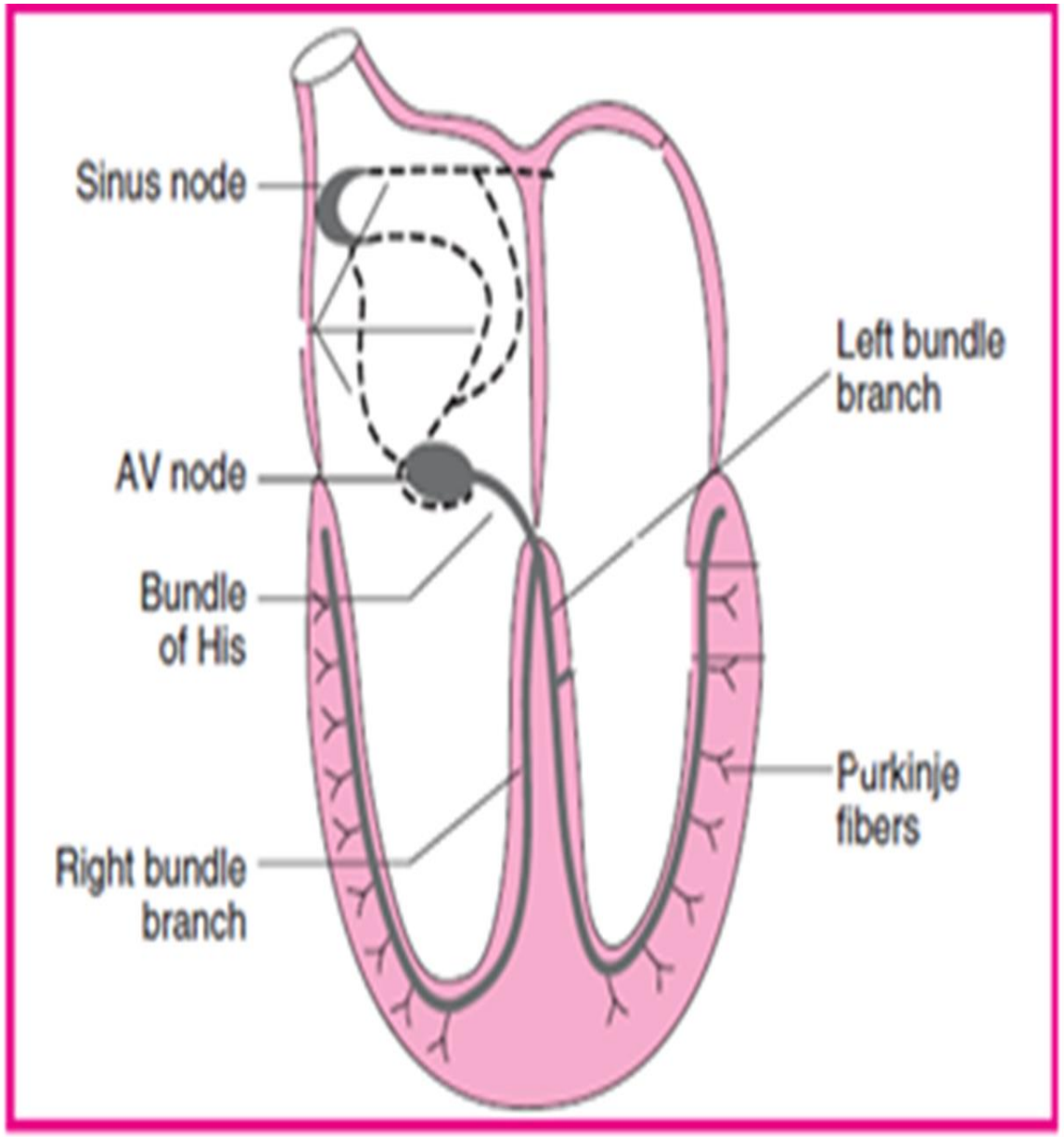
Dr. Muhannad R. M. Salih
B.Sc, M.Pharm (Clinical Pharmacy), Ph.D, RPH
Pharmacy Department, Al-Rasheed University College
muhanad_rmk@yahoo.com

Normal cardiac electrophysiology

- The normal cardiac rhythm, sinus rhythm, is characterized by contraction of first the atria and then the ventricles (systole) followed by relaxation (diastole) during which the heart refills with blood before the next cardiac cycle begins.

- This orderly sequence of contraction and relaxation is regulated by the **heart's electrical activity**.





The cardiac conduction system.

- The heart electrical activity governed by the following key structure:

I. **The sinoatrial (SA) node** located in the right atrium.

II. **The atrioventricular (AV) node** located between the right atria and ventricles.

III. **The bundle of His** it transmits the impulses from the atrioventricular node to the ventricles of the heart.

IV. **The Purkinje fibers** transmits the impulses throughout the ventricular tissue.

Normal cardiac conduction

- In the healthy heart the SA node acts as the **cardiac pacemaker**, generating electrical impulses which are then conducted via the atria to the ventricles, hence the term "sinus rhythm".

- The normal resting heart rate is approximately 70 beats per minute and is maintained by electrical impulses arising from within the SA node.

Etiology

- Arrhythmias result from abnormal **impulse formation** or abnormal **impulse conduction** and these changes may be brought about in several ways.

1. **An infarction** may cause the death of pacemaker cells or conducting tissue.
2. **A cardiac tissue disorder**, e.g. fibrosis or rheumatic fever, disrupts the conduction network.
3. **Sympathetic** or **parasympathetic control changes**, e.g. stress, anxiety, exercise or smoking.
4. **Circulating drugs**, e.g. antiarrhythmic or inotropes or other substances, e.g. caffeine, or alcohol.
5. **Hypothyroidism, hyperthyroidism, hyperkalaemia and hypokalemia** or other electrolyte disturbances may predispose the heart to arrhythmias.

Etiology

- Patients who have pre-existing cardiac disorders including:
  - **heart failure**
  - **hypertension**
  - **a recent infarction**

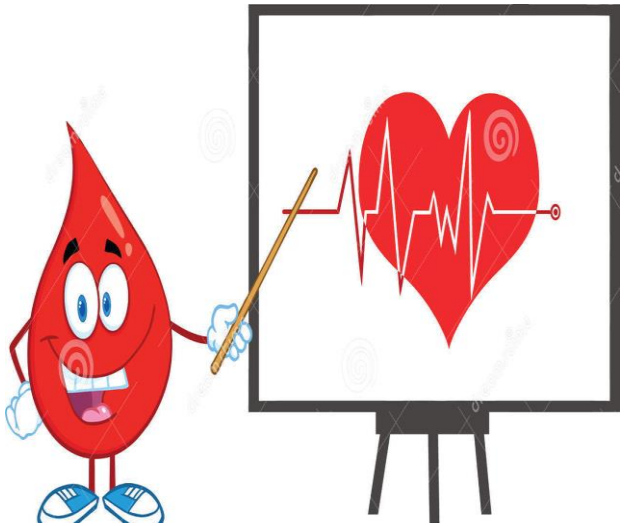
are at greater risk of arrhythmias

Pathogenesis of arrhythmias

- Arrhythmias develop by one of two mechanisms:

1. **Altered impulse generation**, for example, changes in ability of the pacemaker cells in the SA node to generate electrical impulses spontaneously.

2. **Altered impulse conduction**, for example, complete or partial block of conduction pathways within the myocardium.



Classification of arrhythmias

1. **Supraventricular arrhythmias:** occur in the area above the ventricles, usually in the upper chambers of the heart "atria"

2. **Ventricular arrhythmias:** occur in the lower chambers of the heart "ventricles".

- An alternative method of classifying arrhythmias is based on the heart rate:
  - **Bradyarrhythmia** (<60 beats/minute)
  - **Tachyarrhythmia** (>100 beats/minute)

Signs and consequences of arrhythmias

- In general, arrhythmias are associated with increased morbidity and mortality.

- Atrial fibrillation (AF) roughly:
  - **doubles** risk of a person having a **stroke**
  - **triples** the risk of person having a **heart failure**

- Bradycardias low cardiac output symptoms:
  - **fatigue**
  - **lightheadedness**
  - **syncope** (syncope: is a sudden loss of consciousness due to reduced cerebral perfusion).

Signs and consequences of arrhythmias

- Tachycardias cause
  - **rapid palpitation**
  - **dizziness**
  - **chest discomfort**
- Extreme tachycardias can cause **syncope** because the heart is unable to contract or relax properly at extreme rates.
- Extreme bradycardias or tachycardias can precipitate **sudden death** or **cardiac arrest**
- Palpitation is a noticeably rapid, strong, or irregular heartbeat due to agitation, exertion, or illness.

Signs and consequences of arrhythmias

Since these signs are not unique to arrhythmias, arrhythmias are not always easy to diagnose and 24-hour recordings of the ECG (Holter monitoring) may be required.

Diagnosis

- A detailed history should be obtained, covering all of the symptoms listed earlier.
- A history of cardiac disease.
- Other diagnosed medical conditions.
- A full drug history, including over-the-counter medicines and recreational drugs including alcohol.
- A family history of heart disease and of sudden unexpected death.
- Physical examination is essential but often normal between episodes of arrhythmia.

Diagnosis

- Mandatory investigation includes
  - **ECG**
  - **24-hour recordings of the ECG (Holter monitoring)** may be needed up to 7 days at a time if the symptoms occur frequently or some times for 1 to 2 days.
  - **echocardiogram** to detect structural heart disease

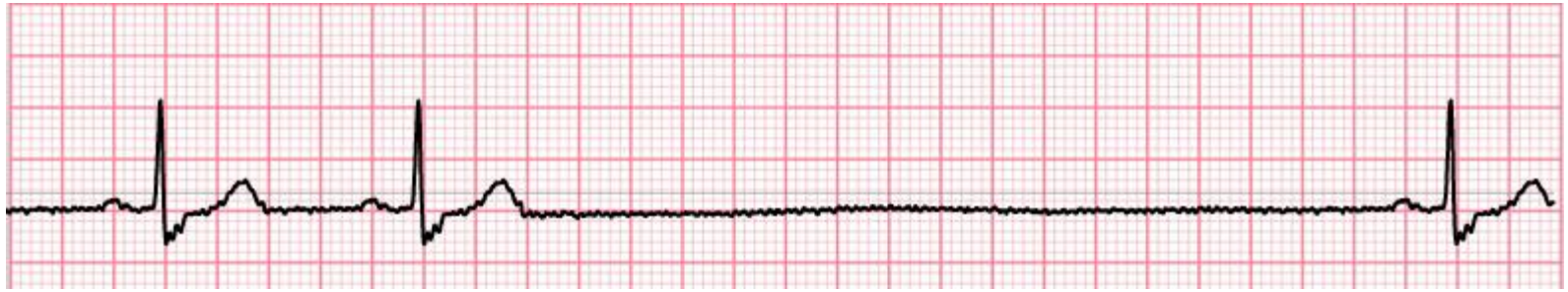
- If the history does not include threatening features such as syncope or a family history of sudden unexpected death at a young age, and the ECG and echocardiogram are normal, then the patient can be reassured that they are extremely unlikely to have a serious heart rhythm disturbance.

Bradycardia

- A heart rate of less than **60 beats per minute** is considered a bradycardia.
- If the heart rate slows but the rhythm remains unchanged this is known as **sinus bradycardia** (i.e., is still controlled by impulses generated in the SA node)
- It can be entirely normal, for example in athletes or during sleep, but it may also occur secondary to
  - **acute myocardial infarction**
  - **sick sinus syndrome** (malfunction of the sinus node)
  - **drug therapy, particularly beta-blockers**
- In this case **sinus bradycardia** is due to a reduction in the frequency of impulse generation within the nodal pacemaker cells (**reduced automaticity**).

Bradycardia

- **Sinus arrest** is another type of bradycardia that the node completely fails to generate an action potential. It is lasting from 2.0 seconds to several minutes



Heart block

- Bradycardias can be caused by **heart block**.
- **AV node block** is the most commonly identified cause of heart block in clinical practice.
- In this situation, the electrical impulse generated by the SA node travels across the atria but is blocked at the level of the AV node before it can be conducted to the ventricles.

AV block

- AV block may be classified into three types.

1. **First degree AV block:** there are **no missed beats**. Every atrial impulse is transmitted to the ventricles, resulting in a regular ventricular rate but with **some delay**. This does not require treatment but may be a warning to avoid drugs that would worsen the block, such as β-blockers and class IV agents (verapamil, diltiazem).
2. **Second degree AV block:** is characterized by disturbance, delay, or interruption of atrial impulse conduction through the AV node to the ventricles. Although patients with second-degree AV block may be asymptomatic, they may experience some significant symptoms and **may progress to complete heart block, with an associated increased risk of mortality**.

AV block

3. **Third degree AV block**, or complete heart block, is a disorder of the cardiac conduction system where there is no conduction through the atrioventricular node.

Tachycardias

- A heart rate of more than 100 beats per minute is considered a tachycardia.
- They can be divided into: Supra-ventricular arrhythmias and Ventricular arrhythmias.

Supra-ventricular arrhythmias

1. **Sinus tachycardia** occurs if the heart rate increases but the rhythm remains unchanged. It is usually due to an increase in **sympathetic activity.**

- **Sinus tachycardia** is common during
  - **exercise or excitation**
  - **Infection**
  - **Hypovolemia**
  - **Anemia**
  - **Thyrotoxicosis**
  - **Shock**
  - **side effect of many drugs, such as beta-2 agonists, thyroxin and aminophylline**

Supra-ventricular arrhythmias

2. **Inappropriate sinus tachycardia** is a syndrome in which the sinus heart rate **is strangely faster than expected**. The heart rate at rest, even in a supine position, can exceed 100 beats/min; minimal activity accelerates the rate rapidly and substantially.

Supra-ventricular arrhythmias

3. **Atrial ectopic beats** These usually cause **no symptoms** but can give the sensation of a missed beat or an abnormally strong beat.

- In most cases these are of no consequence. Treatment is rarely necessary.

Supra-ventricular arrhythmias

4. **Atrial flutter** occurs less frequently than atrial fibrillation (AF).

- The **atrial rate** is approximately **300/min**.

- The resulting **ventricular rate is usually regular**, but **slower** than the atrial rate as the AV nodal prevents these rapid atrial impulses from being conducted to the ventricles.

- The **rapid atrial rate** and **disturbance of conduction pathways** in atrial flutter increases the risk of **localized thrombus formation** and secondary embolic events (i.e., **thrombotic stroke**) in this group of patients.

Supra-ventricular arrhythmias

5. **Atrial fibrillation (AF)** is one of the most common arrhythmias and it is a major cause of morbidity and mortality.

- Atrial fibrillation incidence increases with
  - **age**
  - **hypertension**
  - **coronary artery disease**
  - **heart failure**
  - **hyperthyroidism**
  - **high alcohol consumption**

- Atrial rates of between **350** and **600 beats** per **minute** result.

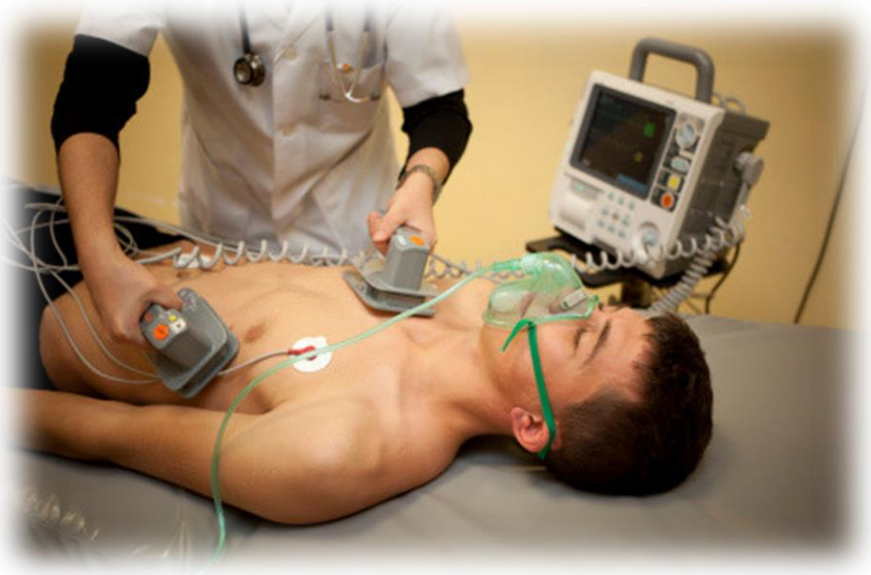
- The ventricular rate is usually **rapid** (around 100-180 beats per minute) and **irregular**.

Supra-ventricular arrhythmias

- In general, when compared with **Atrial Flutter**, **AF** is associated with
  - **higher atrial rates**
  - **irregular ventricular rhythm**
- The condition is not acutely life threatening but failure of coordinated atrial contraction results in stasis of blood within the atria.
- This can lead to the formation of local thrombi. As a result, one of the most important complications of AF is the increased risk of thromboembolic stroke.

Supra-ventricular arrhythmias

- The risk of stroke increases after restoration of normal sinus rhythm (by **drugs** or by **direct current cardioversion (DCC)** which allows more efficient cardiac contractility and expulsion of the thrombus.



Ventricular arrhythmias

1. **Ventricular ectopic beats** Ectopic beats produce a low stroke volume because **left ventricular contraction occurs before filling is complete**. The pulse is therefore irregular, with weak or missed beats.

- Patients are usually asymptomatic but may complain of an irregular heartbeat, missed beats, or abnormally strong beats (due to the **increased output** of the **post-ectopic beat**).

Ventricular arrhythmias

- The significance of ventricular ectopic beats depends on the **presence** or **absence** of underlying heart disease.

A. **Ventricular ectopic beats in healthy subjects:** Treatment is not necessary unless the patient is highly symptomatic, in which case ß-blockers can be used.

B. **Ventricular ectopic beats associated with heart disease:** (e.g. recent MI or heart failure): Treatment is usually needed.

Ventricular arrhythmias

2. Ventricular tachycardias (VT)

- Ventricular tachycardia is defined as three or more consecutive ventricular ectopic beats.
- Ventricular tachycardia is defined as **non-sustained** if it lasts less than 30 seconds and terminates spontaneously.
- **Sustained VT** lasts greater than 30 seconds and does not terminate spontaneously, but rather requires therapeutic intervention for termination.
- Ventricular rates during episodes of VT vary from **120-250 beats per minute.**

Ventricular arrhythmias

- **Torsades de pointes** is a specific form of VT that is occur mostly secondary to drug therapy, particularly
  - ***antiarrhythmic***
  - ***erythromycin***
  - ***clarithromycin***
  - ***antidepressants particularly tricyclic***

- Torsades de pointes can rapidly degenerate into **ventricular fibrillation** and must therefore be treated as a medical emergency.

Ventricular arrhythmias

3. **Ventricular fibrillation** is a **rapid** and **uncoordinated** contraction of the ventricular tissue. It severely compromises cardiac output (resulting in **no cardiac output**) to the extent that patients usually lose consciousness within 10-20 seconds of onset.

- It is responsible for **most deaths** caused by **myocardial infarction** and there is high risk of ventricular fibrillation in patients with **severe ischemic heart disease**.

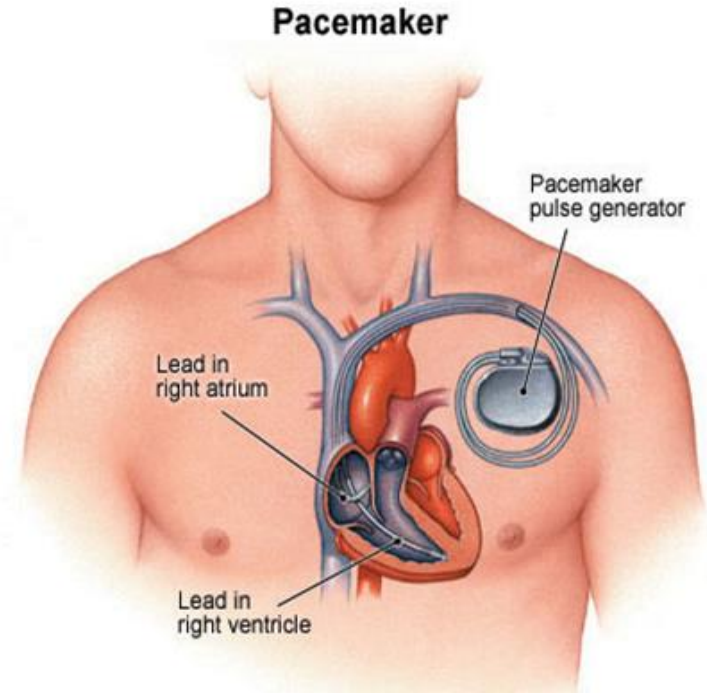
- Ventricular fibrillation is a medical emergency, because without prompt treatment **irreversible cerebral** and **myocardial damage will occur.**

Management

Non-pharmacological Treatment

1. **Non-pharmacological therapy of bradyarrhythmia: cardiac pacemakers**

- Artificial cardiac pacemakers are devices that deliver a small electrical impulse to a localized region of the heart, thus initiating an action potential that spreads to the remainder of the heart.



Non-pharmacological Treatment

- These devices can be used **temporarily** to treat a transient bradyarrhythmia resulting from a **reversible cause** or can be implanted **permanently** to treat **irreversible disorders** of impulse formation or conduction that result in recurrent or persistent bradyarrhythmia.

Non-pharmacological Treatment

2. Non-pharmacological therapy of tachyarrhythmia

A. Direct current cardioversion (DCC) and defibrillation

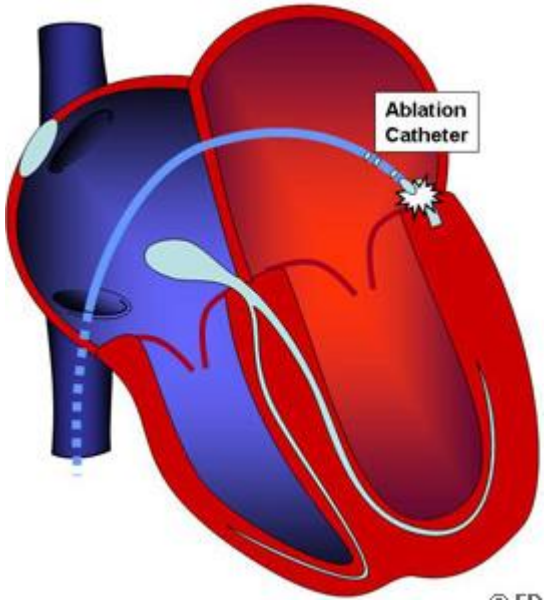
- Cardioversion refers to the process of restoring the heart's normal rhythm. This can be done chemically using drugs (chemical or pharmacological cardioversion) or by application of an electric shock across the chest (electrical cardioversion). This involves the delivery of a low voltage shock to the heart through the chest wall (e.g., using paddles). The aim is to disturb the abnormal electrical conduction pathways in order to convert an arrhythmia to sinus rhythm.

Non-pharmacological Treatment

B. Radiofrequency ablation

- Radiofrequency energy is used in heart tissue to **destroy abnormal electrical pathways** that are contributing to a cardiac arrhythmia.

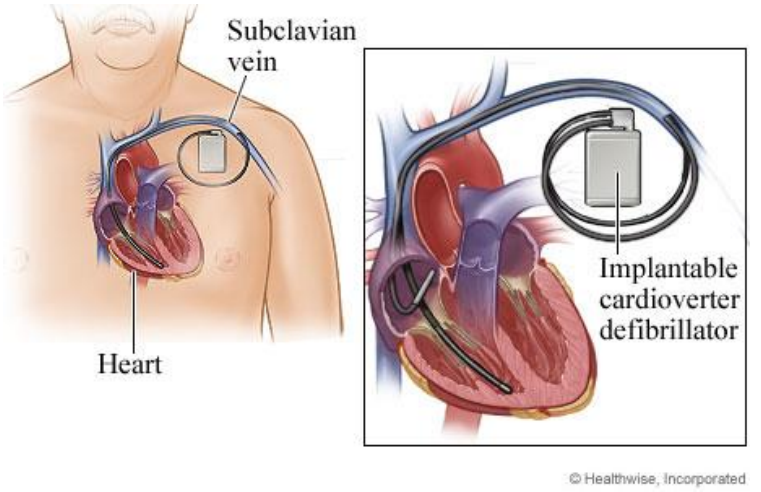
- The energy-emitting probe (**electrode**) is at the **tip of a catheter** which is placed into the heart, usually through a vein. This catheter is called the **ablator**. The procedure has a high success rate and patients can return to normal activities in a few days.



Non-pharmacological Treatment

C. Implantable cardioverter defibrillator (ICD)

- It is a small device that's placed in the chest or abdomen. The ICD is the first-line treatment and prophylactic therapy for patients at risk for sudden cardiac death due to **ventricular fibrillation** and **ventricular tachycardia**.



Pharmacological therapy

Classification of antiarrhythmic drugs

Vaughn Williams classification

- It is the most frequently used classification system, which categorizes these drugs on the basis of their **in vitro electrophysiological effect on normal Purkinje fibers**.

Class	Mechanism	Example
Class I	Na-channel blockers	Quinidine, procainamide, lidocaine, flecainide, phenytoin, propafenone
Class II	β-blockers	Propranolol, metoprolol
class III	K-channel blockers	Sotalol, amiodarone
class IV	Ca-channel blockers	Verapamil, diltiazem

Pharmacological therapy

Bradycardia

- Patients with sinus bradycardia due to underlying correctable disorders (**electrolyte abnormalities** or **hypothyroidism**), management consists of correcting those disorders.

- Treatment of sinus bradycardia is **only necessary** in patients who become **symptomatic**.

- If the patient is taking any medication(s) that may cause sinus bradycardia, the drug(s) should be discontinued whenever possible.

- In certain circumstances, discontinuation of the medication(s) may be undesirable. In these patients, a **permanent pacemaker** may be implanted in order to allow the patient to maintain therapy with **β-blockers**.

Pharmacological therapy

- Acute treatment of the symptomatic patient consists **primarily** of administration of the **anticholinergic drug**
  - **Atropine 0.5 mg intravenously (IV) every 3 to 5 minutes.**

- The maximum recommended total dose of atropine is 3 mg.

Pharmacological therapy

- In patients with
  - hemodynamically unstable (i.e., unstable blood pressure)
  - severely symptomatic sinus bradycardia

that is unresponsive to **atropine** and in whom **temporary pacing** is not available or is ineffective, **epinephrine** or **dopamine infusion** may be administered to increase heart rate.

- Long-term management of patients with **sick sinus syndrome** requires implantation of a **permanent pacemaker**.

Pharmacological therapy

AV-Block

- Treatment of **first-degree AV** nodal blockade is rarely necessary, because symptoms rarely occur.

- **Second** or **third-degree AV** nodal blockade requires treatment, because bradycardia usually results in symptoms.

A. In patients with second- or third-degree AV block due to underlying correctable disorders (such as **electrolyte abnormalities** or **hypothyroidism**), management consists of correcting those disorders.

B. If the patient is taking any **medication(s)** that may cause AV nodal blockade, the drug(s) should be discontinued whenever possible. However, in certain circumstances, discontinuation of a medication may be undesirable. In these patients, a **permanent pacemaker** may be implanted in order to allow the patient to maintain therapy with **β-blockers**.

Pharmacological therapy

C. **Acute treatment** of patients with second- or third-degree AV nodal blockade consists primarily of administration of **atropine**.

D. In patients with **hemodynamically unstable or severely symptomatic** AV nodal blockade that is unresponsive to atropine and in whom **temporary pacing is not available** or is ineffective, **epinephrine** or **dopamine** infusion may be administered.

E. **Long-term management** of patients with AV nodal blockade due to idiopathic degeneration of the AV node requires implantation of a permanent pacemaker.

Pharmacological therapy

Tachycardias

A. Sinus tachycardia

- In most cases, sinus tachycardia can be addressed by treating the underlying cause, for example,
  - using antibiotics to treat infections
  - fluid replacement to correct hypotension and hypovolemia
  - beta-blockers and anti-thyroid agents to manage thyrotoxicosis

- Management of Inappropriate Sinus Tachycardia relies on the use of rate-controlling agents such as beta-blockers or calcium channel blockers. In some cases, radiofrequency ablation may be necessary to modify the sinus node activity.

Pharmacological therapy

B. Atrial ectopic beats

- These usually cause no symptoms but can give the sensation of a missed beat or an abnormally strong beat.
- Treatment is rarely necessary other than treatment of the underlying disease or avoidance of precipitants.
- Symptomatic cases usually produce palpitations or the sensation of missed beats and can usually be controlled with β-blockers.

Pharmacological therapy

C. Atrial fibrillation (AF)

i. Hemodynamically unstable AF

- Patients with shock or severe hypotension, pulmonary edema, or ongoing myocardial infarction or ischemia, emergent conversion to sinus rhythm is necessary using direct current cardioversion (DCC).

- There is a potential risk of thromboembolism in patients undergoing cardioversion who have not received anticoagulation therapy if atrial fibrillation has been present for > 48 hours; however, in hemodynamically unstable patients the need for immediate rate control outweighs that risk.

Pharmacological therapy

i. **Hemodynamically stable AF patient**

Rate Control → Versus ← **Rhythm Control**

- **Ventricular Rate Control** drugs that are effective for ventricular rate control are those that inhibit AV nodal impulse conduction:
  - Class II (β-blockers)
  - Class IV (diltiazem, verapamil) and digoxin.

- **Rhythm Control** (Restoration of sinus rhythm) can be achieved with DCC or with antiarrhythmic agents (type I, and III agents). DCC is generally more effective than drug therapy for conversion to sinus rhythm.

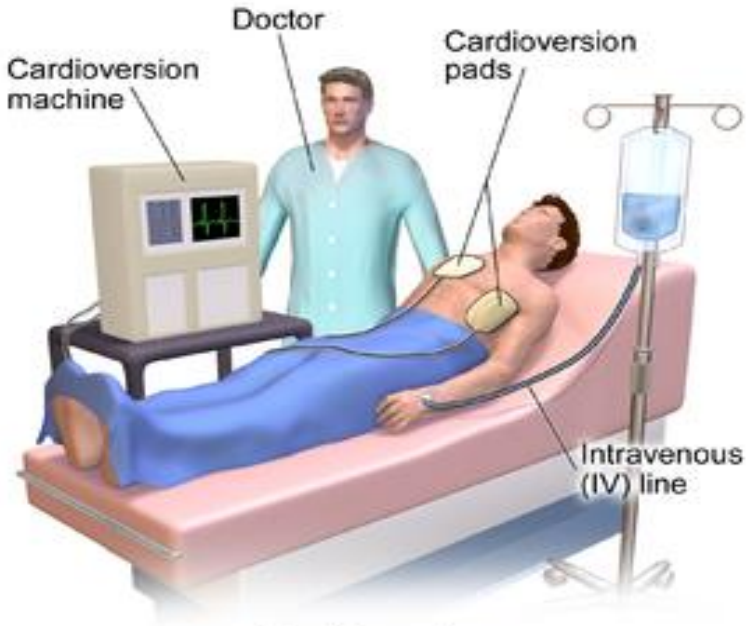
Pharmacological therapy

Treatment strategy for most patients should be a rate control strategy. However, rhythm control is necessary when patients experience symptoms despite adequate rate control

Conversion to normal sinus rhythm

- The cardioversion decision strategy depends greatly on the **duration of AF**.

- If the **AF is less than 48 hours in duration**, then the likelihood of atrial clot formation is low and conversion to sinus rhythm is safe and may be attempted with DCC or specific drug therapy.

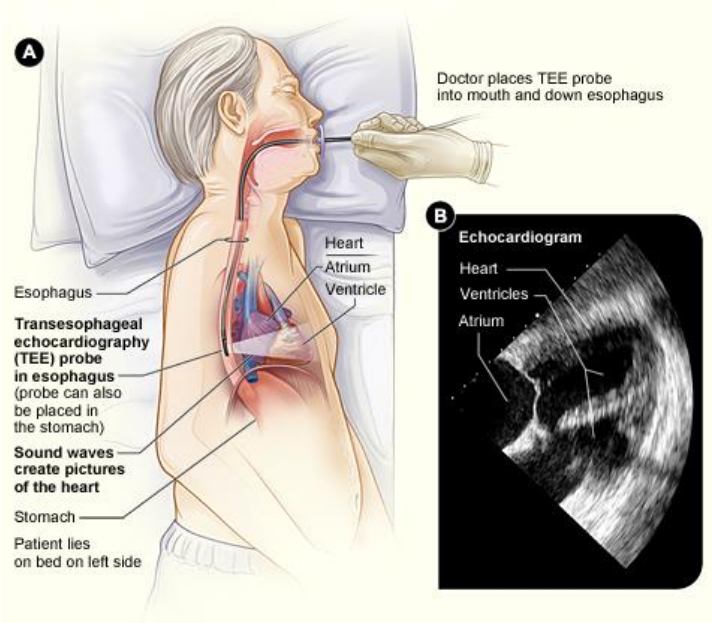


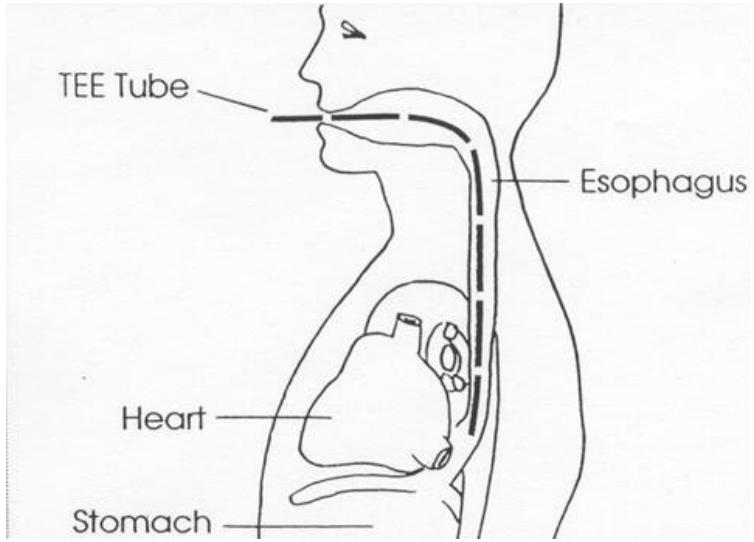
Cardioversion

Conversion to normal sinus rhythm

- However, if the duration of the **AF episode is longer than 48 hours** or if there is uncertainty regarding the duration of the episode, the following strategy for conversion may be considered:

- a **transesophageal echocardiogram (TEE)** can be used to determine whether atrial clots have formed. If no clot is observed on TEE, then there is low risk for stroke with cardioversion of AF.

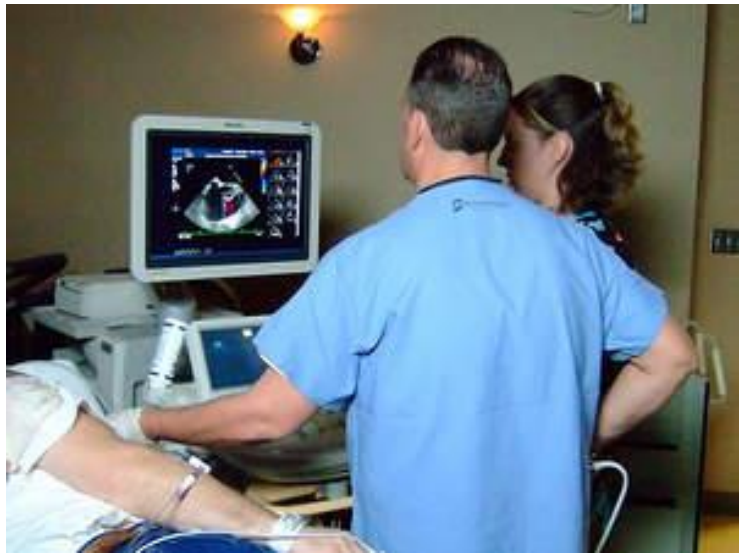




Conversion to normal sinus rhythm

- However, if an **atrial clot is evident on TEE**, the patient need to be adequately **anticoagulated for 3 weeks** before cardioversion to prevent embolization of the clot and stroke.

- Patients should remain on **warfarin for at least 4 weeks after cardioversion** because normal atrial contraction may not return for up to 3 weeks.

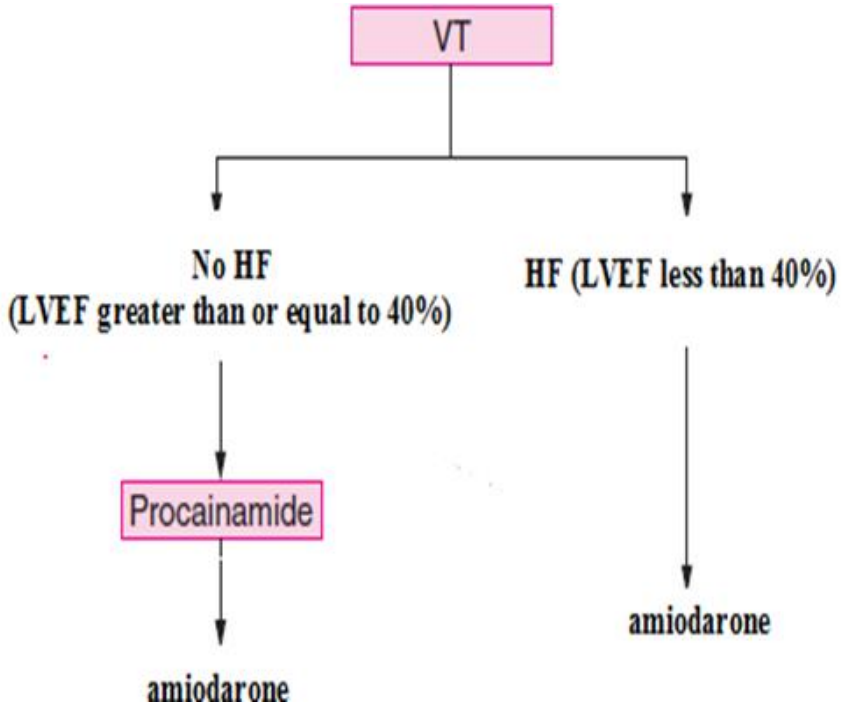


Pharmacological therapy

D. **Ventricular tachycardia**

i. **Hemodynamically unstable VT** should be terminated immediately using direct current cardioversion (DCC).

ii. A decision algorithm for management of **Hemodynamically stable** VT is presented below



Pharmacological therapy

- Procainamide is considered the first-line agent for management of VT in patients with normal left ventricular function, amiodarone may be used for refractory cases.

- However, in patients with heart failure due to left ventricular dysfunction, **procainamide should be avoided, due to negative inotropic activity**.

- If VT is associated with a transient initiating factor (e.g., acute myocardial ischemia, digitalis toxicity), there is no need for long-term antiarrhythmic therapy after precipitating factors are corrected.

- Patients with **chronic recurrent sustained VT** are at extremely high risk for death. The ICD is a highly effective method for preventing sudden death due to recurrent VT or ventricular fibrillation .

Pharmacological therapy

E. Torsade de Pointes

- Management of drug-induced Torsades de pointes includes **discontinuation of the potentially causative agent**.

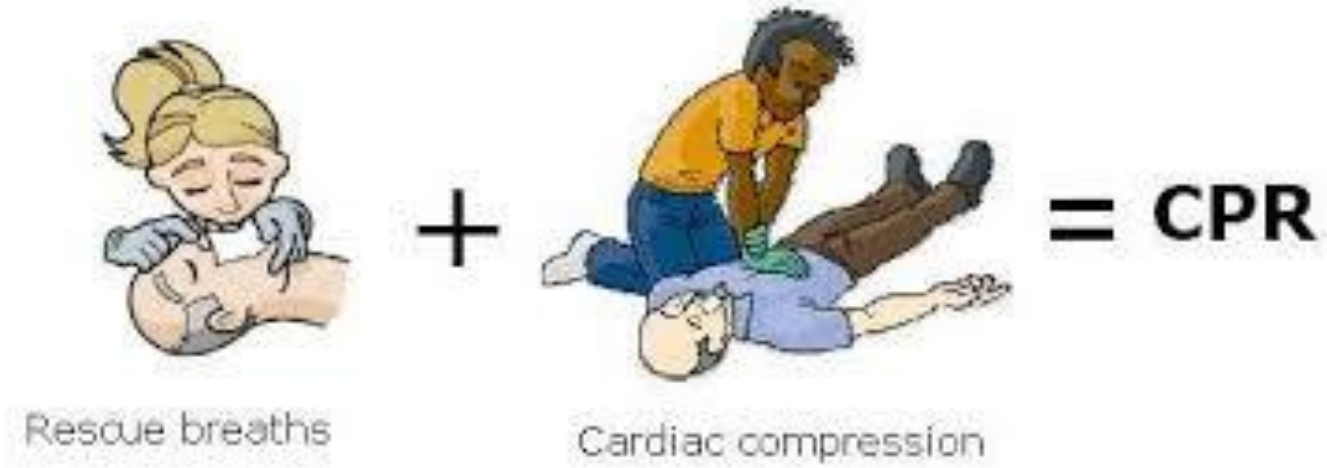
- Patients with **hemodynamically unstable** Torsades de pointes should undergo immediate DCC.

- **Hemodynamically stable** Torsades de pointes is often treated with I.V magnesium, irrespective of whether the patient is hypomagnesemic; magnesium has been shown to terminate Torsades de pointes in normo-magnesemic patients.

Pharmacological therapy

F. Ventricular fibrillation

- Due to the absence of pulse and blood pressure, ventricular fibrillation is considered a hemodynamically unstable state.
- Initial management includes providing of the basic life support, including calling for help and initiation of cardiopulmonary resuscitation (CPR).



Pharmacological therapy

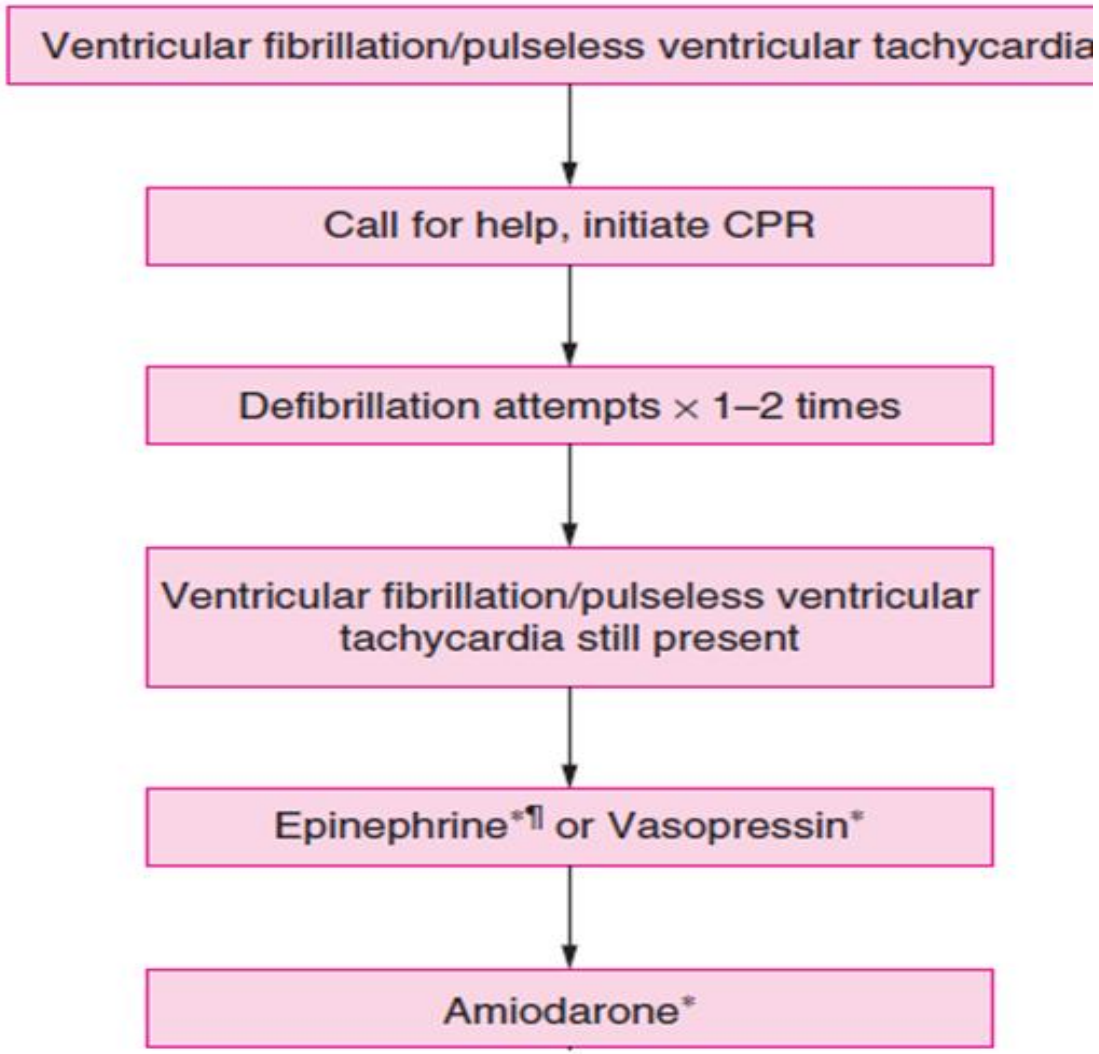
- Oxygen should be administered as soon as it is available.
- The only means of successfully terminating VF and restoring sinus rhythm is **electrical defibrillation (DCC)**.
- If **VF persists** following **one or two defibrillation shocks**, drug therapy may be administered.
- The purpose of drug administration for treatment of VF is to facilitate successful defibrillation. Drug therapy alone will not result in termination of VF.
- A defibrillation attempt should be made after every dose of drug.

Pharmacological therapy

- The vasopressor agents epinephrine or vasopressin are administered initially, because it has been shown that a critical factor in successful defibrillation is maintenance of coronary perfusion pressure, which is achieved via the vasoconstriction effects of these drugs.

Drug	Dose
Epinephrine	1 mg IV every 3–5 minutes
Vasopressin	40 units IV single dose
Amiodarone	300 mg IV diluted in 20–30 mL D_5W One subsequent dose of 150 mg IV may be administered

Decision algorithm for resuscitation of ventricular fibrillation or pulseless ventricular tachycardia



***A defibrillation attempt should be made after every dose of drug administration.**

Enjoy your life with healthy heart