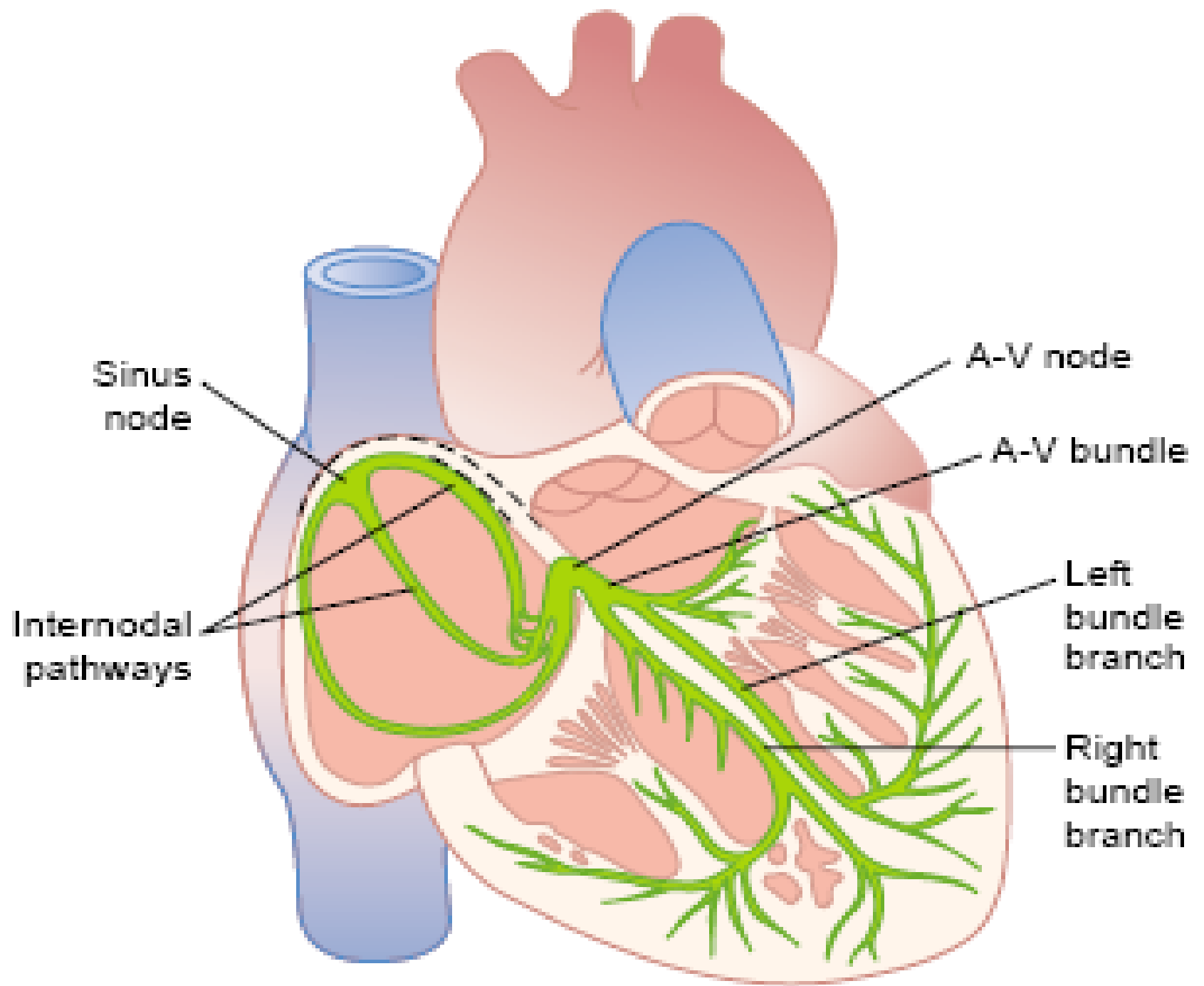

Pharmacotherapy of **Arrhythmias**

Tessema Tsehay (B.Pharm., M.Pharm., RPh.)

Introduction: The Heart

- The heart has two basic properties, namely an
 - **Electrical property**
 - **Mechanical property**
- Electrical activity is initiated by the sinoatrial (SA) node and moves through cardiac tissue by a **tree-like conduction network**.
- The **SA node initiates cardiac rhythm** under normal circumstances because this tissue possesses the highest degree of automaticity or rate of spontaneous impulse generation.



Characteristics of Cardiac Muscle

- **Automaticity**
 - ability to generate an electrical impulse spontaneously & repetitively
- **Excitability**
 - ability to be electrically stimulated or respond to an electrical stimulus
- **Conductivity**
 - ability to receive an electrical stimulus and transmit to other cardiac cells
- **Contractility/rhythmicity**
 - the ability to shorten and cause contraction in response to an electrical stimulus-coordination of contraction to produce a regular heartbeat

Cont...

Automaticity






- **SA nodal cells:** Highest intrinsic rate, primary pacemaker of the heart (100-120/min)
- **AV nodal cell:** Second highest intrinsic rate, secondary pacemaker of the heart (40-60/min)
- **Purkinje cells:** Slowest intrinsic rate (30-40/min)

Cont...

• Electrical Conduction System of the Heart

- The heart is supplied with an electrical conduction system that generates and conducts electrical impulses along specialized pathways.

– Normal conduction pathway

- SA node  internodal pathway  AV node  bundle of His  Left and Right Bundle Branches  purkinji fibers

Action potential

- Momentary change in the electrical charge stored on the surface of a cell.
- It is a cyclic of depolarization and repolarization
- Resting state - K^+ inside and Na^+ outside cell (Na^+/K^+ pump)
- AP occurs when Na^+ enters the cell and sets up a depolarising current

Phases of Action Potential

- The action potential can be described in **five** phases.
- **Phase 0**
 - rapid depolarization in response to influx of sodium ions
 - determines the velocity of impulse conduction
 - Drugs that decrease the rate of phase 0 depolarization (by blocking sodium channels)
 - slow impulse conduction through the His-Purkinje system and myocardium
- **Phase 1**
 - rapid (but partial) repolarization takes place
 - has no relevance to antidysrhythmic drugs

Cont...

- **Phase 2**
 - consists of a prolonged plateau in which the membrane potential remains relatively stable
 - calcium enters the cell and promotes contraction of atrial and ventricular muscle
 - Drugs that reduce calcium entry during phase 2 do not influence cardiac rhythm
 - can reduce myocardial contractility

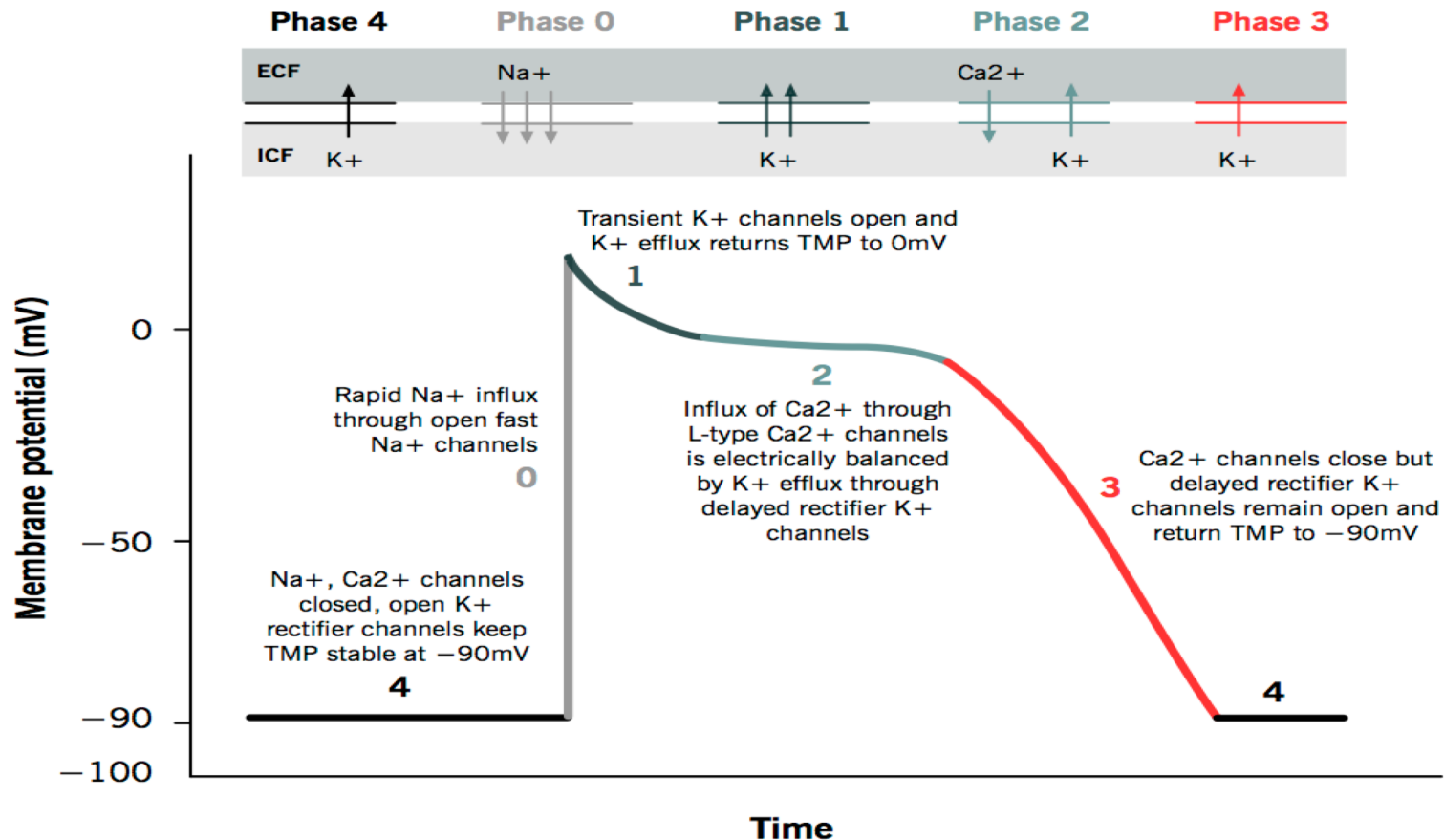
Cont...

- **Phase 3**
 - rapid repolarization takes place
 - extrusion of potassium from the cell
 - relevant in that delay of repolarization prolongs the action potential duration, and
 - thereby prolongs the effective refractory period (ERP)
 - ERP is the time during which a cell is unable to respond to excitation and initiate a new action potential
- **Phase 4**
 - two types of electrical activity are possible:
 - the membrane potential may remain stable or
 - the membrane may undergo spontaneous depolarization

Cont...

Action potential of cardiac muscles

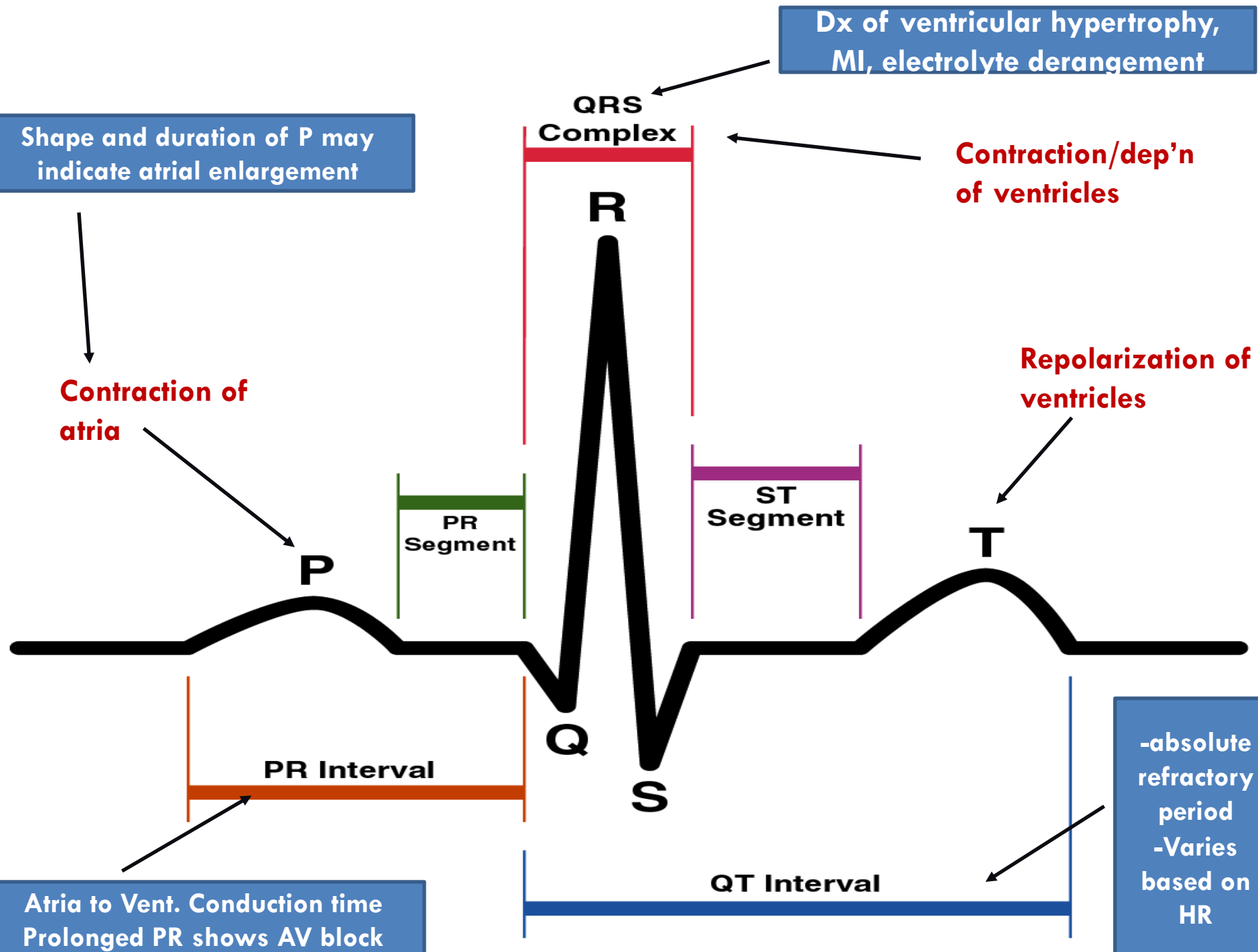
Grigoriy Ikonnikov and Eric Wong



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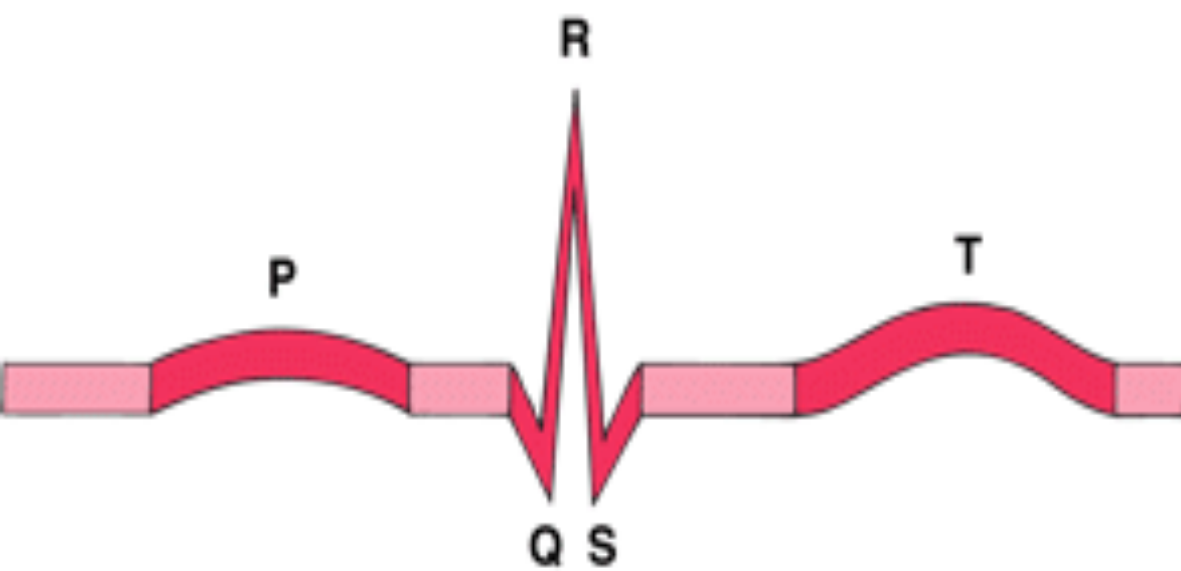
- **ECG**

- A recording of the electrical activity of the heart over time.
- is a non-invasive means of measuring the electrical activity of the heart.
- Gold standard for diagnosis of cardiac arrhythmias
- Net sum of depolarisation and repolarisation potentials of all myocardial cells
- P-QRS-T pattern

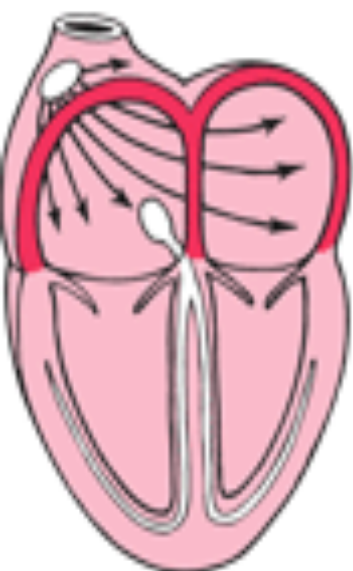


Definition

- An abnormality of the cardiac rhythm: rate and regularity
- Arrhythmias may cause sudden death, syncope, heart failure, dizziness, palpitations or no symptoms at all.
- In general, cardiac arrhythmias are classified into two broad categories:
 - **Supraventricular** (those occurring above the ventricles)
 - **Ventricular** (those occurring in the ventricles).
- base on the hear rate:
 - **bradycardia**: the HR is slow (< 60 b.p.m).
 - **tachycardia**: the HR is fast (> 100 b.p.m).

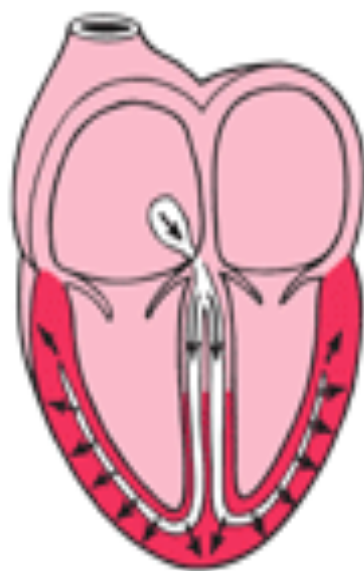


P Wave



Activation of the
atria

QRS Complex



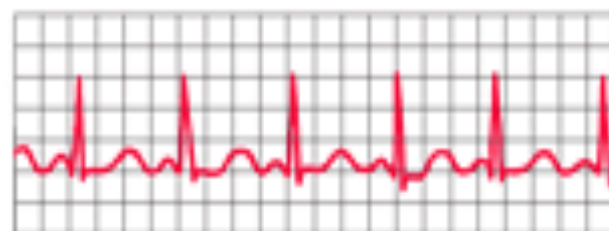
Activation of the
ventricles

T Wave

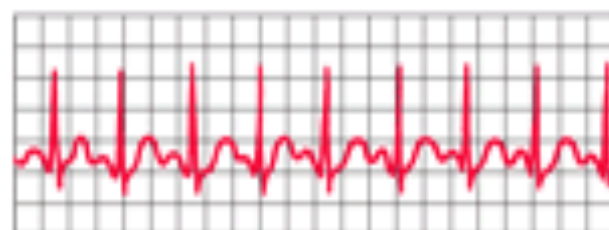


Recovery wave

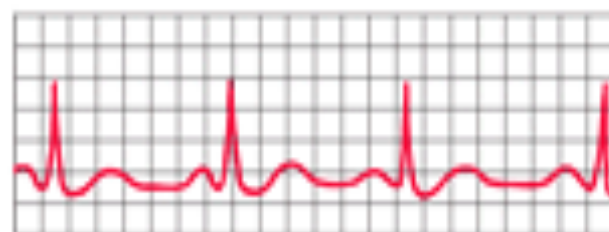
Normal Heartbeat



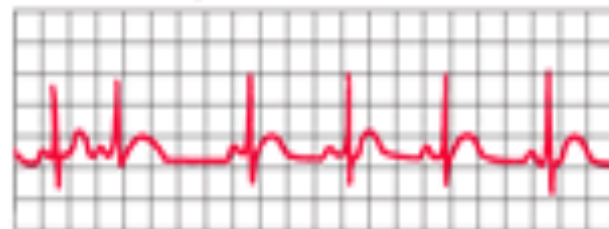
Fast Heartbeat



Slow Heartbeat



Irregular Heartbeat



Mechanisms of Cardiac Arrhythmias

- **Mechanisms generating bradycardia**
 - Sinus bradycardia is a result of **abnormally slow automaticity**
 - AV block -by **abnormal conduction** within the AV node or the distal AV conduction system.
- **Mechanisms generating tachycardia**
 - Accelerated automaticity
 - Triggered activity
 - Re-entry (or circus movements)

Accelerated automaticity

- It occurs due to increasing the rate of depolarization or changing the threshold potential.
- Such changes are thought to produce sinus tachycardia, escape rhythms and accelerated AV nodal (junctional) rhythms.
- an increased slope of phase 4 depolarization in cardiac tissues other than the SA node due to the following drugs and conditions;
 - digitalis glycosides, catecholamines , hypoxemia, electrolyte abnormalities, fiber stretch (cardiac dilation)

Triggered activity

- Transient membrane depolarizations that occur during repolarization [EADs]) or after repolarization [LADs]) but prior to phase 4 of the AP
- Presence of an increased Ca^{2+} load
- EADs is by: hypokalemia/ K^+ blockers, type Ia antiarrhythmic drugs.
 - Ex. Torsades de pointes
- LADs is by: digitalis or catecholamines, ischemia and suppressed by CCBs.
 - Ex. exercise-provoked VT

Re-entry (or circus movement)

- An Indefinite propagation of the impulse and continued activation of previously refractory tissue.
- Reentry may occur as a consequence of anatomic or functional variants in the normal conduction system
- Heart diseases (e.g., IHD, LV dysfunction) can result in changes in conduction in the pathways of a suitable reentrant substrate.

Pathophysiology

Supraventricular Arrhythmias

- Common supraventricular tachycardias **requiring drug treatment** are
 - atrial fibrillation (AF) or atrial flutter
 - paroxysmal supraventricular tachycardia (PSVT) and
 - automatic atrial tachycardias
- Other common supraventricular arrhythmias that usually **do not require drug therapy** are
 - premature atrial complexes
 - wandering atrial pace-maker
 - sinus arrhythmia
 - sinus tachycardia

Atrial Fibrillation and Atrial Flutter

- AF
 - is characterized as an extremely rapid (400 to 600 atrial beats/min) and disorganized atrial activation.
 - There is a loss of atrial contraction (atrial kick) and
 - supraventricular impulses penetrate the atrioventricular (AV) conduction system in variable degrees,
 - resulting in irregular ventricular activation and **irregularly irregular** pulse (120 to 180 beats/min).

Cont...

- Atrial flutter
 - is characterized by rapid (270 to 330 atrial beats/min) but regular atrial activation.
 - The ventricular response usually has a regular pattern and a pulse of 300 beats/min.
 - This arrhythmia occurs less frequently than AF but
 - has similar precipitating factors, consequences, and drug therapy.

Cont...

- The predominant mechanism of AF and atrial flutter is **reentry**,
 - which is usually associated with organic heart disease that causes atrial distention (e.g., ischemia or infarction, hypertensive heart disease, valvular disorders).
 - Additional associated disorders include
 - acute pulmonary embolus and chronic lung disease, resulting in pulmonary hypertension and cor pulmonale and
 - states of high adrenergic tone such as thyrotoxicosis, alcohol withdrawal, sepsis or excessive physical exertion

PSVT

- Caused by Reentry
- PSVT arising by reentrant mechanisms includes arrhythmias caused by
 - AV nodal reentry
 - AV reentry incorporating an anomalous AV pathway
 - sinoatrial (SA) nodal reentry and
 - intraatrial reentry

Automatic Atrial Tachycardias

- Automatic atrial tachycardias such as multifocal atrial tachycardia appear to arise from
 - **supraventricular foci with enhanced automatic properties.**
- Severe pulmonary disease is the underlying precipitating disorder in 60% to 80% of patients.

Ventricular Arrhythmias

- **Premature Ventricular Complexes (PCVs)**
 - are common ventricular rhythm disturbances that occur in patients with or without heart disease and may be elicited experimentally by
 - abnormal automaticity
 - triggered activity or
 - reentrant mechanisms

Cont...

Ventricular tachycardia (VT)

- defined by three or more repetitive PVCs occurring at a rate greater than 100 beats/min
- It occurs most commonly in acute myocardial infarction (MI)
- other causes are severe electrolyte abnormalities (e.g., hypokalemia), hypoxemia and digitalis toxicity
- The chronic recurrent form is almost always associated with underlying organic heart disease
 - e.g., idiopathic dilated cardiomyopathy or remote MI with left ventricular aneurysm

Cont...

- **Sustained VT** : which requires therapeutic intervention to restore a stable rhythm
- **Non-sustained VT** : self-terminates after a brief duration (usually less than 30 seconds).
- **Incessant VT** : refers to VT occurring more frequently than sinus rhythm, so that VT becomes the dominant rhythm.
- **Monomorphic VT** : has a consistent QRS configuration
- **Polymorphic VT** : has varying QRS complexes.
- **Torsade de pointes (TdP)** : is a polymorphic VT in which the QRS complexes appear to undulate around a central axis.

Ventricular Proarrhythmia

- Proarrhythmia refers to development of a significant new arrhythmia such as VT, ventricular fibrillation [VF] or TdP) or worsening of an existing arrhythmia.
- Proarrhythmia results from the same mechanisms that cause other arrhythmias or due to the antiarrhythmic agent.

Ventricular Fibrillation

- VF is electrical anarchy of the ventricle resulting in no cardiac output and cardiovascular collapse.
- Sudden cardiac death occurs most commonly in patients with IHD and primary myocardial disease associated with LV dysfunction.
- VF associated with acute MI may be classified as either
 - primary (an uncomplicated MI not associated with HF or
 - secondary or complicated (an MI complicated by HF)

Bradyarrhythmias

- **Asymptomatic sinus bradyarrhythmias**
 - (heart rate less than 60 beats/min) are common especially in young, athletically active individuals.
 - However, some patients have sinus node dysfunction (sick sinus syndrome) because of underlying organic heart disease and the normal aging process, which attenuates SA nodal function.

Cont...

- Sinus node dysfunction is usually representative of diffuse conduction disease,
 - which may be accompanied by AV block AF.
- Alternating bradyarrhythmias and tachyarrhythmias are referred to as the **tachy-brady syndrome**.

Cont...

- AV block or conduction delay may occur in any area of the AV conduction system.
- AV block may be found in patients without underlying heart disease (e.g., trained athletes) or during sleep when vagal tone is high.
- It may be transient when the underlying etiology is reversible
 - e.g., myocarditis, myocardial ischemia, after cardiovascular surgery, during drug therapy

Cont...

- β -Blockers, digoxin, or nondihydropyridine calcium antagonists may cause AV block, primarily in the AV nodal area.
- Type I antiarrhythmics may exacerbate conduction delays below the level of the AV node.
- AV block may be irreversible if the cause is
 - acute MI
 - rare degenerative disease
 - primary myocardial disease or
 - a congenital condition

Clinical Presentations

- Supraventricular tachycardias may cause a variety of clinical manifestations ranging from
 - no symptoms to minor palpitations and/or irregular pulse to
 - severe and even life-threatening symptoms.
- Patients may experience
 - dizziness or acute syncopal episodes
 - symptoms of HF
 - anginal chest pain or
 - more often a choking or pressure sensation during the tachycardia episode

Cont...

- AF or atrial flutter
 - may be manifested by the entire range of symptoms associated with other supraventricular tachycardias,
 - but syncope is not a common presenting symptom.
 - An additional complication of AF is arterial embolization resulting from atrial stasis and poorly adherent mural thrombi,
 - which accounts for the most devastating complication: embolic stroke.
 - Patients with AF and concurrent mitral stenosis or severe systolic HF are at particularly high risk for cerebral embolism.

Cont...

- PVCs
 - often cause no symptoms or only mild palpitations.
- VT
 - The presentation of VT may vary from totally asymptomatic to pulseless hemodynamic collapse.
- proarrhythmia
 - Consequences of proarrhythmia range from no symptoms to worsening of symptoms to sudden death.
- VF
 - results in hemodynamic collapse, syncope, and cardiac arrest

Cont...

- bradyarrhythmias
 - Patients with bradyarrhythmias experience symptoms associated with
 - hypotension such as dizziness, syncope, fatigue, and confusion.
 - If LV dysfunction exists, symptoms of congestive HF may be exacerbated.

Diagnosis

- The surface electrocardiogram (ECG) is the cornerstone of diagnosis for cardiac rhythm disturbances.
- Less sophisticated methods are often the initial tools for detecting qualitative and quantitative alterations of heartbeat.
 - For example, direct auscultation can reveal the irregularly irregular pulse that is characteristic of AF.
- Proarrhythmia can be difficult to diagnose because of the variable nature of underlying arrhythmias.
- TdP is characterized by long QT intervals or prominent U waves on the surface ECG.

Desired Outcome

- The desired outcome depends on the underlying arrhythmia.
- For example, the ultimate treatment goals of treating AF or atrial flutter are
 - restoring sinus rhythm
 - preventing thromboembolic complications and
 - preventing further recurrences

Treatment

General Approach

- The use of antiarrhythmic drugs in the United States is declining because of major trials that showed
 - increased mortality
 - proarrhythmia as a significant side effect
 - the advancing technology of nondrug therapies such as ablation and the implantable cardioverter-defibrillator (ICD)

Classification of Antiarrhythmic Drugs

- Drugs may have antiarrhythmic activity by directly altering conduction in several ways.
 - may depress the automatic properties of abnormal pacemaker cells
 - by decreasing the slope of phase 4 depolarization and/or by elevating threshold potential.
 - may alter the conduction characteristics of the pathways of a reentrant loop.

ANTIARRHYTHMIC DRUGS

CLASS I (Na⁺ channel blockers)

- *Disopyramide (IA)*
- *Flecainide (IC)*
- *Lidocaine (IB)*
- *Mexiletine (IB)*
- *Procainamide (IA)*
- *Propafenone (IC)*
- *Quinidine (IA)*
- *Tocainide (IB)*

CLASS II (β -adrenoreceptor blockers)

- *Esmolol*
- *Metoprolol*
- *Propranolol*

CLASS III (K⁺ channel blockers)

- *Amiodarone*
- *Dofetilide*
- *Sotalol*

CLASS IV (Ca²⁺ channel blockers)

- *Diltiazem*
- *Verapamil*

OTHER ANTI-ARRHYTHMIC DRUGS

- *Adenosine*
- *Digoxin*

Cont...

- The most frequently used classification system is that proposed by Vaughan Williams.
- **Type Ia drugs**
 - slow conduction velocity
 - prolong refractoriness and
 - decrease the automatic properties of sodium-dependent (normal and diseased) conduction tissue.
 - Type Ia drugs are **broad-spectrum** antiarrhythmics, being effective for both supraventricular and ventricular arrhythmias

Cont...

- **type Ib drugs**
 - Although categorized separately, type Ib drugs probably act similarly to type Ia drugs, except that type Ib agents are considerably **more effective in ventricular than supraventricular arrhythmias**.
- **Type Ic drugs**
 - profoundly slow conduction velocity **while leaving refractoriness relatively unaltered**.
 - Although effective for both ventricular and supraventricular arrhythmias, their use for ventricular arrhythmias has been limited by the risk of **proarrhythmia**
- Collectively, type I drugs can be referred to as **sodium channel blockers**.

Cont...

- **Type II drugs**
 - **β -adrenergic antagonists** ; clinically relevant mechanisms result from their antiadrenergic actions.
 - β -Blockers are most useful in tachycardias in which nodal tissues are abnormally automatic or are a portion of a reentrant loop.
 - These agents are also helpful in slowing ventricular response in atrial tachycardias (e.g., AF) by their effects on the AV node.

Cont...

- **Type III drugs**

- specifically **prolong refractoriness** in atrial and ventricular fibers and include very different drugs that share the common effect of delaying repolarization by **blocking potassium channels**.
- are effective in most supraventricular and ventricular tachycardias.

Cont...

- **Amiodarone**

- impressive effectiveness and low proarrhythmic potential
- It is a sodium channel blocker
- has nonselective β -blocking actions,
- blocks potassium channels, and
- has slight calcium antagonist activity.

Cont...

- **Type IV drugs**

- inhibit calcium entry into the cell, which

- slows conduction,
 - prolongs refractoriness, and
 - decreases SA and AV nodal automaticity.

- CCBs hence are effective for automatic or reentrant tachycardias that arise from or use the SA or AV nodes.

TABLE 1

Classification of Antiarrhythmic Drugs

Type	Drug	Conduction Velocity ^a	Refractory Period	Automaticity	Ion Block
Ia	Quinidine Procainamide Disopyramide	↓	↑	↓	Sodium (intermediate) Potassium
Ib	Lidocaine Mexiletine	0/↓	↓	↓	Sodium (fast on/off)
Ic	Flecainide Propafenone ^b Moricizine ^c	↓↓	0	↓	Sodium (slow on/off) Potassium ^d
II ^e	β-Blockers	↓	↑	↓	Calcium (indirect)
III	Amiodarone ^f Dofetilide Sotalol ^b Ibutilide	0	↑↑	0	Potassium
IV ^e	Verapamil Diltiazem	↓	↑	↓	Calcium

0, no change; ↑, increased; ↓, decreased.

^aVariables for normal tissue models in ventricular tissue.

^bAlso has type II, β-blocking actions.

^cClassification controversial.

^dNot clinically manifest.

^eVariables for sinoatrial and atrioventricular nodal tissue only.

^fAlso has sodium, calcium, and β-blocking actions.

TABLE 2 Typical Maintenance Doses of Oral Antiarrhythmic Drugs		
Drug	Dose	Dose Adjusted
Quinidine	200–300 mg sulfate salt q 6 h 324–648 mg gluconate salt q 8–12 h	HEP, age >60 years
Procainamide	500–1,000 mg q 6 h (Pronestyl SR) 1,000–2,000 mg q 12 h (Procanbid)	HEP, REN ^a
Disopyramide	100–150 mg q 6 h 200–300 mg q 12 h (SR form)	HEP, REN
Mexiletine	200–300 mg q 8 h	HEP
Flecainide	50–150 mg q 8 h	HEP, REN
Propafenone	150–300 mg q 8 h	HEP
Moricizine	200 mg q 8 h	HEP, REN
Sotalol	80–160 mg q 12 h	REN ^b
Dofetilide	500 mcg q 12 h	REN ^c
Amiodarone	400 mg two to three times daily until 10 g total, then 200–400 mg daily ^d	

HEP, hepatic disease; REN, renal dysfunction; SR, sustained-release.

^aAccumulation of parent compound or metabolite (e.g., NAPA) may occur.

^bShould not be used for atrial fibrillation when creatinine clearance <40 mL/min.

^cDose should be based upon creatinine clearance; should not be used when creatinine clearance <20 mL/min.

^dUsual maintenance dose for atrial fibrillation is 200 mg/day (may further decrease dose to 100 mg/day with long-term use if patient clinically stable in order to decrease risk of toxicity); usual maintenance dose for ventricular arrhythmias is 300–400 mg/day.

Drug	Clinical Situation	Dose
Amiodarone	Pulseless VT/VF	300 mg IV/IO push (can give additional 150 mg IV/IO push if persistent VT/VF), followed by infusion of 1 mg/min for 6 hours, then 0.5 mg/min
	Stable VT (with a pulse)	150 mg IV over 10 minutes, followed by infusion of 1 mg/min for 6 hours, then 0.5 mg/min
	AF (termination)	5 mg/kg IV over 30 minutes, followed by infusion of 1 mg/min for 6 hours, then 0.5 mg/min
Diltiazem	PSVT; AF (rate control)	0.25 mg/kg IV over 2 minutes (may repeat with 0.35 mg/kg IV over 2 minutes), followed by infusion of 5–15 mg/hour
ibutilide	AF (termination)	1 mg IV over 10 minutes (may repeat if needed)
Lidocaine	Pulseless VT/VF	1–1.5 mg/kg IV/IO push (can give additional 0.5–0.75 mg/kg IV/IO push every 5–10 minutes if persistent VT/VF [maximum cumulative dose = 3 mg/kg]), followed by infusion of 1–4 mg/min (1–2 mg/min if liver disease or HF)
	Stable VT (with a pulse)	1–1.5 mg/kg IV push (can give additional 0.5–0.75 mg/kg IV push every 5–10 minutes if persistent VT [maximum cumulative dose = 3 mg/kg]), followed by infusion of 1–4 mg/min (1–2 mg/min if liver disease or HF)
Procainamide	AF (termination); stable VT (with a pulse)	15–18 mg/kg IV over 60 minutes, followed by infusion of 1–4 mg/min
Verapamil	PSVT; AF (rate control)	2.5–5 mg IV over 2 minutes (may repeat up to maximum cumulative dose of 20 mg); can follow with infusion of 2.5–15 mg/hour

AF, atrial fibrillation; HF, heart failure; IO, intraosseous; PSVT, paroxysmal supraventricular tachycardia; VF, ventricular fibrillation; VT, ventricular tachycardia.

Quinidine	Cinchonism, diarrhea, abdominal cramps, nausea, vomiting, hypotension, TdP, aggravation of underlying HF, conduction disturbances or ventricular arrhythmias, fever, hepatitis, thrombocytopenia, hemolytic anemia
Procainamide	Systemic lupus erythematosus, diarrhea, nausea, vomiting, TdP, aggravation of underlying HF, conduction disturbances or ventricular arrhythmias, agranulocytosis
Disopyramide	Anticholinergic symptoms (dry mouth, urinary retention, constipation, blurred vision), nausea, anorexia, TdP, HF, aggravation of underlying conduction disturbances and/or ventricular arrhythmias, hypoglycemia
Lidocaine	Dizziness, sedation, slurred speech, blurred vision, paresthesia, muscle twitching, confusion, nausea, vomiting, seizures, psychosis, sinus arrest, aggravation of underlying conduction disturbances
Mexiletine	Dizziness, sedation, anxiety, confusion, paresthesia, tremor, ataxia, blurred vision, nausea, vomiting, anorexia, aggravation of underlying conduction disturbances or ventricular arrhythmias
Moricizine	Dizziness, headache, fatigue, insomnia, nausea, diarrhea, blurred vision, aggravation of underlying conduction disturbances or ventricular arrhythmias
Flecainide	Blurred vision, dizziness, dyspnea, headache, tremor, nausea, aggravation of underlying HF, conduction disturbances, or ventricular arrhythmias
Propafenone	Dizziness, fatigue, bronchospasm, headache, taste disturbances, nausea, vomiting, bradycardia or AV block, aggravation of underlying HF, conduction disturbances, or ventricular arrhythmias
Amiodarone	Tremor, ataxia, paresthesia, insomnia, corneal microdeposits, optic neuropathy/neuritis, nausea, vomiting, anorexia, constipation, TdP (<1%), bradycardia or AV block (IV and oral use), pulmonary fibrosis, liver function test abnormalities, hepatitis, hypothyroidism, hyperthyroidism, photosensitivity, blue-gray skin discoloration, hypotension (IV use), phlebitis (IV use)
Dofetilide	Headache, dizziness, TdP
Ibutilide	Headache, TdP, hypotension
Sotalol	Dizziness, weakness, fatigue, nausea, vomiting, diarrhea, bradycardia, TdP, bronchospasm, aggravation of underlying heart failure

Treatment

Atrial Fibrillation or Atrial Flutter

- Many methods are available for restoring sinus rhythm, preventing thromboembolic complications, and preventing further recurrences
 - however, treatment selection depends in part on onset and severity of symptoms.
 - If symptoms are severe and of recent onset, patients may require direct-current cardioversion (DCC) to restore sinus rhythm immediately

Cont...

- If patients are hemodynamically stable, the focus should be directed **toward control of ventricular rate**.
 - Drugs that slow conduction and increase refractoriness in the AV node should be used as initial therapy.
- In patients with normal LV function (left ventricular ejection fraction $>40\%$),
 - IV β -blockers (propranolol, metoprolol, esmolol), diltiazem or verapamil is recommended.

Cont...

- If a high adrenergic state is the precipitating factor,
 - IV β -blockers can be highly effective and should be considered first.
- In patients with left ventricular ejection fraction $\leq 40\%$,
 - IV diltiazem and verapamil should be avoided and IV β -blockers should be used with caution.

Cont...

- In patients having an exacerbation of HF symptoms,
 - IV digoxin or amiodarone should be used as first-line therapy for ventricular rate control.
 - IV amiodarone can also be used in patients who are refractory or have contraindications to BBs, nondihydropyridine CCBs and digoxin.
- After treatment with AV nodal blocking agents and a subsequent decrease in ventricular response,
 - the patient should be evaluated for the possibility of restoring sinus rhythm if AF persists.

Cont...

- If sinus rhythm is to be restored,
 - anticoagulation should be **initiated prior to cardioversion** because return of atrial contraction increases risk of thromboembolism.
 - Patients with AF for longer than 48 hours or an unknown duration should receive warfarin
 - target INR 2 to 3
 - for at least 3 weeks prior to cardioversion and continuing for at least 4 weeks after effective cardioversion and return of normal sinus rhythm.

Cont...

- Patients with AF less than 48 hours in duration do not require warfarin,
 - but it is recommended that these patients receive either IV UH or a LMWH (subcutaneously at treatment doses) at presentation prior to cardioversion.
- After prior anticoagulation (or after TEE demonstrated the absence of a thrombus, thereby obviating the need for warfarin)
 - methods for restoring sinus rhythm in patients with AF or atrial flutter are **pharmacologic cardioversion and DCC**

Cont...

- DCC is quick and more often successful, but it requires prior sedation or anesthesia and has a **small risk** of serious complications such as sinus arrest or ventricular arrhythmias.
- Relatively strong evidence for efficacy of pharmacological cardioversion
 - type III pure K⁺ blockers (ibutilide, dofetilide),
 - type Ic drugs (e.g., flecainide, propafenone), and
 - amiodarone (oral or IV).
- Disadvantages of drug therapy are
 - significant side effects such as drug-induced TdP,
 - drug–drug interactions, and
 - lower cardioversion rate for drugs compared with DCC

Cont...

- The ACCP recommends chronic warfarin treatment (target INR 2.5; range 2 to 3) for all patients with AF who are at **high risk for stroke**
 - rheumatic mitral valve disease
 - previous ischemic stroke, transient ischemic attack, or other systemic embolic event
 - age >75 years
 - moderate or severe LV systolic dysfunction and/or congestive HF
 - hypertension or
 - prosthetic heart valve

Cont...

- Those at **intermediate risk** (age 65 to 75 years with none of the high-risk factors)
 - should receive either warfarin (target INR 2.5; range 2 to 3) or aspirin 325 mg/day.
- Those at **low risk** (age <65 years with none of the high-risk factors)
 - should receive aspirin 325 mg/day.
- **Chronic antithrombotic therapy** should be considered for
 - all patients with AF and risk factors for stroke regardless of whether or not they remain in sinus rhythm

Cont...

- AF often **recurs after initial cardioversion** because most patients have irreversible underlying heart or lung disease.
- Consequently, chronic anti-arrhythmic drugs should be reserved
 - for patients with recurrent AF associated with intolerable symptoms during episodes of AF

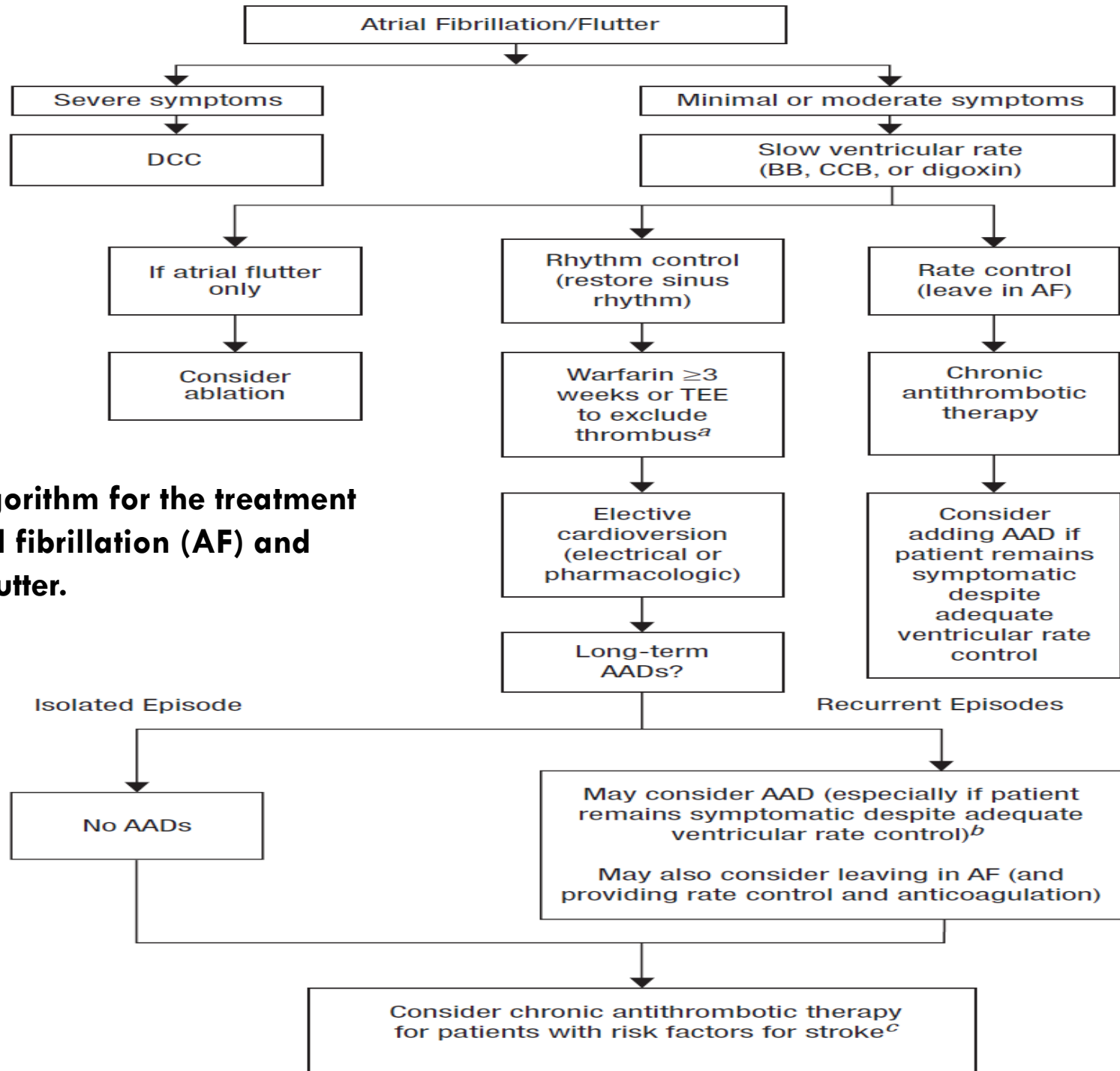


Fig: Algorithm for the treatment of atrial fibrillation (AF) and atrial flutter.

Paroxysmal Supraventricular Tachycardia

- The choice between pharmacologic and non-pharmacologic methods for treating PSVT depends on symptom severity.
- **Synchronized DCC** is the treatment of choice if symptoms are **severe**
 - e.g., syncope, near syncope, anginal chest pain, severe HF
- **Nondrug measures** that increase vagal tone to the AV node (e.g., unilateral carotid sinus massage, Valsalva maneuver) can be used for **mild to moderate symptoms**.
- If these methods fail, drug therapy is the next option.

Cont...

- Drugs can be divided into three broad categories:
 - those that directly or indirectly increase vagal tone to the AV node
 - e.g., digoxin
 - those that depress conduction through slow, calcium-dependent tissue
 - e.g., adenosine, β -blockers, calcium channel blockers
 - those that depress conduction through fast, sodium-dependent tissue
 - e.g., quinidine, procainamide, disopyramide, flecainide

Cont...

- **Adenosine** has been recommended as the drug of first choice in patients with PSVT
 - because its short duration of action will not cause prolonged hemodynamic compromise in patients with wide QRS complexes

Cont...

- After acute PSVT is terminated, long-term preventive treatment is indicated
 - if frequent episodes necessitate therapeutic intervention or
 - if episodes are infrequent but severely symptomatic.
- Serial testing of antiarrhythmic agents can be evaluated in the ambulatory setting

Automatic Atrial Tachycardias

- Underlying precipitating factors should be corrected by
 - ensuring proper oxygenation and ventilation and
 - correcting acid–base or electrolyte disturbances.
- If tachycardia persists, the need for additional treatment is determined by symptoms.
- Patients with asymptomatic atrial tachycardia and relatively slow ventricular response usually require **no drug therapy**.

Cont...

- In symptomatic patients, medical therapy can be tailored either
 - to control ventricular response or
 - to restore sinus rhythm.
- Nondihydropyridine calcium antagonists (e.g., verapamil) are considered first-line drug therapy for **decreasing ventricular response**.
 - DCC is ineffective and β -blockers are usually contraindicated because of coexisting severe pulmonary disease or uncompensated HF.

Premature Ventricular Complexes

- In apparently healthy individuals, **drug therapy is unnecessary**
 - because PVCs without associated heart disease carry little or no risk.
- In patients with risk factors for arrhythmic death (recent MI, LV dysfunction, complex PVCs),
 - chronic drug therapy should be restricted to **β -blockers** because only they have been conclusively proven to prevent mortality in these patients.

Ventricular Tachycardia

- **Acute Ventricular Tachycardia**
 - If severe symptoms are present, synchronized DCC should be instituted immediately to restore sinus rhythm.
 - Precipitating factors should be corrected if possible.
 - Patients with mild or no symptoms can be treated initially with antiarrhythmic drugs.
 - **IV amiodarone** is now recommended as first-line therapy in this situation.
 - Procainamide or lidocaine given IV is a suitable alternative.

Cont...

- **Sustained Ventricular Tachycardia**

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

Cont...

- **Torsade de Pointes**

- For an acute episode of TdP, most patients require and respond to DCC.
- However, TdP tends to often recurs rapidly after DCC.
- **IV magnesium sulfate** is considered the drug of choice for preventing recurrences of TdP.
- Agents that prolong the QT interval should be discontinued, and exacerbating factors (e.g., hypokalemia, hypomagnesemia) corrected.

Cont...

- **Ventricular Fibrillation**

- After successful resuscitation, antiarrhythmics should be continued until the patient's rhythm and overall status are stable.
- Long-term antiarrhythmics or ICD implantation may or may not be required.

Bradyarrhythmias

- Sinus node dysfunction

- Treatment of sinus node dysfunction involves
 - elimination of symptomatic bradycardia and possibly
 - managing alternating tachycardias such as AF.
- Asymptomatic sinus bradyarrhythmias usually do **not require** therapeutic intervention.
- In general, long-term therapy of choice for patients with significant symptoms is a **permanent ventricular pacemaker**.

Cont...

- Drugs commonly employed to treat supraventricular tachycardias should be used with caution.
- Symptomatic carotid sinus hypersensitivity also should be treated with **permanent pacemaker therapy**.
- Patients who remain symptomatic may benefit from adding an **α -adrenergic stimulant such as midodrine**

Atrioventricular block :

- > **First degree AV block** : PR interval $\geq 0.20\text{sec}$
 - AV nodal decrease conduction, acute myocardial infraction, enhanced vagal tone.
- > **Secondary block**
 - Mobitz I (Wenckebach) : Progressive PR prolongation until QRS complex is dropped.
 - Mobitz II : Absence of QRS complex.
- > **Third-degree block** : Absence of AV conduction.

Cont...

- If patients with Mobitz II or third-degree AV block develop signs or symptoms of poor perfusion (e.g., altered mental status, chest pain, hypotension, shock) associated with bradycardia or AV block,
 - **transcutaneous pacing** should be initiated immediately.
- **Atropine**
 - 0.5 mg IV given every 3 to 5 minutes, up to 3 mg total dose should be given as the pacing leads are being placed.

Cont...

- Infusions of **epinephrine** (2 to 10 mcg/min) or **dopamine** (2 to 10 mcg/kg/min) can be used in the event of atropine failure.
- These agents will not help if AV block is below the AV node (Mobitz II or trifascicular AV block)
- Chronic symptomatic AV block warrants insertion of a **permanent pace-maker**.
- Patients without symptoms can sometimes be followed closely without the need for a pacemaker.

Evaluation Of Therapeutic Outcomes

- The most important monitoring parameters include
 - mortality (total and due to arrhythmic death)
 - arrhythmia recurrence (duration, frequency, symptoms)
 - hemodynamic consequences (rate, blood pressure, symptoms) and
 - treatment complications (need for alternative or additional drugs, devices or surgery).