

ANTI-ARRHYTHMICS AND WARFARIN

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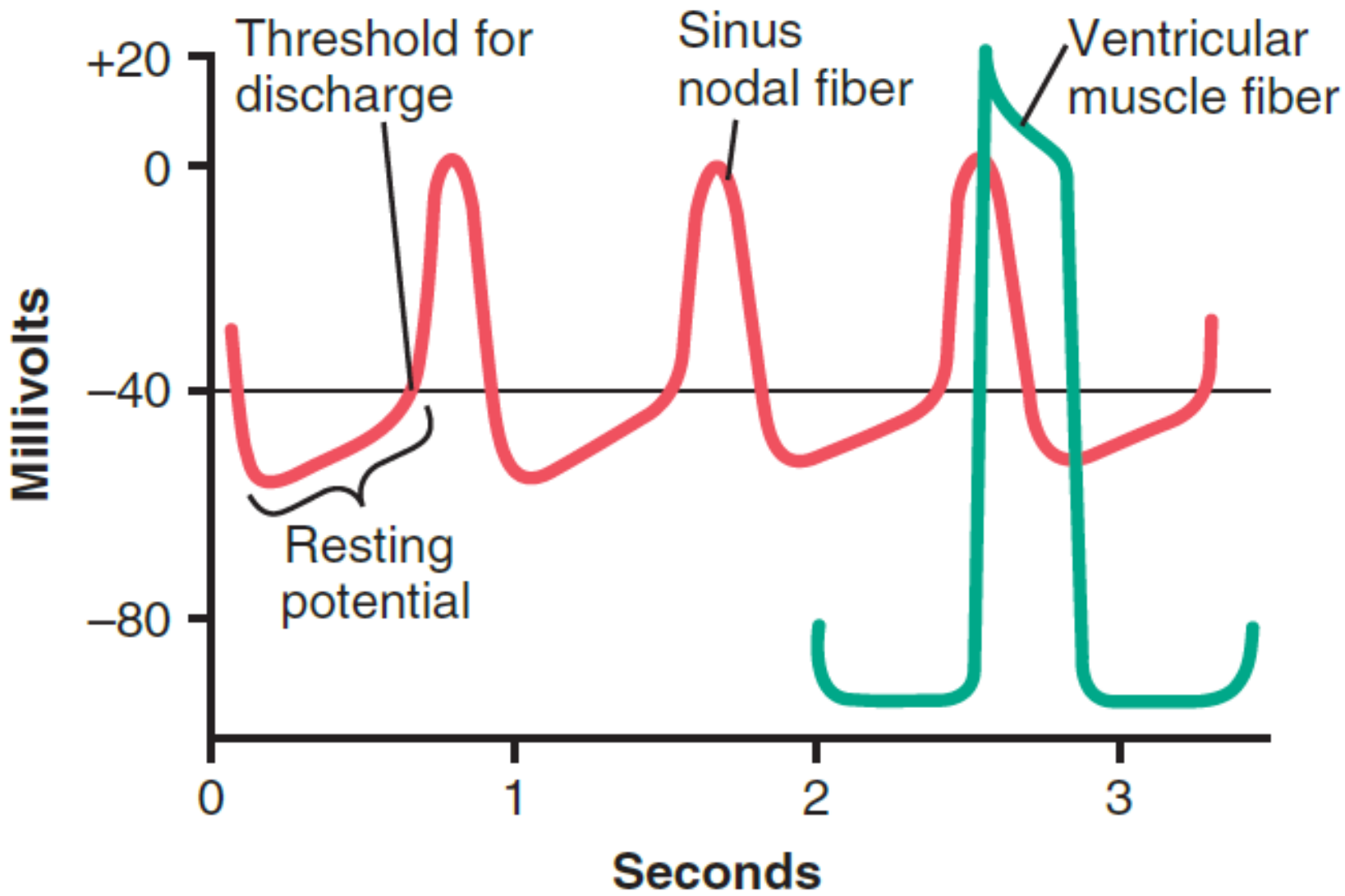
Pacemaker & myocardial potentials

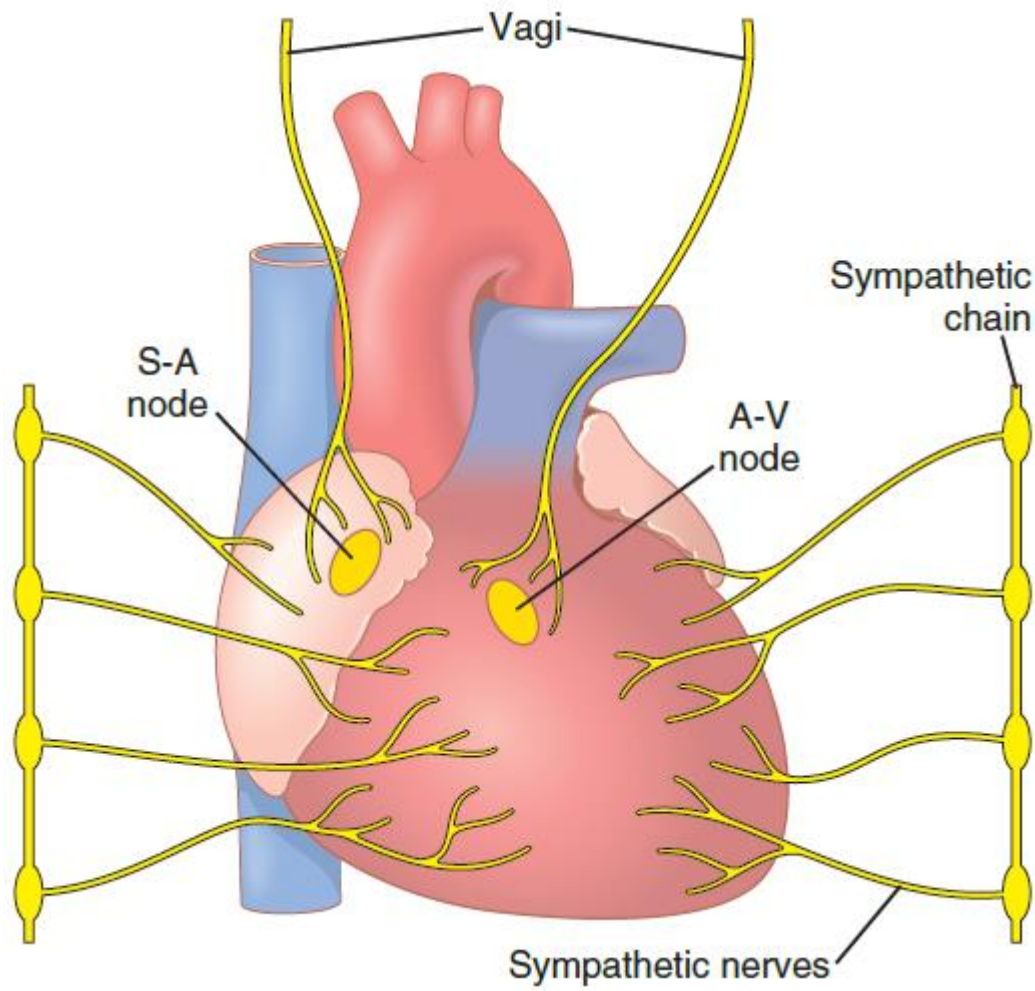
➤ Pacemaker potentials

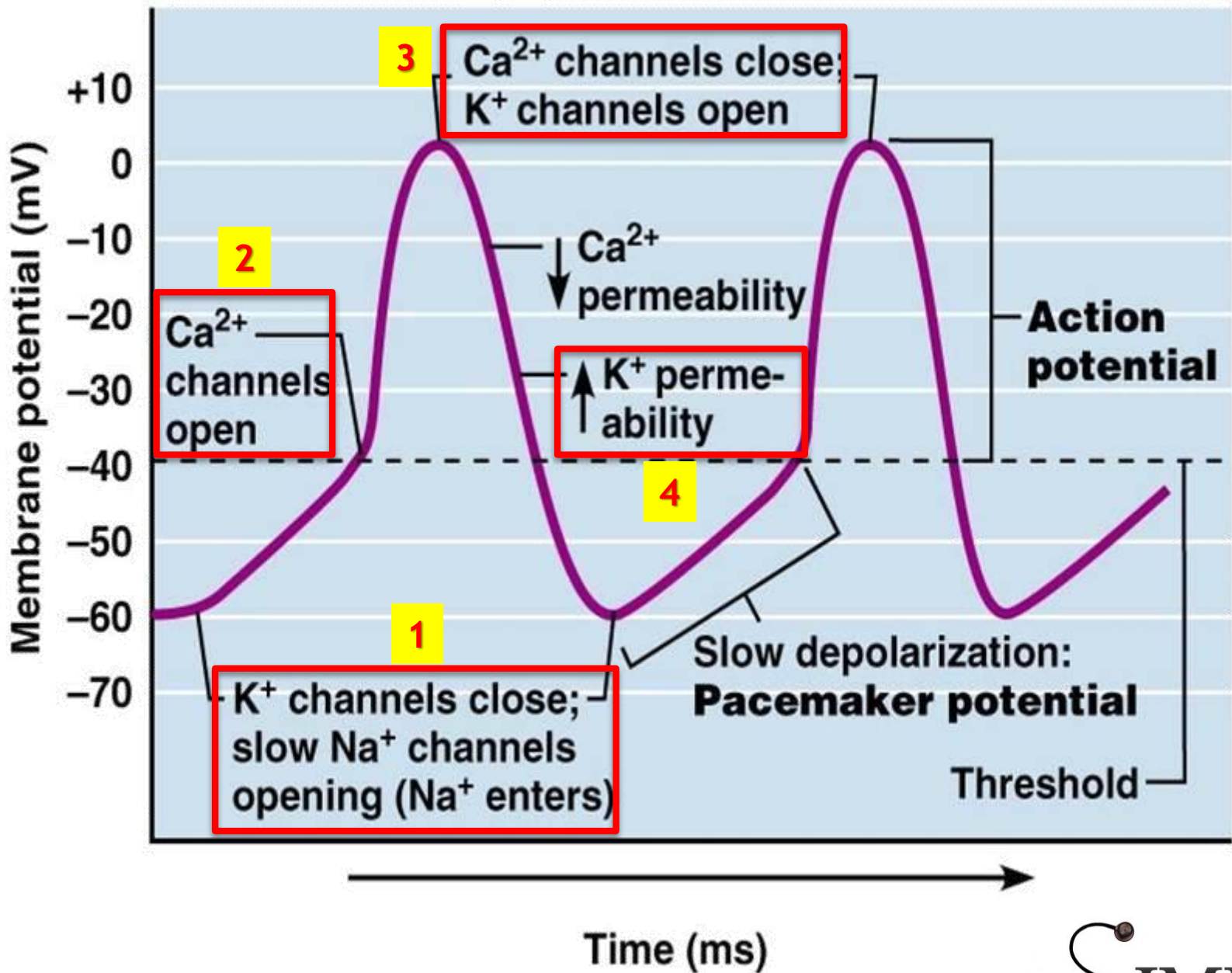
- Originate at rapidly conducting tissue
- SAN → AVN → Bundle of His → Ventricular fibres
- SAN ordinarily sets the pace [70-80/min]
- Sympathetic and parasympathetic input

➤ Myocardial potentials

- Stimulated by pacemaker potentials
- Atrial and ventricular muscle
- Sympathetic input only







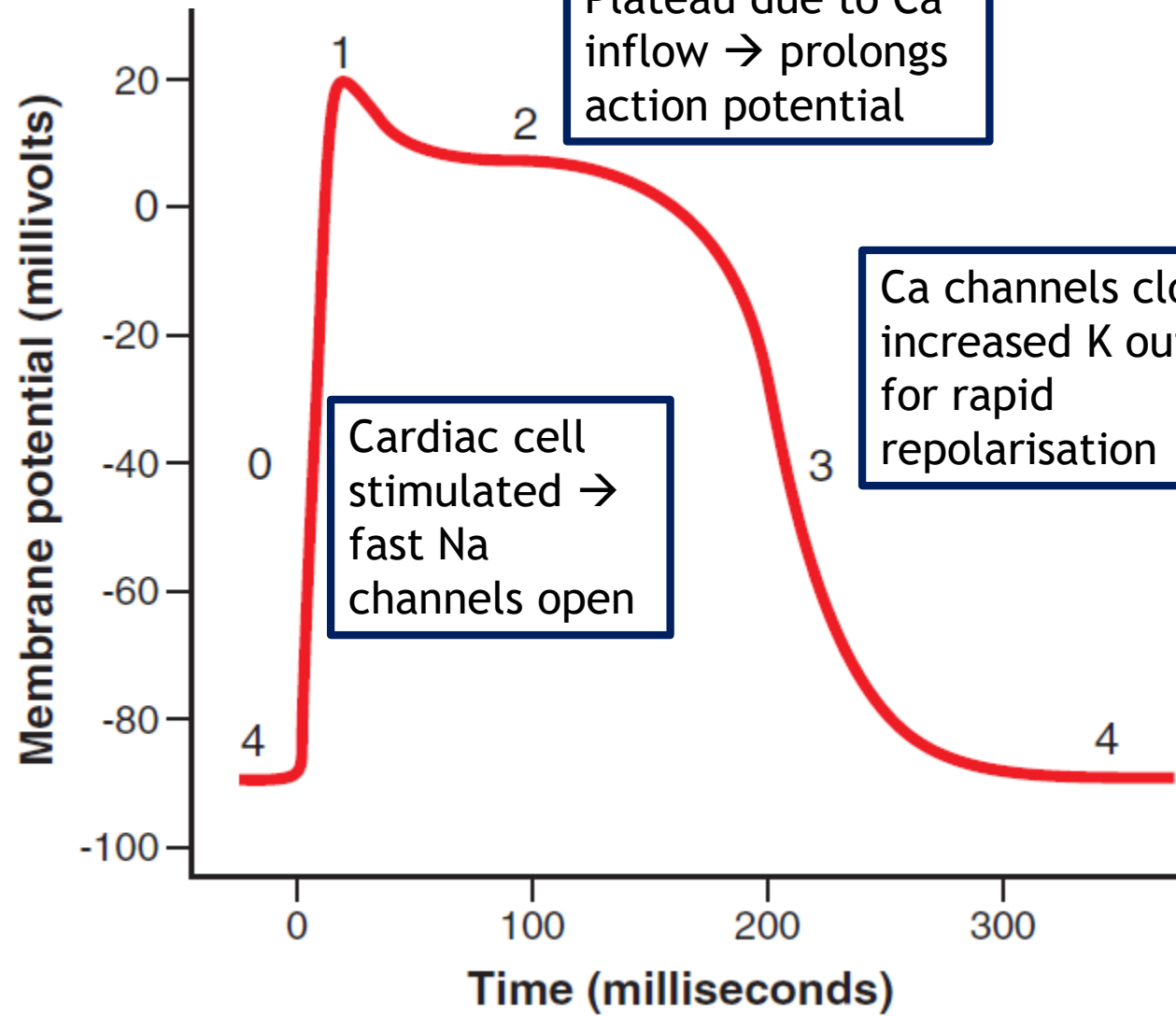
Fast Na closes
→ K channels
open

Plateau due to Ca
inflow → prolongs
action potential

Ca channels close →
increased K outflow
for rapid
repolarisation

Cell membrane
returns to resting
potential

Cardiac cell
stimulated →
fast Na
channels open



Anti-arrhythmics

- Vaughan-Williams classification
 - According to predominant mechanism of action
- 4 classes
- Amiodarone; digoxin; adenosine
- Rx for tachyarrhythmias
- [Atropine]

Tachyarrhythmias

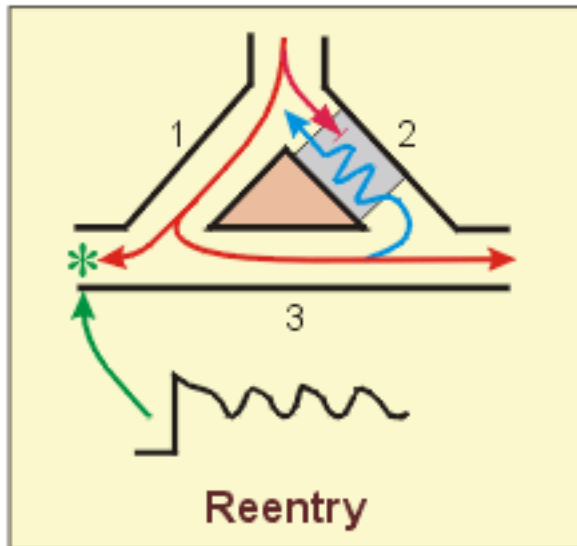
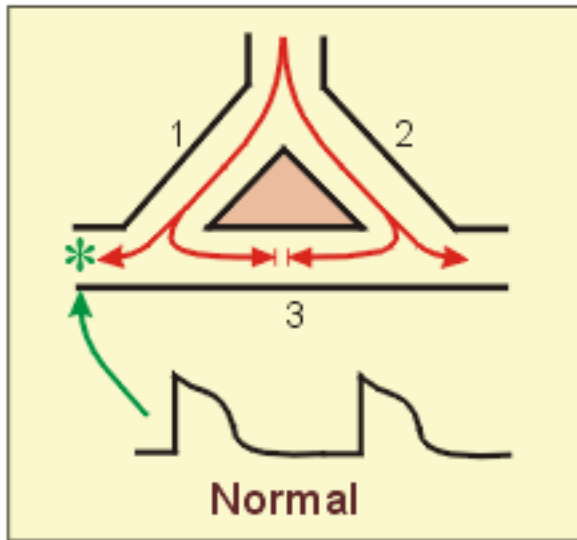
➤ Enhanced automaticity

- More active than usual (catecholamines; sepsis; electrolyte imbalance)

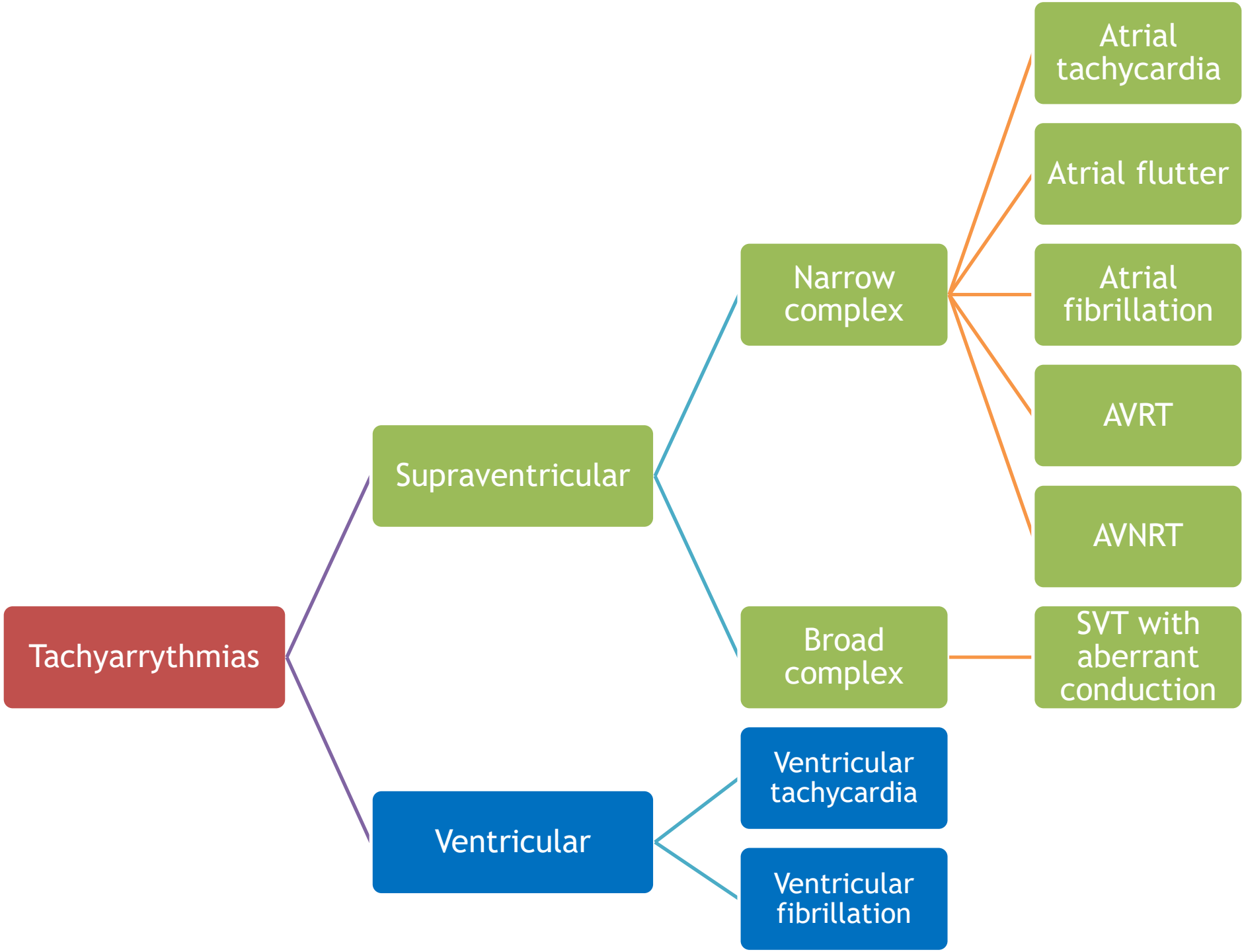
➤ Triggered activity

➤ Re-entry

- A propagating impulse fails to die out after normal activation of the heart and persists to re-excite the heart after expiration of the refractory period

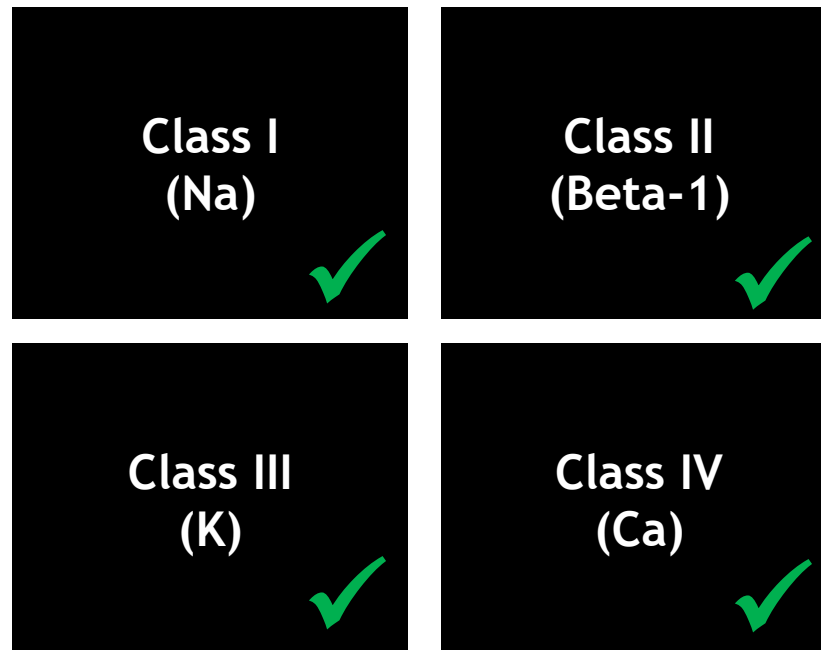


Class	Site	Mechanism	Example
I [Ia; Ib; Ic]			
II			
III			
IV			



Atrial fibrillation

- Multiple re-entry mechanisms



Atrial fibrillation

➤ Rate vs rhythm control

Flecainide	
<i>Indication in AF</i>	Paroxysmal AF ('pill in the pocket')
<i>Mechanism</i>	Class Ic
<i>Contraindications</i>	Structural heart disease LVF
<i>Side-effects</i>	Proarrhythmic AV blocks Dizziness

Atrial fibrillation

➤ Rate vs rhythm control

Amiodarone	
<i>Indication in AF</i>	Maintain sinus rhythm
<i>Mechanism</i>	Class III [all classes]
<i>Contraindications</i>	AV block
<i>Side-effects</i>	Pneumonitis Bradycardia/AV block Hepatitis Photosensitivity Hypo/hyperthyroidism Prolongs QT

A



B



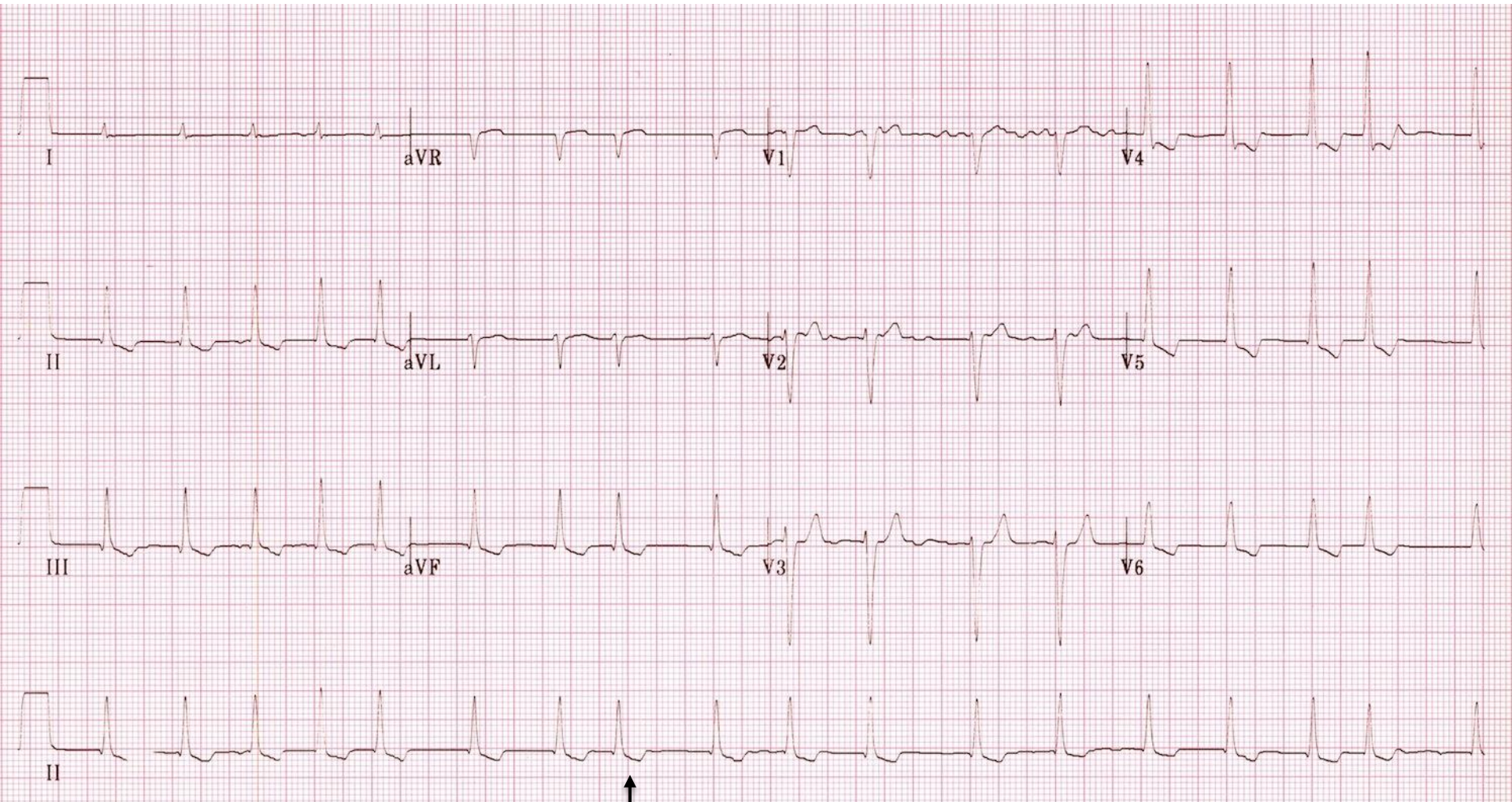
Atrial fibrillation

- Heart failure and AF
 - Avoid class IV (negatively chronotropic)
 - Rate control with beta-blocker ideal
 - Digoxin is alternative when other rx failed

Digoxin

<i>Indication in AF</i>	Rate control in heart failure
<i>Mechanism</i>	Increases vagal tone (less so in exercise) Na/K-ATPase inhibitor - positively inotropic
<i>Side-effects</i>	GI s/e - anorexia; N&V; diarrhoea AV block Dizziness
<i>Monitoring</i>	Heart rate Renal function - renal clearance Hypokalaemia

Digoxin effect - therapeutic doses



Reverse-tick ST depression

Digitalis toxicity

Clinical features

- Cardiac → any arrhythmia; PVC / brady
- GI symptoms → anorexia; N&V; diarrhoea
- CNS symptoms
 - Visual changes [yellow-green distortion]
 - Drowsiness
 - Lethargy
 - Headache

Biochemical features

- Hyperkalaemia
- [renal dysfunction]
- Serum digoxin level

Management

- Digifab (digoxin-specific antibody fragments)

AVNRT

- Re-entry mechanism
 - AVN is focus of re-entry

Class I (Na)	Class II (Beta-1) ✓
Class III (K)	Class IV (Ca) ✓

AVNRT

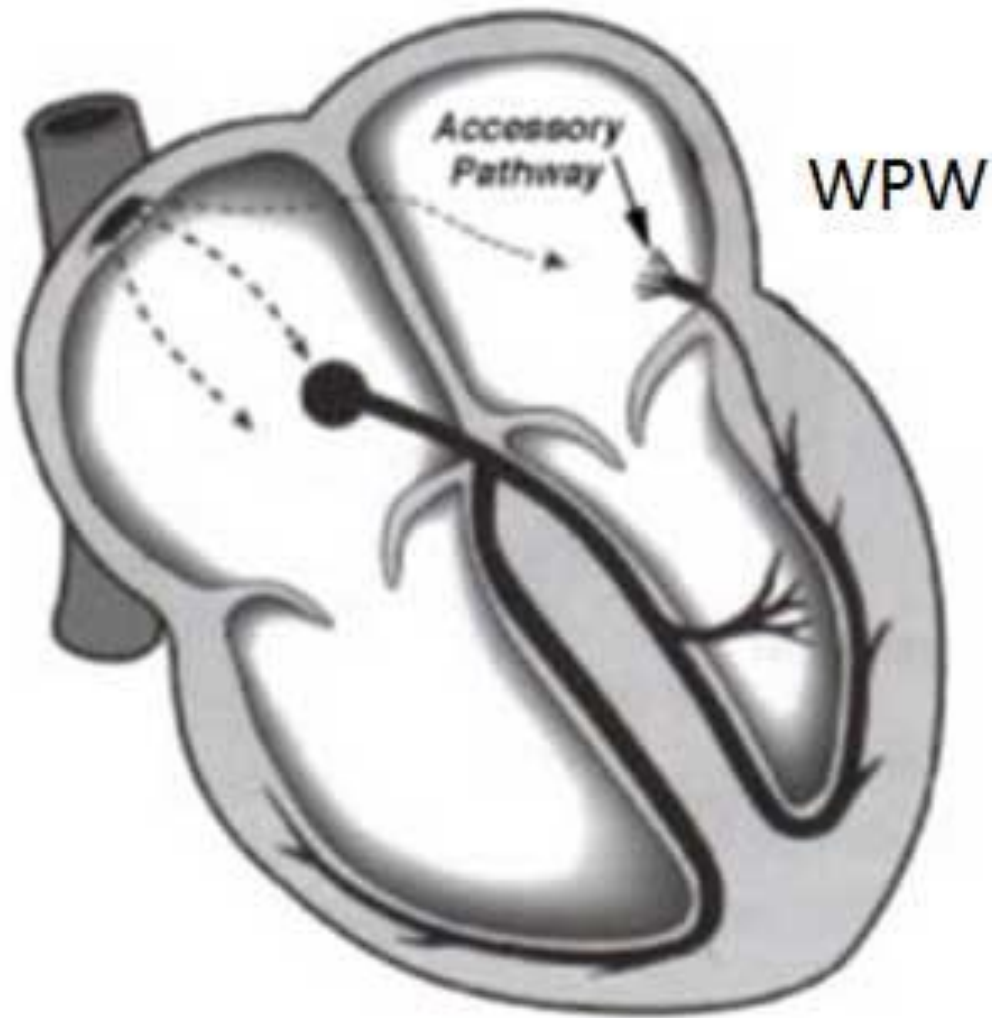
➤ Vagal maneuvers → adenosine → BB/CaCB/dig

Adenosine	
Indication in AVNRT	Termination
Mechanism	- A1 receptors at SAN → opens K channels - Ca blocker at AVN
Contraindications	AF in WPW Severe asthma Severe coronary artery disease
Side-effects	Flushing Chest pain Bronchospasm AV block

AF in WPW

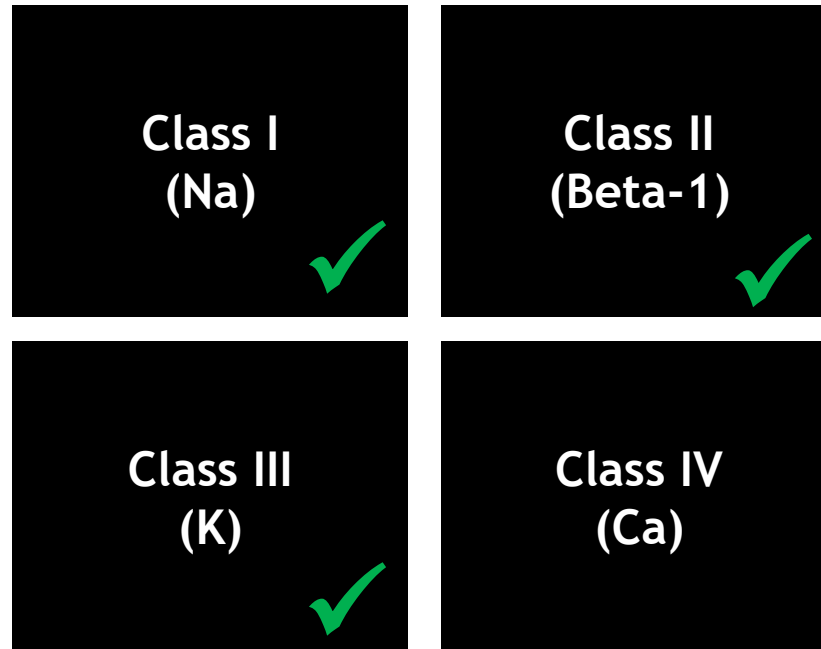
- Accessory pathway with antegrade conduction

Class I (Na) ✓	Class II (Beta-1) ✗	Adenosine ✗
Class III (K) ✓	Class IV (Ca) ✗	



VT

- Usually secondary to structural heart disease



VT

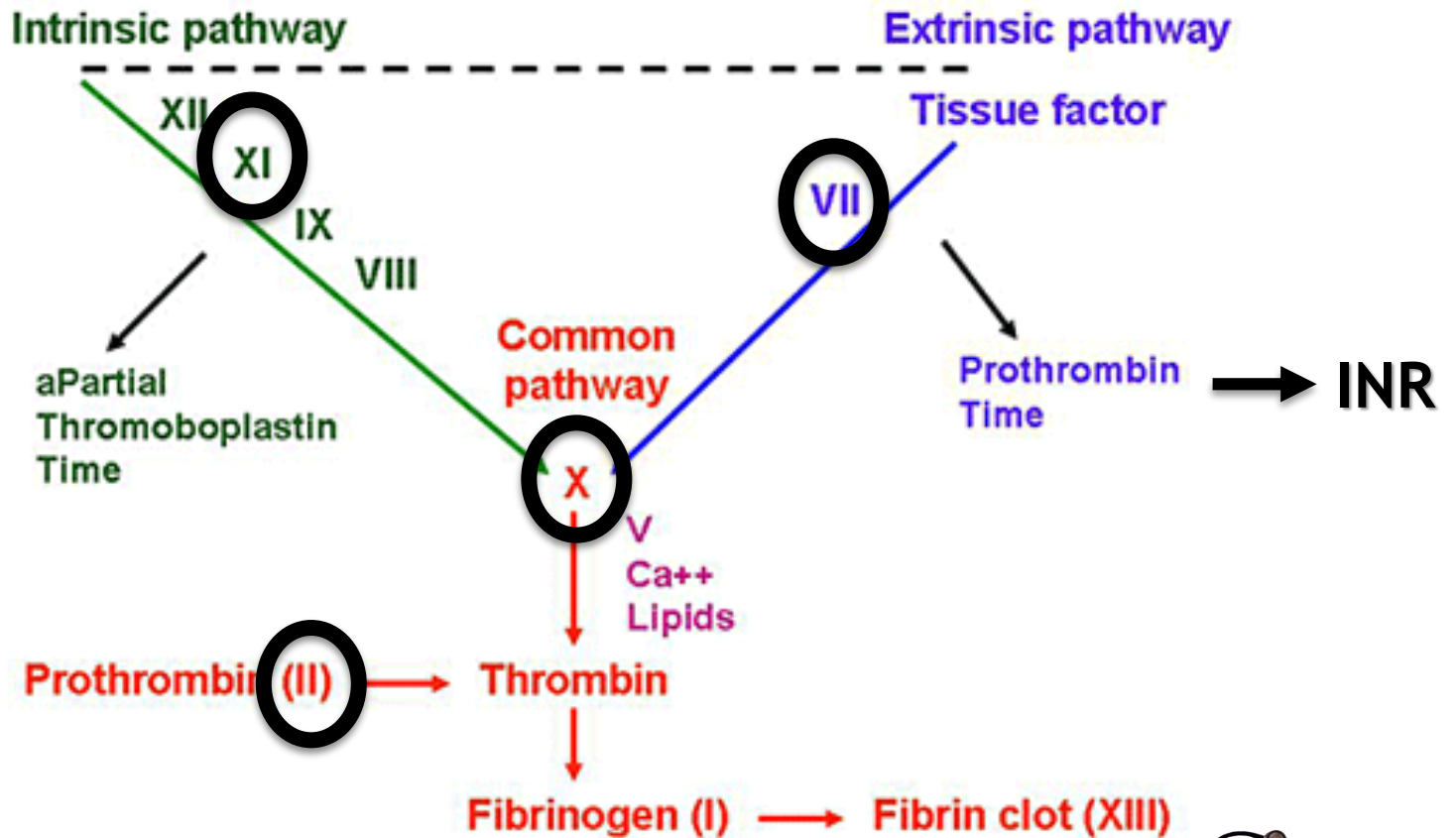
- Electrical cardioversion
- Amiodarone
 - Indicated in haemodynamically unstable/pulseless (as per ALS) and haemodynamically stable VT
- Lidocaine
 - Class Ib

Atropine

Atropine	
Indication	Symptomatic bradyarrhythmias
Mechanism	Muscarinic receptor antagonist - Inhibits vagal activation at nodes
Contraindications	Glaucoma Ileus BPH
Side-effects	Anticholinergic effects: - Dilated pupils - Blurred vision - Dry mouth - Tachycardia - Constipation - Urinary retention

Warfarin

Coagulation Cascade



Warfarin

- INR is the standardised measure of prothrombin time
 - PT measures extrinsic and common pathways [VII; X; V; II; fibrinogen]

Warfarin

Indication	Anticoagulation - DVT/PE & AF
Mechanism	Inhibits the conversion of vitamin K to its active form <ul style="list-style-type: none">- Active vitamin K → carboxylates 2, 7, 9, 10 [protein C & S]- Without carboxylation, cannot bind Ca and form effective coagulation complex
Contra-indications	Haemorrhagic stroke Significant bleeding Pregnancy Liver failure
Cautions	<ul style="list-style-type: none">- Increased risk of bleeding [recent surgery; recent ischaemic stroke; recent GI bleed; peptic ulcer; severe hypertension]- Drug interactions [enzyme inducers & inhibitors]- Other interactions [cranberry juice; ETOH]
Side-effects	Bleeding Skin necrosis Hepatic dysfunction GI s/e - N&V; diarrhoea
Monitoring	INR

Warfarin in AF

CHA ₂ DS ₂ -VASc risk factors	Score
Congestive heart failure	1
Hypertension	1
Age ≥75	2
Age 65–74	1
Diabetes mellitus	1
Stroke/TIA/thromboembolism	2
Vascular disease	1
Female gender	1

Table 1.6 The CHA₂DS₂-VASc risk score

CHA ₂ DS ₂ -VASc score	Annual stroke risk (%/year)	Suggested medication
0	0	Nil
1	1.3	Aspirin or warfarin
2	2.2	Warfarin
3	3.2	
4	4.0	
5	6.7	
6	9.8	
7	9.6	
8	6.7	
9	15.2	

Warfarin and bleeding risk

Table 1.8 The HAS-BLED score

Letter	Characteristics	Definition	Score
H	Hypertension	Systolic BP >160 mmHg	1
A	Abnormal renal and liver function	Dialysis, renal transplantation or Cr >200 β mol/L; cirrhosis or ALT/AST more than three times upper normal limit	1 point each (1 or 2)
S	Stroke		1
B	Bleeding	Previous bleeding or predisposition to bleeding	1
L	Labile INRs	INRs out of range >40% time	1
E	Elderly >65 years		1
D	Drugs or alcohol	Concomitant use of NSAIDs, antiplatelet agents or alcohol abuse	1 point each (1 or 2)

Warfarin in DVT/PE

- Initiated with heparins
 - Heparins continued for minimum 5 days post DVT/PE
- Once-daily regimen
- ‘Load’ with 10/5/5 usually (lower in elderly; liver/renal/heart failure)
 - 10mg od → 5mg od → 5mg od
 - Check INR each day
- After initiation → protein C and VII levels fall first → may be initially procoagulant (warfarin skin necrosis - protein C deficiency)
- Heparins stopped when INR in therapeutic range for 2 consecutive days



Warfarin

- INR targets
 - AF → 2.5
 - DVT/PE → 2.5
 - Recurrent DVT/PE → 3.5
 - Metallic valve → 3.0 - 3.5
- Duration of warfarin therapy
 - First DVT/PE, reversible cause = 3 months
 - Idiopathic first DVT/PE = 3 months or long-term
 - Recurrent DVT/PE = indefinite

 - DVT/PE and cancer = LMWH for 3-6 months then long-term
- Anticoagulation clinic referral for regular follow-up
 - Yellow book for INR monitoring

Warfarin reversal

- Major bleeding associated with warfarin:
 - Intracranial haemorrhage
 - GI bleed
- Urgent surgery
 1. Stop warfarin
 2. Vitamin K IV 5mg over 20-60mins (12 hrly)
 3. Prothrombin complex concentrate [2, 7, 9, 10, protein C & S]
 - Alternative is fresh frozen plasma
- PCC corrects the defective coagulopathy without risks of transfusion reactions

Warfarin reversal

- INR >8; minor bleeding
 1. Stop warfarin
 2. Vitamin K IV 1-3mg
 3. Restart warfarin when INR <5.0

- INR >8; no bleeding
 1. Stop warfarin
 2. Vitamin K 1-5mg oral
 3. Restart warfarin when INR <5.0

- INR 5 - 8; minor bleeding
 1. Stop warfarin
 2. Vitamin K IV 1-3mg
 3. Restart warfarin when INR <5.0

- INR 5 - 8; no bleeding
 1. Hold 1 or 2 doses of warfarin
 2. Recheck INR and reduce subsequent maintenance dose

Warfarin reversal

➤ Peri-operative

1. Stop warfarin 5 days in advance
2. If high risk → bridge with LMWH

NOAC

- New oral anti-coagulants
 - Avoids regular monitoring and variable doses
 - Lower risk of intracranial haemorrhage
 - Short half life

- Dabigatran
- Apixaban
- Rivaroxaban

(Factor Xa)

Thanks for listening!

Good luck!

Any questions?

