



# **Current Concepts in Cardiology for Advanced Practitioners Mini Series**

## **Session 1: Mechanisms of Cardiac Arrhythmias Made Easy**

Nuala Summerfield BSc BVM&S DipACVIM(Cardiology)  
DipECVIM-CA (Cardiology) MRCVS  
RCVS & European Recognised Specialist in  
Veterinary Cardiology



Surface ECGs provide us with clues as to potential underlying mechanisms for cardiac arrhythmias. However, the surface ECG has limitations when interpreting complex arrhythmias. Electrophysiology (EP) studies are necessary for a definite diagnosis of underlying arrhythmia mechanism(s) and allow curative treatment with radiofrequency ablation (RFA). EP and RFA are now emerging as viable options for our veterinary (canine) patients.

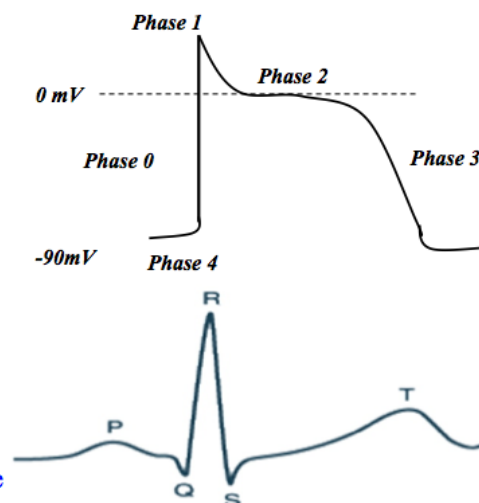
Interpretation of complex arrhythmias requires practice and familiarity with reading ECGs, a logical approach to the complex ECG and an understanding of the various underlying arrhythmia mechanisms. Correct ECG interpretation enables the clinician to narrow down the possibilities, to guide appropriate therapy. However, it is important to realise that the surface ECG diagnosis can still be open to debate.

Cardiac cells are excitable i.e. electrical stimulation results in ion movement across the cell membrane, resulting in the pattern of changes in transmembrane potential over time which is called an action potential (AP). An AP represents the electrical activity occurring in a single cardiac cell. The ECG represents the sum of electrical activity of all cardiac cells in the entire heart.

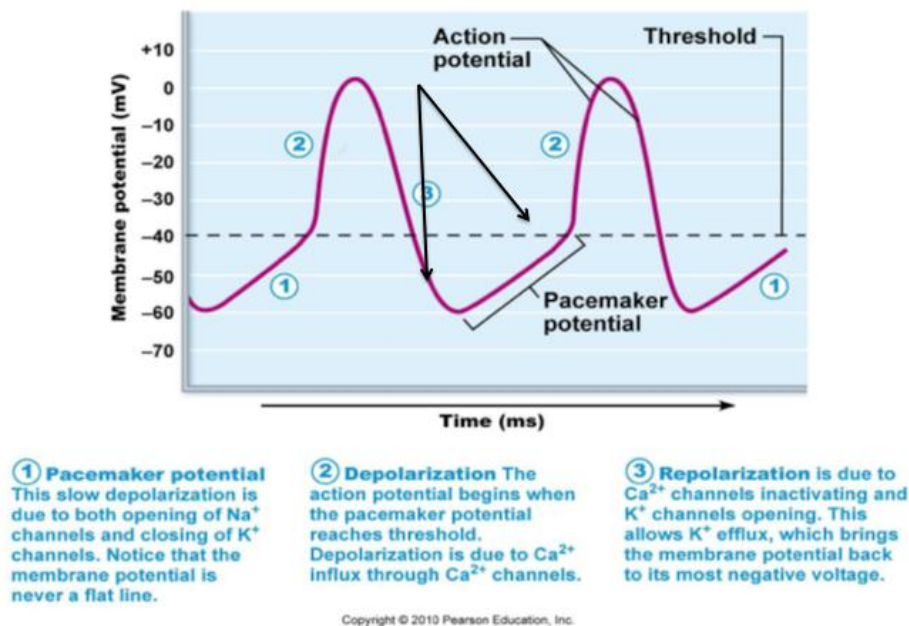
The trans-membrane electrical gradient (potential) is maintained, with the interior of the cell negative with respect to outside the cell. This gradient is the result of unequal distribution of ions inside versus outside the cell i.e. sodium and calcium are higher outside than inside the cell, potassium is higher inside the cell than outside. The resting membrane potential is maintained by ion-selective channels, active pumps and exchangers.

## Phases of cardiac myocyte AP

- **Phase 0** rapid depolarisation (inflow of  $\text{Na}^+$ )
- **Phase 1** partial repolarisation (inward  $\text{Na}^+$  current deactivated, outflow of  $\text{K}^+$ )  
R and S waves on ECG
- **Phase 2** plateau (slow inward calcium current)  
ST segment on ECG
- **Phase 3** repolarisation (calcium current inactivates,  $\text{K}^+$  outflow)  
T wave on ECG
- **Phase 4** resting phase  
Diastolic portion of cardiac cycle



# Phases of cardiac pacemaker cell AP



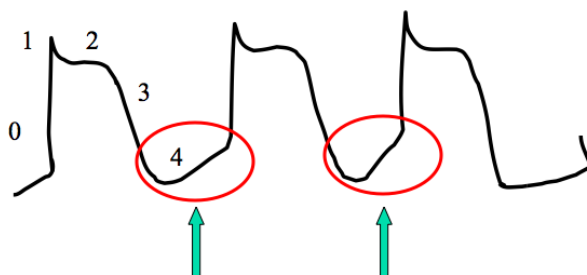
There are three cellular mechanisms of arrhythmias proposed:

- **Automaticity**
- **Triggered activity**
- **Reentry.**

## Automaticity

Automaticity is the property of cardiac cells to generate spontaneous action potentials. The sinoatrial (SA) node normally displays the highest intrinsic rate. All other pacemakers (e.g. AVN, ventricular pacemakers) are referred to as subsidiary or latent pacemakers. They take over the function of initiating excitation of the heart only when the SA node is unable to generate impulses or when these impulses fail to propagate.

## Automaticity



Spontaneous activity is the result of diastolic depolarization caused by a net inward current during phase 4 of the action potential, which progressively brings the membrane potential to threshold.

Abnormal automaticity is an important cause of atrial and ventricular arrhythmias. Like sinus tachycardia (which is a **normal** automatic tachycardia), abnormal automatic tachyarrhythmias display warm up / slow down behaviour. Also like sinus tachycardia, tachycardias due to abnormal automaticity are often seen in acutely ill patients and have metabolic causes, eg. hypoxia, acid-base disorders, electrolyte abnormalities, high sympathetic tone.

Abnormal automaticity can occur in cardiac cells when there are major abnormalities in trans-membrane potentials caused by factors such as:

- Drug toxicities (digoxin)
- Ischaemic cardiac disease
- Electrolyte disturbances
- Changes in autonomic nervous system.

It is therefore important to address the underlying systemic condition that is causing abnormal automaticity.

Parasystole is a benign type of automaticity problem. It affects only a small region of atrial or ventricular cells. It is caused by an independent focus discharging spontaneously. Due to the presence of an entrance block, the parasystolic focus is not overdriven by the normal cardiac impulse. The parasystolic focus will discharge at a regular rate and may cause complete depolarization of the atria or ventricles.

With atrial parasystole, the focus is located within the atrial myocardium and produces small P waves usually unassociated with QRS complexes.

With ventricular parasystole, the focus is located within the ventricular myocardium and produces regularly spaced QRS complexes. When the parasystolic focus discharges during the ventricles' refractory period, a QRS will not be created.

## Atrial parasystole in a dog



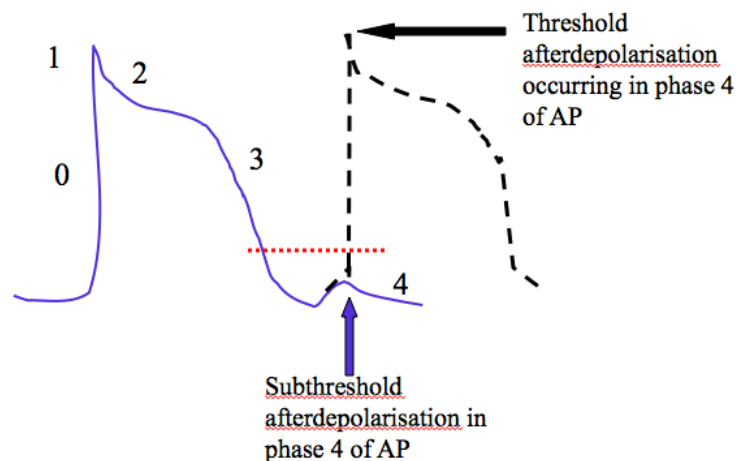
Lead II 25 mm/sec, 10 mm = 1mV

- Parasystolic focus is located within atrial myocardium.
- Produces small P waves unassociated with QRS complexes.

### Triggered activity

Triggered activity involves leakage of positive ions into the cell. This causes a “bump” (oscillation in membrane potential) on the action potential (AP) during phase 2, 3 or 4. This is called an afterdepolarisation (AD). When the AD amplitude suffices to bring the membrane to its threshold potential, a spontaneous AP, referred to as a triggered response, is the result. These triggered events give rise to extrasystoles which can precipitate tachyarrhythmias. Triggered activity displays warm-up / slow-down behaviour (like abnormal automaticity).

## Triggered activity



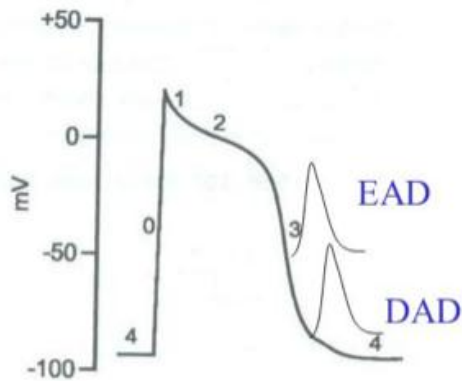
After depolarisations and triggered activity are most likely to occur when heart becomes calcium overloaded. A variety of drugs increase the susceptibility to these arrhythmias:

- Inotropic agents that increase cytosolic calcium
- Antiarrhythmic drugs
- Antidepressants
- Anticonvulsants

Unlike most arrhythmias that are suppressed when the heart is paced rapidly (through a mechanism called overdrive suppression), DADs are made worse when the heart rate increases.

Two subclasses of ADs are traditionally recognized:

- Early afterdepolarizations (EAD) interrupt or retard repolarization during phase 2 or 3 of the AP (when MP ranges between -10 and -30 mV)
- Delayed afterdepolarizations (DAD) occur after full repolarization (phase 4).



There are a number of clinical examples of arrhythmias caused by triggered activity.

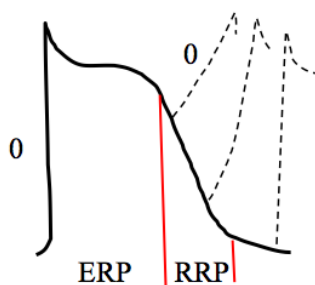
- ADs and triggered activity are thought to be responsible for the initiation of pause-dependent ventricular arrhythmias in the German Shepherd dog model of inherited ventricular arrhythmias and sudden cardiac death (Ref: Jesty et al JVC 2013).
- EADs are the likely initiating cause of Torsade de Pointes (polymorphic, pause dependent VT). There are several published case reports of T de P in horses.
- DADs are thought to be involved in initiation of arrhythmias after exposure to toxic levels of cardiac glycosides (digitalis) or catecholamines (catecholaminergic polymorphic ventricular tachycardia).
- Triggered arrhythmias are common in patients with long QT syndromes (Sudden death associated with QT interval prolongation and KCNQ1 gene mutation in a family of English Springer Spaniels. Ware et al JVIM 2015).

### Reentry

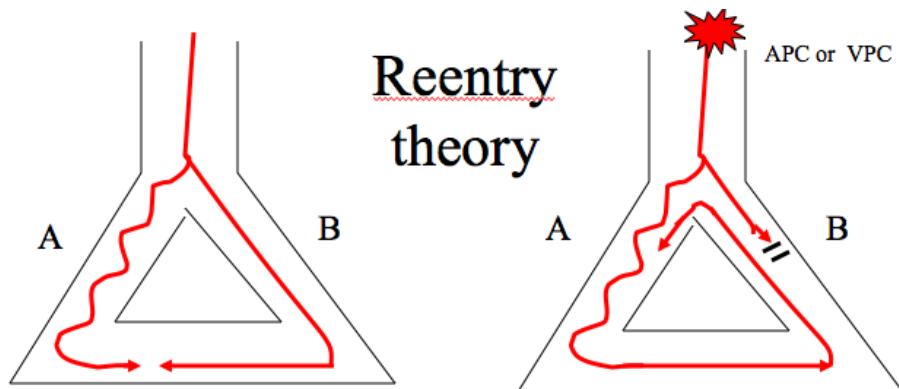
During each cardiac cycle, electrical activity normally starts in the sinoatrial node (SAN). Each cell becomes activated in turn. This continues until the entire heart has been depolarised ("excited"). The electrical impulse "dies out" when all cardiac fibres have been depolarised and are then completely refractory. In the refractory period (RP), the electrical impulse has "no place to go". The electrical impulse is therefore extinguished and is started again by next SAN impulse.

The RP is divided into two parts:

- In Effective Refractory Period (ERP) the cell cannot be depolarised
- In Relative Refractory Period (RRP) the cell can be depolarised but APs have slower phase 0 activity.



However, if a group of fibres are not activated by the initial wave of depolarisation (i.e. they were refractory), they may recover excitability in time to be depolarised by impulse **just before** it dies out. Thus they can serve as link to depolarise areas that were initially depolarised and refractory, but have now had time to recover excitability.



- Need 2 parallel conducting pathways, connected proximally and distally
- A has SLOWER conduction velocity
- B has LONGER refractory period
- Initiation by appropriately timed premature beat
- Establishes continually circling impulse
- Impulse exits circuit at some point during each loop to depolarise surrounding myocardium

Reentry is the most common mechanism. It is probably the mechanism underlying a lot of tachyarrhythmias:

- **Congenital circuits**
  - AV nodal re-entry, pre-excitation syndrome/accessory pathways.
- Reentrant circuits **acquired with heart disease** (as a result of scar tissue formation within myocardium?)
  - Atrial fibrillation, atrial flutter, ventricular fibrillation, some ventricular tachycardias.

#### Relating the electrophysiology to the surface ECG findings

##### ECG features of SVTs:

The QRS morphology is characteristically narrow but can have wide QRS complex if there is **aberrant conduction** through the ventricle e.g. with an accessory pathway or bundle branch block (pre-existing BBB or rate dependent BBB).

The rhythm can be regular or irregular e.g. AV block may result in irregularity of QRS interval; AVN conduction pattern may be **regularly irregular** due to influences of autonomic tone; the rhythm may be **irregularly irregular** with atrial fibrillation.

Identification of P' waves is important. P' waves indicate atrial depolarisation that does NOT originate in the SAN. May be hard to see with rapid SVT and it depends on ventricular rate and QRS duration. Run all possible leads at normal and maximal sensitivity (limb leads and chest leads) as P' waves may be more visible in chest leads.

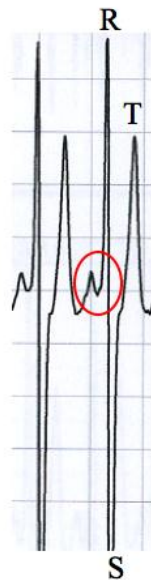
The relationship of P' wave to **preceding QRS** is an important feature.

If P' closer to preceding QRS than to subsequent QRS (i.e. RP' interval is less than or equal to 50% of RR interval)

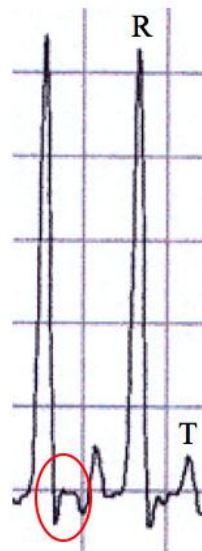
- SHORT RP' / LONG P'R SVT.

If P' closer to subsequent QRS than to preceding QRS (i.e. RP' interval is greater than 50% of RR interval)

- LONG RP' / SHORT P'R SVT.



LONG RP' / SHORT P'R SVT



SHORT RP' / LONG P'R SVT

Initiation  
and

termination of the tachycardia provide important information as to their likely mechanism:  
Sudden onset and offset (paroxysmal) vs, gradual rate acceleration and deceleration.

Response to AV block

- AV nodal dependent – SVT terminates
- AV nodal independent – SVT continues.



# Typical ECG characteristics of SVTs

SVT mechanism	Visible P' waves	P' wave morphology	RP' Interval	Initiation / Termination	Response to AV block
AAT (FAT)	Yes	Differs from sinus P wave	Long	Gradual	SVT continues
Atrial flutter	Flutter waves	N/A	N/A	Abrupt	SVT continues
Atrial fibrillation	Fibrillation waves	N/A	N/A	Abrupt (but often incessant)	SVT continues
AVNRT*	No	Retrograde, II, III, aVF	Short	Abrupt	SVT terminates
OAVRT	Yes	Retrograde II, III, aVF	Short	Abrupt	SVT terminates

\*AVNRT has not been confirmed with electrophysiological studies clinically in veterinary medicine yet

## Focal Atrial Tachycardia (FAT)

Focal atrial tachycardia (FAT) arises from a single site within the left or right atrium. This is in contrast to macro-reentrant atrial arrhythmias (eg, atrial flutter) and atrial fibrillation, which involve multiple sites or larger circuits. Traditionally, FAT was considered to be due predominantly to abnormal automaticity (often referred to as automatic AT).

Now known that FAT can be caused by automatic, triggered, and micro-reentrant aetiologies, which cannot be distinguished easily on the surface ECG.

According to one EP study, dogs have mainly right-sided FAT. The majority of FATs are automatic and can trigger AF, particularly in the case of PV location (Ref: Santilli et al JVIM 2010).

Typical ECG Features:

- Visible P' waves
- Long RP' interval, short P' R interval
- Gradual rate acceleration/deceleration
- AV node independent



•Visible P' waves

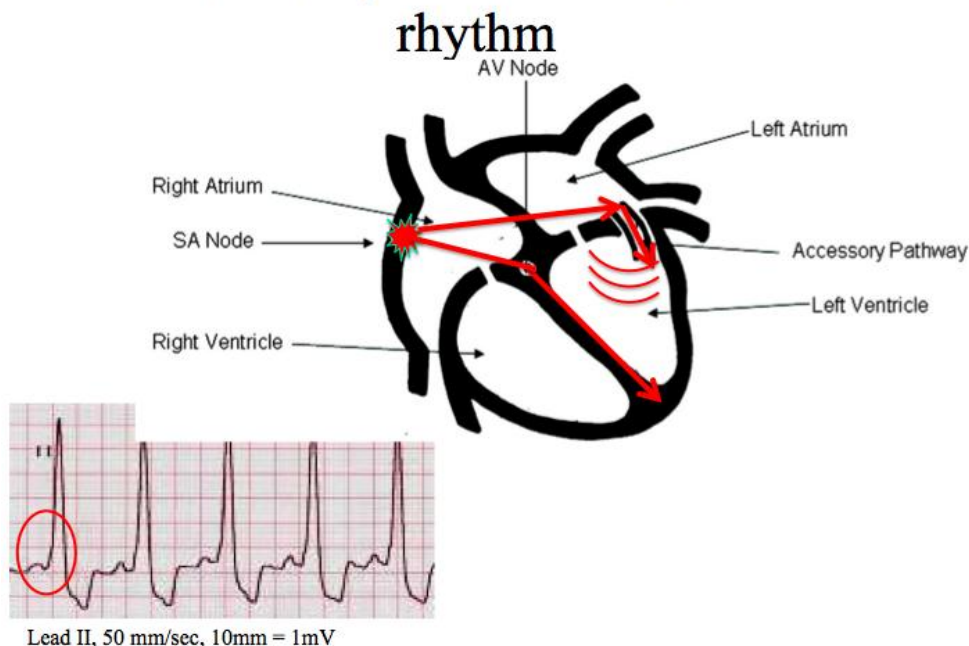
•Long RP' interval, short P' R interval

### Accessory pathway mediated tachycardias

Accessory pathways (AP) contain working myocardial fibres (embryonic remnants). The AP connects atrium to ventricle and bypasses AV node. The AP has **FASTER** conduction than AVN, but has **LONGER** refractory period. It may conduct unidirectionally or bidirectionally. Anterograde (atrium to ventricle) conduction allows all or part of ventricle to be depolarised earlier than would occur if the impulse had travelled down usual slower route through AV node (i.e. this is called ventricular pre-excitation).

Wolff-Parkinson White (WPW) syndrome is the term given to individuals with an AP which conducts in an **anterograde** direction in sinus rhythm. This ventricular pre-excitation allows diagnosis of condition from surface ECG in sinus rhythm i.e. there is a **short PR** and a slurred upstroke to QRS in some leads (**delta wave**).

## Ventricular pre-excitation in sinus rhythm



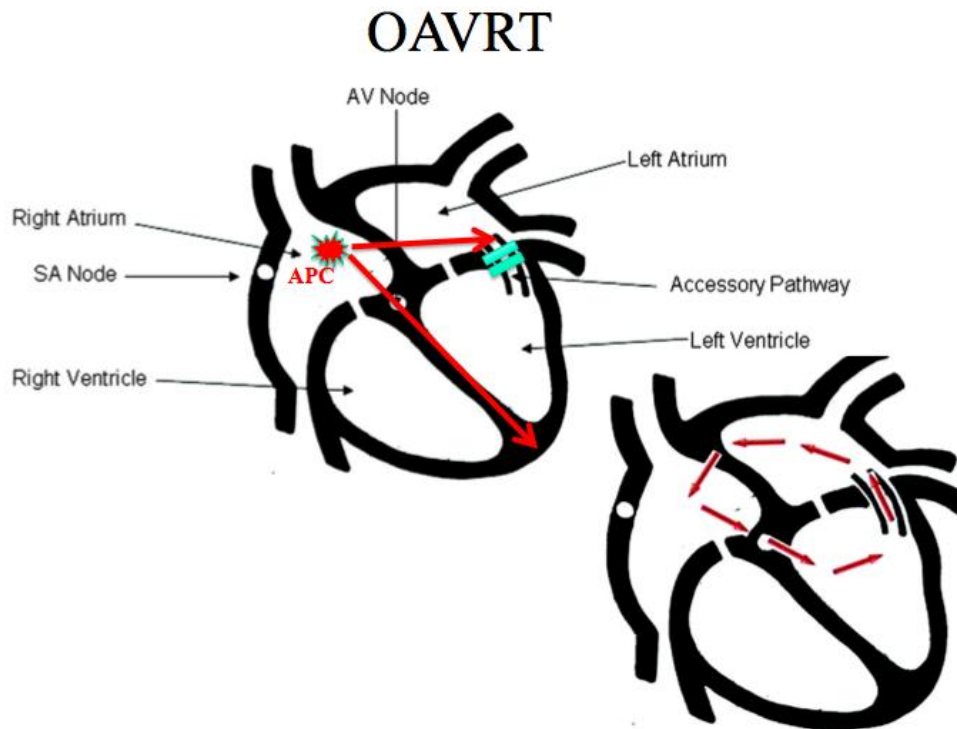
If AP only conducts unidirectionally from V to A (retrograde), will not see pre-excitation on surface ECG in sinus rhythm i.e. no manifestations of WPW are evident and the pathway is termed “concealed”. Remember that OAVRT can still occur with a concealed pathway, as long as it conducts retrogradely during the tachycardia (see OAVRT section below). EP studies suggest that in dogs most APs are:

- Right-sided
- Unidirectional with retrograde conduction (i.e. approx. 75% are concealed)
- Are associated with various arrhythmias, including orthodromic atrioventricular reciprocating tachycardia (OAVRT) and atrial fibrillation (Ref: Santilli et al JAVMA 2007).

Accessory pathways have been described predominantly in young Labradors and Boxers. Typically these dogs will present with a history of narrow QRS complex tachycardia causing exercise intolerance, episodic weakness, or heart failure secondary to tachycardia-induced cardiomyopathy. It is possible also to occasionally find what appear to be delta waves on ECG in cats and dogs as “incidental findings”.

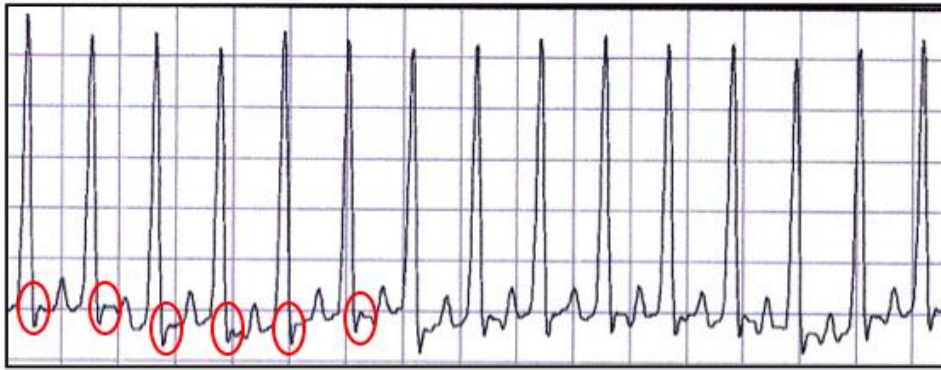
### Orthodromic AV Reciprocating Tachycardia (OAVRT)

OAVRT is usually initiated by APC. The APC blocks in refractory accessory pathway (as RP of AP is longer than AVN) but conducts anterograde through AVN. It then conducts retrograde (ie. from V to A) through the recovered accessory pathway. This results in a macro-reentrant narrow complex tachycardia.



OAVRT ECG features include:

- Rapid, regular SVT.
- Narrow, normal morphology QRS (unless BBB).
- P' waves retrograde (-) II, III, aVF.
- P' waves within ST segment.
- Short RP', long P'R.
- Abrupt onset and offset.
- AV nodal dependent (ie. SVT ceases with AV block).

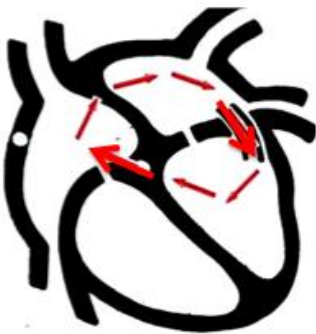


- Rapid, regular SVT HR = 280 bpm 25 mm/sec, 10 mm = 1mV
- Narrow, normal morphology QRS
  - Unless BBB
- P' waves retrograde and within ST segment
- Short RP' , long P' R

#### Antidromic AVRT

This is an unusual situation (rare in humans). AP conducts anterograde during SVT. Impulse travels retrograde through AVN. Therefore the tachycardia has a wide QRS morphology as the total ventricular activation occurs over AP.

There is a single report of anterograde conduction through an AP during tachycardia in a dog (confirmed by EP). The dog had pre-excited atrial fibrillation (Ref: Santilli et al ECG of the month JAVMA 2010).

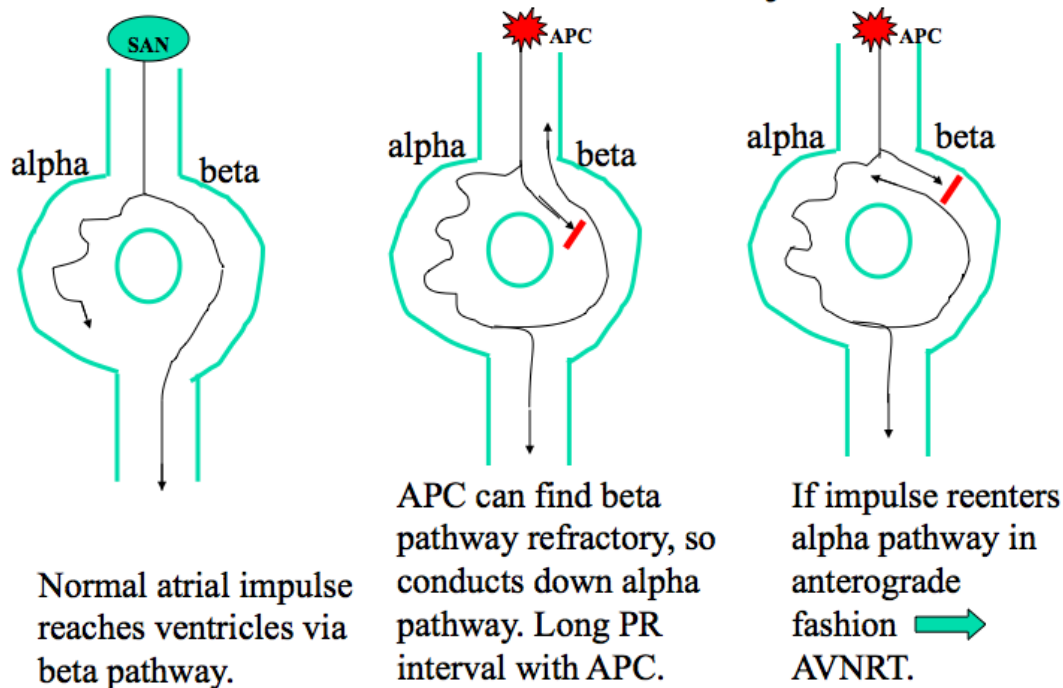


### AV nodal reentrant tachycardia (AVNRT)

In patients with this condition, the AV node is functionally divided into 2 pathways (alpha and beta). Alpha pathway has SLOWER conduction and has SHORTER refractory period. Beta pathway has FASTER conduction and has a LONGER refractory period.

### Atrial flutter

## AV nodal re-entrant tachycardia



Atrial flutter (AFL) is a macro-reentrant atrial tachycardia. It is characterised by an organized atrial rhythm typically > 300 bpm, with a classical “saw tooth” pattern in leads II, III and/or aVF. There are two forms of cavo-tricuspid isthmus (CTI)-dependent AFL, termed typical and reverse typical:

- During typical AFL the activation wave front turns counterclockwise around the tricuspid valve annulus
- During reverse typical AFL it turns clockwise.

Both can be treated with RFA (Ref: Santilli et al JVC 2010).

Recently, atypical AFL was confirmed in dogs and treated with RFA. This is non-CTI-dependent, usually more rapid and irregular, with variable flutter wave morphology and in humans often proven to be prefibrillatory (Ref: Santilli et al JVC 2014).

### Atrial fibrillation

Sinus impulses are “overdrive suppressed” by disorganised electrical impulses originating in atria and pulmonary veins. In dogs, AF typically occurs secondary to significant underlying structural heart disease. In this situation it is often persistent, although some dogs seem to develop paroxysmal AF.

Dogs with structurally normal hearts can develop AF in situations that enhance vagal tone e.g. after morphine administration. The proposed mechanism is vagally induced shortening of atrial AP duration and increase in heterogeneity of refractoriness (Ref: Moise et al JVC 2005). There is a recent report of changes of autonomic nervous balance during presumed reflex syncope inducing paroxysmal vagal atrial fibrillation in dogs (Ref: Porteiro Vazquez et al JVC 2016).

It is important to differentiate SVTs with wide QRS complexes from VT

Wide complex SVT can be caused by:

- Acceleration (tachycardia) dependant block (ie. impulses are conducted with aberrancy at rapid heart rates as a result of incomplete recovery of refractoriness - this is the usual mechanism for premature P' waves that conducts with a functional BBB.
- Pre-existing BBB (ie. also present in sinus rhythm)

Assessment of previous ECGs from the same patient or performing vagal manoeuvre to attempt to terminate SVT to assess QRS morphology when patient in sinus rhythm can be helpful.

#### Ventricular tachyarrhythmias

The same mechanisms underlie ventricular tachyarrhythmias ie. abnormal automaticity, triggered activity and re-entry.

Accelerated idioventricular rhythm is due to abnormal automaticity within the ventricular myocardium. It is frequently seen in association with systemic disease:

- Splenic disease
- Traumatic myocarditis (secondary to road traffic accident or other blunt thoracic trauma)
- IMHA
- GDV

Torsade de Pointes is initiated by triggered activity (EADs).

It has characteristic upward and downward deflections of the QRS complexes around the baseline - the term Torsade de Pointes means "twisting about the points."

Caused by:

- Drugs which lengthen the QT interval such as quinidine
- Electrolyte imbalances, particularly hypokalemia
- Myocardial ischemia

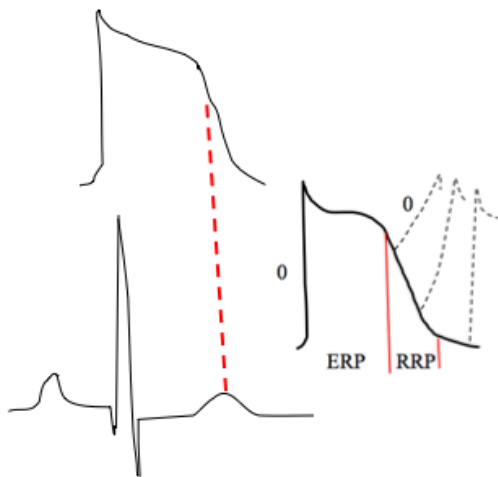
Treatment:

- Synchronized cardioversion is indicated when the patient is unstable.
- IV magnesium
- IV Potassium to correct an electrolyte imbalance
- Overdrive pacing

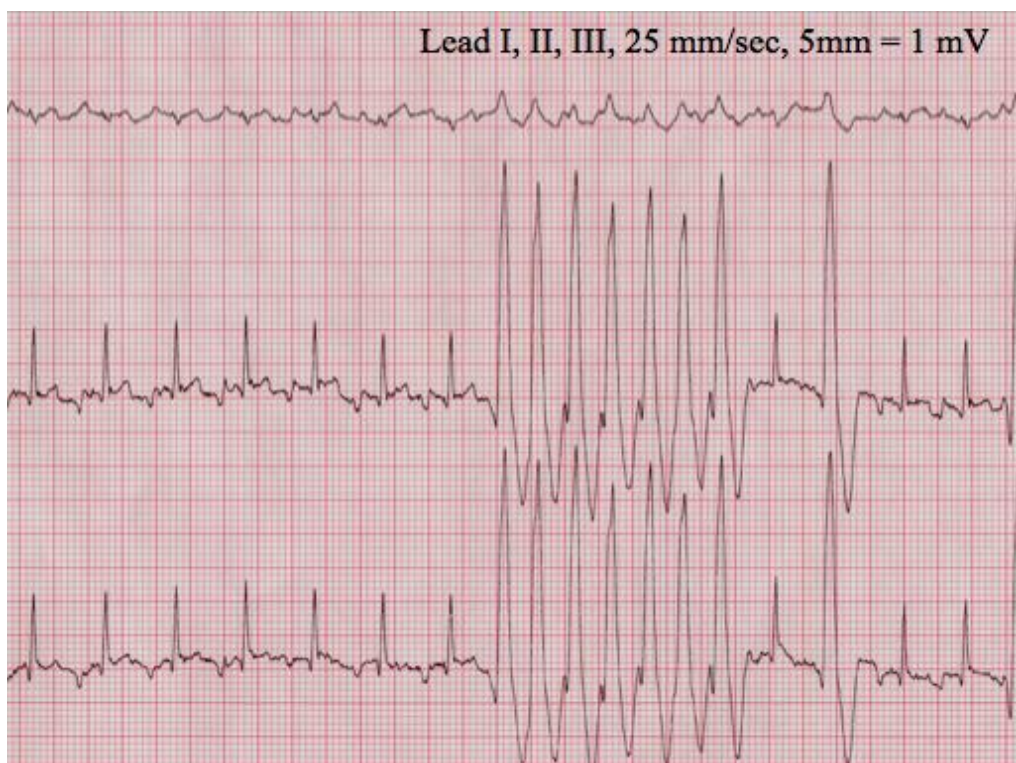
R on T phenomenon is associated with ventricular re-entry.

Premature impulses elicited during the peak of the T wave result in dispersion of refractoriness within the ventricular myocardium. Can be accentuated by cardiac disease and can lead to ventricular fibrillation.





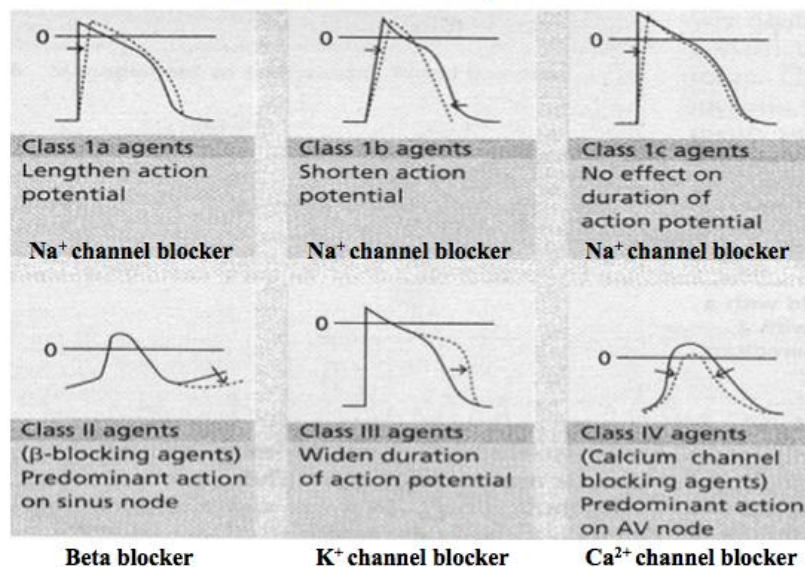
If impulse occurs during  
RRP, will produce AP  
with slow phase 0



## Antiarrhythmic drugs and their effect on the cardiac action potential

The cardiac rhythm is largely determined by the shape of the cardiac action potential. The effect of antiarrhythmic drugs is determined by how they change that action potential shape.

### Antiarrhythmic drugs have distinct characteristics depending on which ion channels they block



## Classification of antiarrhythmic drugs

**Class I:** Sodium channel blockers (membrane-stabilizing agents)

**1 a:** Block  $\text{Na}^+$  channel and prolong action potential (quinidine, procainamide)

**1 b:** Block  $\text{Na}^+$  channel and shorten action potential (lignocaine)

**1 c:** Block  $\text{Na}^+$  channel with no effect on action potential (flecainide)

**Class II:**  $\beta$ - blockers (esmolol, atenolol, propranolol)

**Class III:** Potassium channel blockers - main effect is to prolong the action potential (amiodarone, sotalol)

**Class IV:** Slow (L-type) calcium channel blockers (diltiazem)

Vaughan Williams classification



Other miscellaneous antiarrhythmics:

Digoxin is not in the Vaughan Williams classification. It is a cardiac glycoside (digitalis, foxglove). It acts on Na/K-ATPase of cell membrane (inhibits  $\text{Na}^+/\text{K}^+$  pump, increases intracellular  $\text{Na}^+$  and calcium)/ increases vagal activity. Therefore it increases cardiac contraction and slows AV conduction by increasing AV node refractory period.

Magnesium is also not in the Vaughan Williams classification. The mechanism of action is not known. It is used for digitalis-induced arrhythmias and in Torsade de pointes, even if serum magnesium is normal.

In summary, anti-arrhythmic drugs are classified by their effect on the cardiac AP. Not all drugs fit this classification. In clinical practice, treatment of arrhythmias is determined by the type of arrhythmia (SVT, VT) and clinical condition of the patient.

The biggest problem is that antiarrhythmics can cause arrhythmia! e.g. treatment of a non-life threatening tachycardia may cause fatal ventricular arrhythmia.

Therefore it is important to be vigilant in determining dosing, blood levels and in follow-up when prescribing antiarrhythmics to our patients.