



Drugs Used In The Management Of Atrial Fibrillation

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Outline of session

- *Unfortunately individual cases cannot and will not be discussed!*
- Beta-blockers
- Calcium channel blockers
- Flecainide & propafenone
- Amiodarone
- Little about Dronedronarone

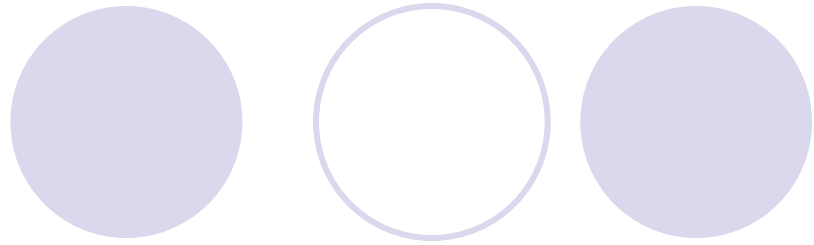
Vaughn-Williams Classification

- I - sodium channel blockers
- II - Beta blockers
- III – Potassium channel blockade
- IV – calcium channel blockers
- Ia – e.g. procainamide
- Ib – e.g. lignocaine
- Ic – e.g. flecainide
- III – e.g. Amiodarone, dofetilide
- NB Sotalol is II and III



Beta blockers

- **Propranolol**
- **Metoprolol**
- Acebutalol
- Labetalol
- **Atenolol**

- 
- Oxprenolol
 - ***Sotalol***
 - **Esmolol**
 - **Bisoprolol**

Beta Blockers – decrease sympathetic tone

● Action

- Antagonise the effects of catecholamines (hormones like adrenaline) on the heart.
- They block beta adrenoreceptors, hence name (duh!)
- Catecholamines, via the so-called *sympathetic nervous system*, are like the “accelerator” on heart and blood vessels

Beta-receptors

A decorative graphic consisting of two groups of three circles. The first group on the left has a solid light purple circle, a white circle with a light purple outline, and another solid light purple circle. The second group on the right has a solid light purple circle, a white circle with a light purple outline, and another solid light purple circle.

- There are many different types of **beta-receptor**, but basically some are more prevalent in the heart, and others in the lung
- However, they are found basically *everywhere* in the body

Side effects

A decorative graphic consisting of two overlapping circles on the left and three separate circles on the right. The circles are light purple with a thin white outline. The first circle on the left is solid purple, while the second is hollow. The three circles on the right are also solid purple.

- Slow pulse, too low blood pressure, cold hands/toes, tiredness/lethargy
- Dose-dependent on which beta blocker used, and varies between individuals

Uses



- Good for AF rate control (NICE 1st line)
- May prevent/reduce attacks of paroxysmal AF in patients with catecholamine-sensitive triggers
- Some used in heart failure treatment (bisoprolol, carvedilol) – a concept that was heresy only as far back as 1995

Verapamil – Calcium (Ca) Antagonist

● Action

- Inhibits slow inward Ca current in smooth muscle and cardiac cells,
- Slows AV node conduction [main 'junction box' in the heart...]
- ... Hence slows ventricular response to atrial fibrillation/flutter
- May suppress Sinus node function [natural pacemaker]



Other points to consider

- Has negative inotropic effect – i.e. decreases **force** of contraction in the heart
- **Caution...**
 - ...if patient has received beta blocker!
 - Also care required in patients with poor myocardial function- hypotension or VT

Uses



- Good for prevention of SVT, but does not prevent AF.
- Excellent rate control for AF in those unable to take Beta-blockers
- Good drug to combine with Digoxin, but not beta-blockers

Verapamil – Bluffer's guide



- Like all Calcium channel blockers, Verapamil is in Vaughn-Williams Class IV
- It primarily acts on AV node and His-purkinje system

Other calcium channel blockers



- Diltiazem – very similar to verapamil
- Amlodipine – little effect on heart conduction, better on relaxing arteries, hence excellent for Blood pressure treatment, and useless for rate control

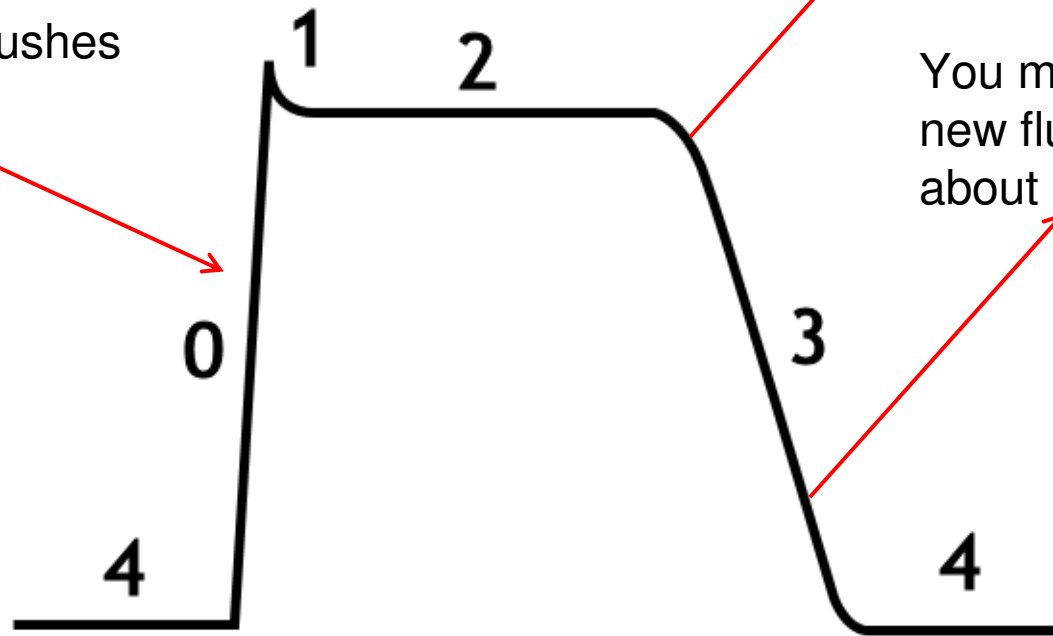
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Cardiac Action Potential – a bit like a toilet flush!

Cistern just about refilled

Chain pulled, loo flushes



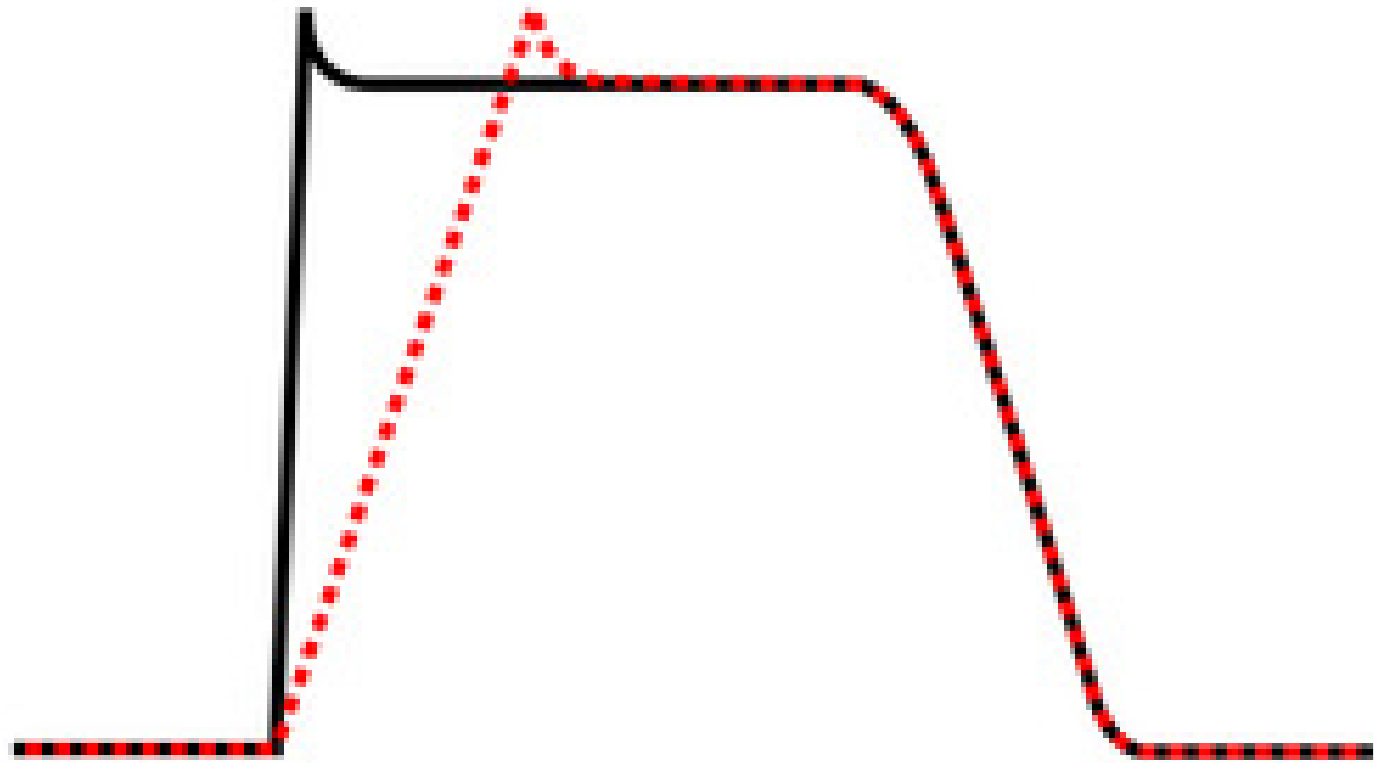
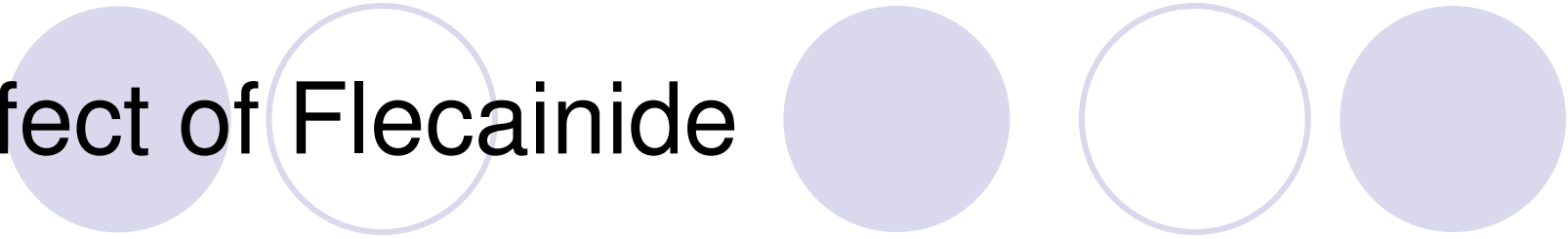
You might manage a new flush anywhere about here

Flecainide- Class 1c Antiarrhythmic

- **Action**

- Binds to sodium channel, decreases speed of depolarisation (phase 1 of action potential)
- **Slows conduction** in the atria, His-purkinje fibres, accessory pathways and ventricles
- Causes slight prolongation of QRS complex, but not QT interval

Effect of Flecainide





Flecainide

- Effective and safe in treatment of atrial fibrillation with structurally normal hearts
- However effects often wane after 2 or 3 years for some patients...

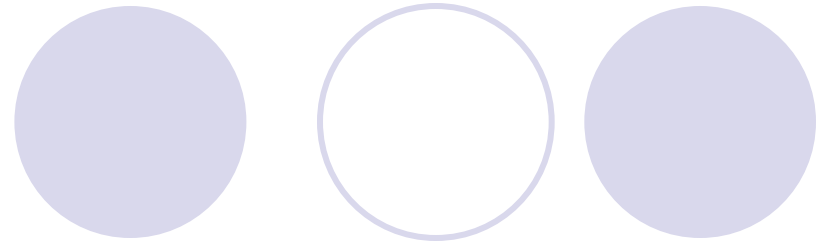
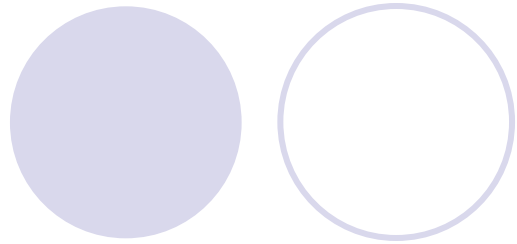
Flecainide – bluffer's guide

- F1ecainide – class Ic
- For 'Action' think:
 - for AF, it's like tadpoles (AF wavelets) swimming in water (spreading across the atria); flecainide turns the pond water into syrup!



Caution!

- Due to negative inotropic effect should be avoided in patients with heart failure (but see below anyway)
- Can be pro arrhythmic – especially in LV dysfunction and acute ischaemia
- Can paradoxically worsen atrial arrhythmias – slowing of atrial rate may facilitate 1:1 conduction of flutter



- **Side effects**

- Visual disturbance

- Light headedness

- nausea

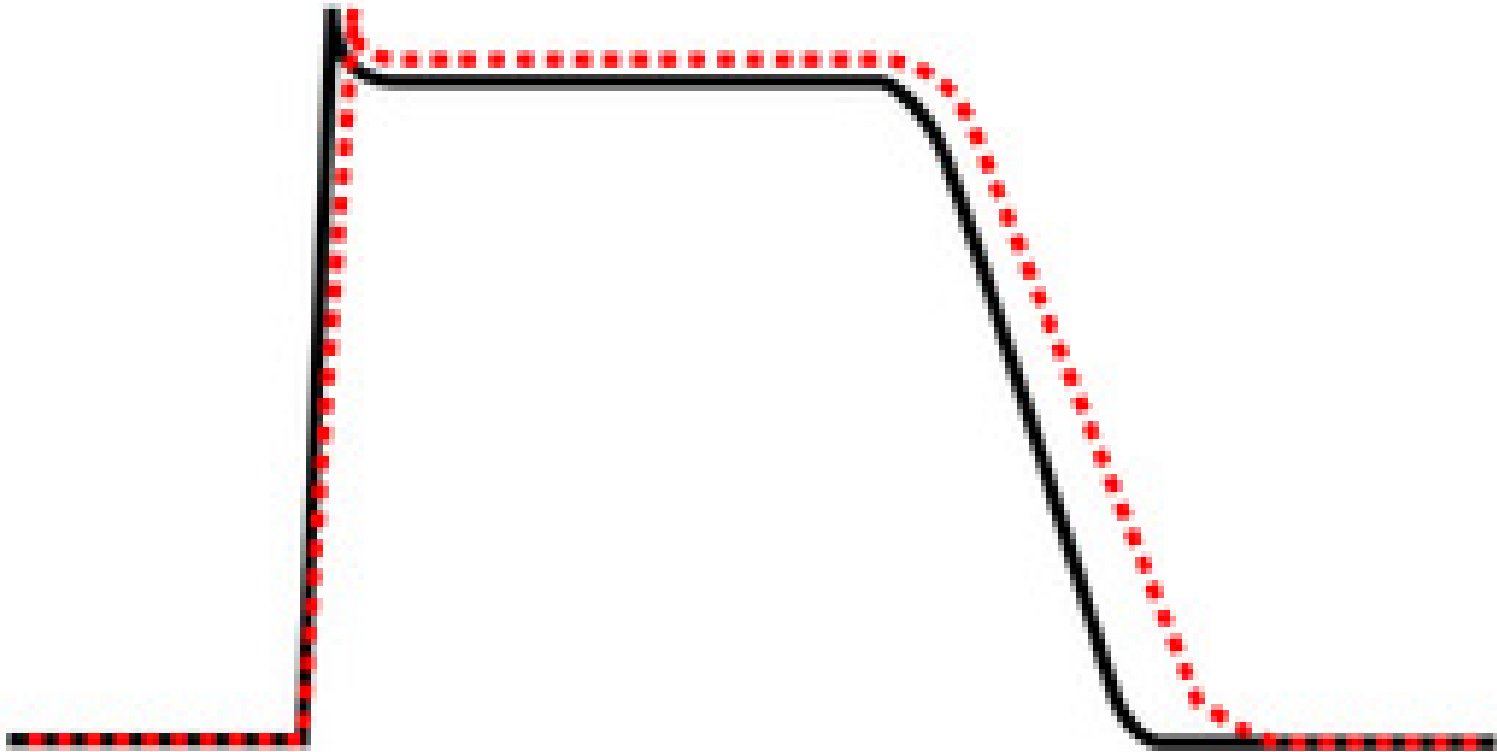
- Can increase pacing threshold in those with pacemakers implanted

Amiodarone- Class III Antiarrhythmic

- **Action**

- “Broad spectrum” antiarrhythmic highly effective in treatment of supraventricular and ventricular rhythm disorders
- Utterly over-used, especially by non-cardiologists!
- Prolongs refractoriness (makes cells lazier)

Effect of Amiodarone





Amiodarone – Bluffer's guide

Class III drug

Think:

after flushing your toilet, it takes longer to re-fill the cistern, so you cannot flush it again quite so quickly

Most amiodarone in the body just 'hangs around' in muscles doing nothing...

...active drug in blood is a small fraction



- **Caution!**

- Sinus bradycardia
- Thyroid dysfunction
- Iodine sensitivity
- Pregnancy

Side Effects

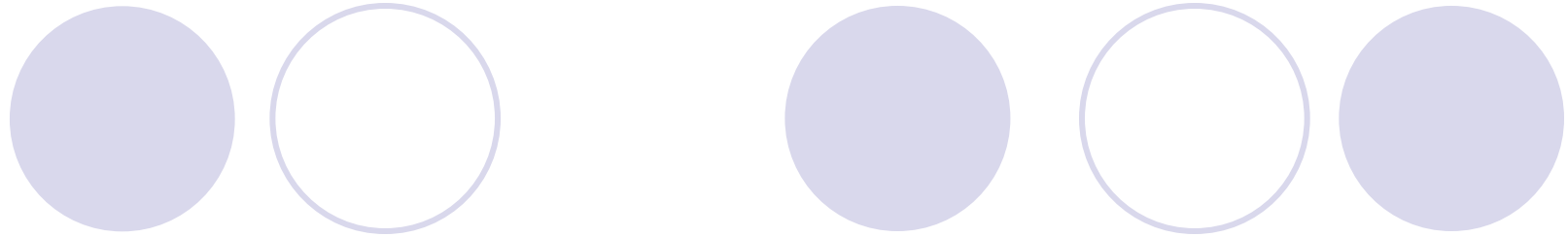


- Reversible corneal deposits (disappear if drug stopped)
- Skin photosensitivity/slate grey skin discoloration
- Hypo/hyperthyroidism
- Lung fibrosis
- Bradycardia and conduction disturbances
- Can effect liver function
- Can effect renal function/thrombocytopenia
- Nausea, rash, alopecia, tremor, insomnia, nightmares



Other points to consider

- Can potentiate warfarin
- Can increase blood levels of digoxin, quinidine and flecainide
- Liver function, thyroid function test required before treatment and every 6 months
- Chest X ray performed prior to commencing drug



- **Half Life** 2 weeks to 3 months
- **Dosage** (oral)
 - Loading dose often required
 - Action may take 1-3 weeks to occur even after loading doses

A decorative graphic consisting of six circles arranged in a horizontal line. The first circle is solid light purple. The second circle is white with a light purple outline. The third circle is solid light purple. The fourth circle is white with a light purple outline. The fifth circle is solid light purple. The sixth circle is solid light purple.

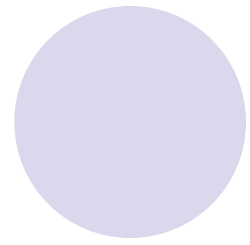
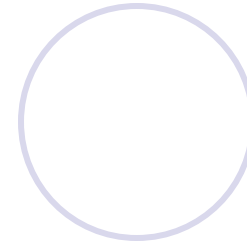
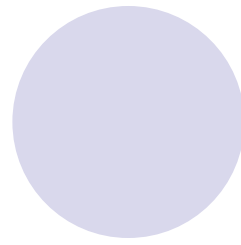
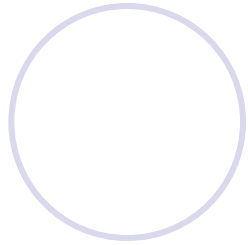
Drodenarone

- Amiodarone without the side effects!
- May become 'gold standard' in AF, but...
- ...possibly less good in AF with heart failure.

Digoxin

- Enhances vagal tone [the “brakes” on the heart via the so-called *parasympathetic nervous system*]
- Vagal tone is withdrawn first at the onset of exercise...
- ...hence Digoxin is not a great 1st line treatment in active patients

Digoxin



- Most of the drug ‘hangs around in muscles’ doing nothing, with small fraction in blood that is active
- Hence interacts with amiodarone
- Too much is poisonous!
- Works extremely well in combination with verapamil

Digoxin is weakly positively inotropic...

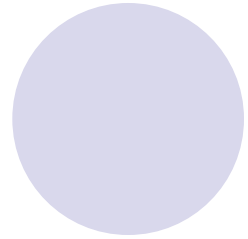
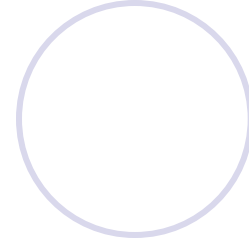
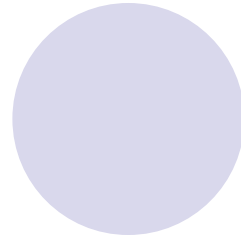
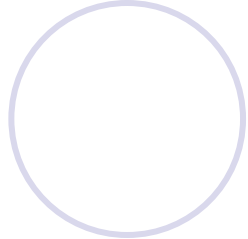
- In other words it has a weak tonic effect on the heart...
- ...this is in contrast to every other anti-arrhythmic drug

Warfarin



- Block Vitamin K in the gut, which is required to make clotting factors
- INR is a ratio as to how much longer the blood will take to clot as compared to 'normal' (an average)
- Works in the liver, where clotting factors are made...
- ...hence influenced by other drugs and foods!

Aspirin



- Makes platelets less sticky
- Has no effect on clotting factors



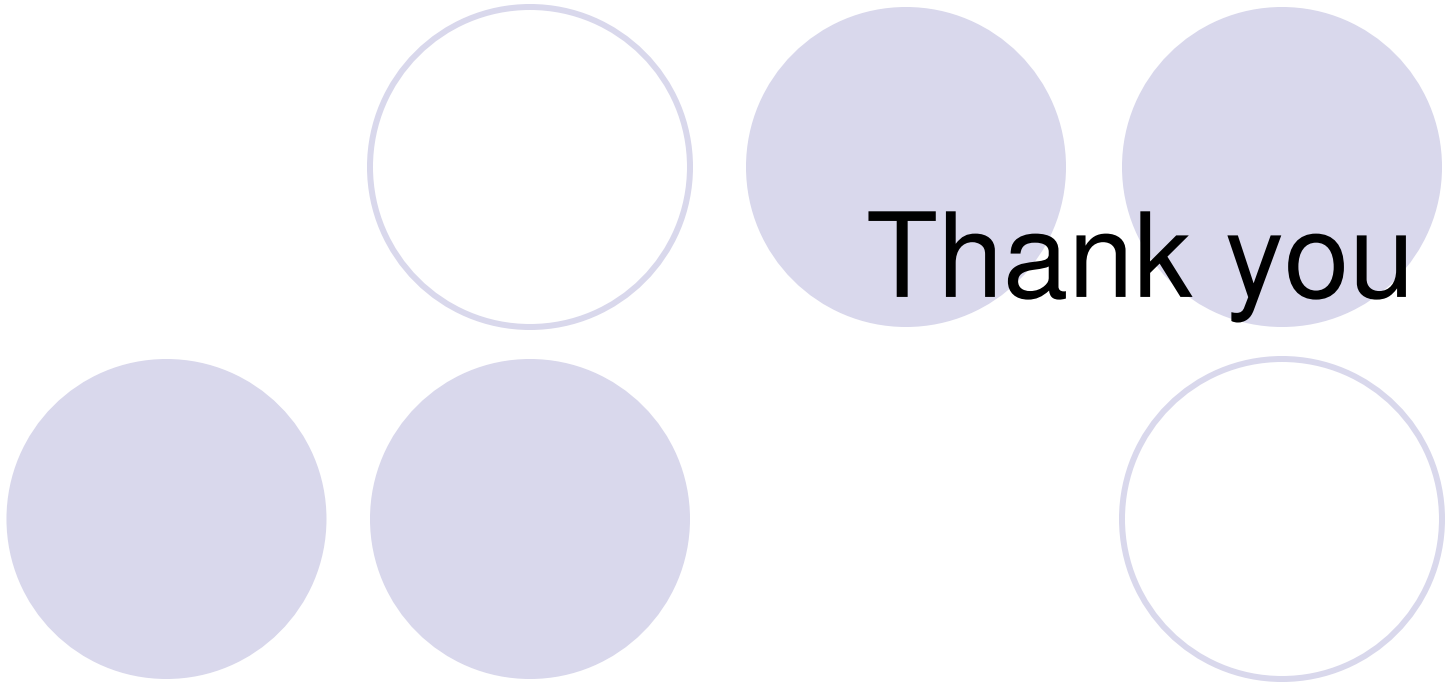
Summary

- All anti-arrhythmic drugs act by altering conduction in the heart.
- The receptors and nerves influenced by these drugs are often found in other tissues outside the heart...hence side effects

Summary



- Some important drugs ‘fill up seats’ in muscles or fat tissue doing nothing, and it’s only when all the ‘seats are taken’ that the drug spills out into blood where it is active.
- Some drugs ‘compete for these seats’ and thus can influence active levels of each other



Thank you

Adenosine



- **Action**

- Blocks AV node conduction
- Shortens atrial refractoriness –
“recover quicker/less lazy”
(hence may promote AF)
- May have some effect on SA
node

Adenosine - Uses



- Clinically:

- Terminate SVTs via nodal block
- Differentiate VT (*NB at high enough dose*)
- Unmask a latent accessory pathway

- In EP lab:

- May aid in assessing a septal concealed accessory pathway

Adenosine – miscellanea



- May terminate around:
 - 15% of automatic atrial tachycardias
 - 10-15% of fascicular VT
 - 10-15% RVOT VT
 - 5-10% typical atrial flutter
- Beware the ‘rebound sympathetic drive’ and resultant sinus tachycardia!

Caution!



- May cause sinus bradycardia, which may be more prolonged in patients with sick sinus syndrome
- In patients with asthma may cause bronchospasm (*but this is rare, and often overplayed*)
- It should only be given with crash trolley to hand
 - *and with this caveat, it is safe to give to pre-excited AF in my opinion*



- **Half Life - 20-30seconds**

- **Side Effects**

- Chest tightness

- Dyspnoea

- Flushing

- Patient may experience impending sense of doom

- **Administration-Rapid bolus, with defib on hand**

Adenosine doses



- **Manufacturer's recommended Dose:-**
Rapid 3mg bolus, if no reversion to sinus rhythm after 1 min give 6mg, then 12mg, then 18mg this is the maximum dose
- **Real life:** Start at least at 6mg, and 'personal best' is 36mg



Atropine

- **Action**

- Blocks vagal stimulation – hence may alleviate vagally-mediated bradycardia & vaso-vagal symptoms in lab

- NB it will not reverse heart block due to conduction tissue disease, or damage from RF!



When would we use it in the lab?

- If patient has vagal event i.e during vascular access / following sheath removal
- May aid initiation of SVT (“slick-up” the AV node)

Side Effects

A decorative graphic consisting of two overlapping circles on the left and three separate circles on the right. The circles are light purple, with the leftmost one being solid and the others being hollow outlines.

- Urinary retention
- Dry mouth
- Dilated pupils
- Visual disturbances
- Confusion
- **Dose**
- 500/600mcg rapid bolus; at 3mg vagus is maximally blocked