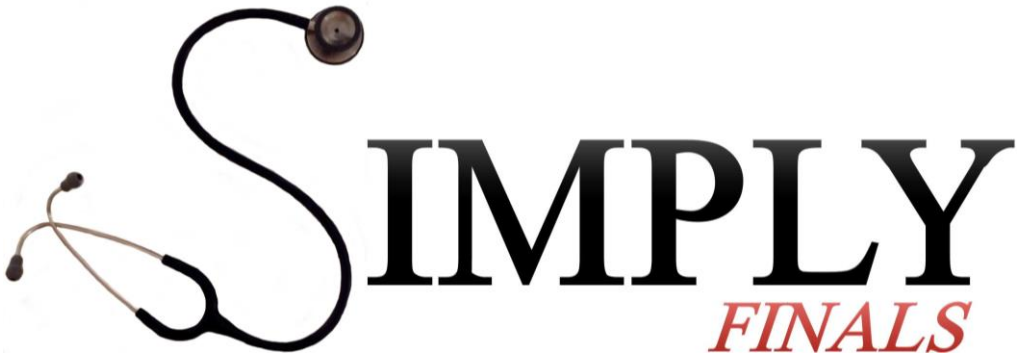
ANTI-ARRHYTHMICS AND WARFARIN

Dr Nithish Jayakumar



Contents

1. Anti-arrhythmics
   - ~~Pacemaker and myocardial potentials~~
   - Drug classes – mechanisms; s/e; contra-indications
   - Management of common arrhythmias

2. Warfarin
   - ~~Coagulation cascade~~
   - Warfarin in VTE – mechanisms; s/e; contra-indications; monitoring
   - Warfarin reversal

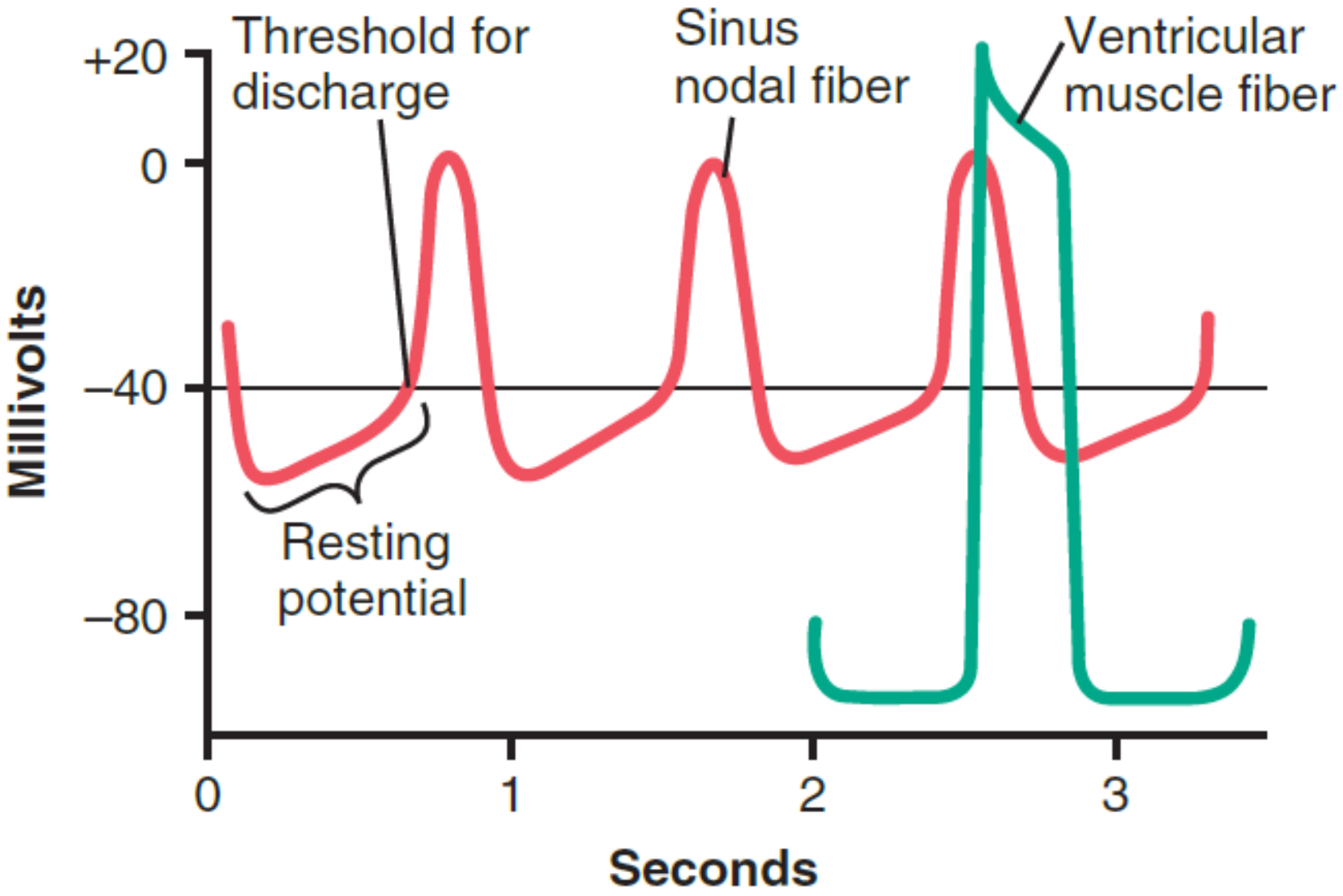
3. NOACs

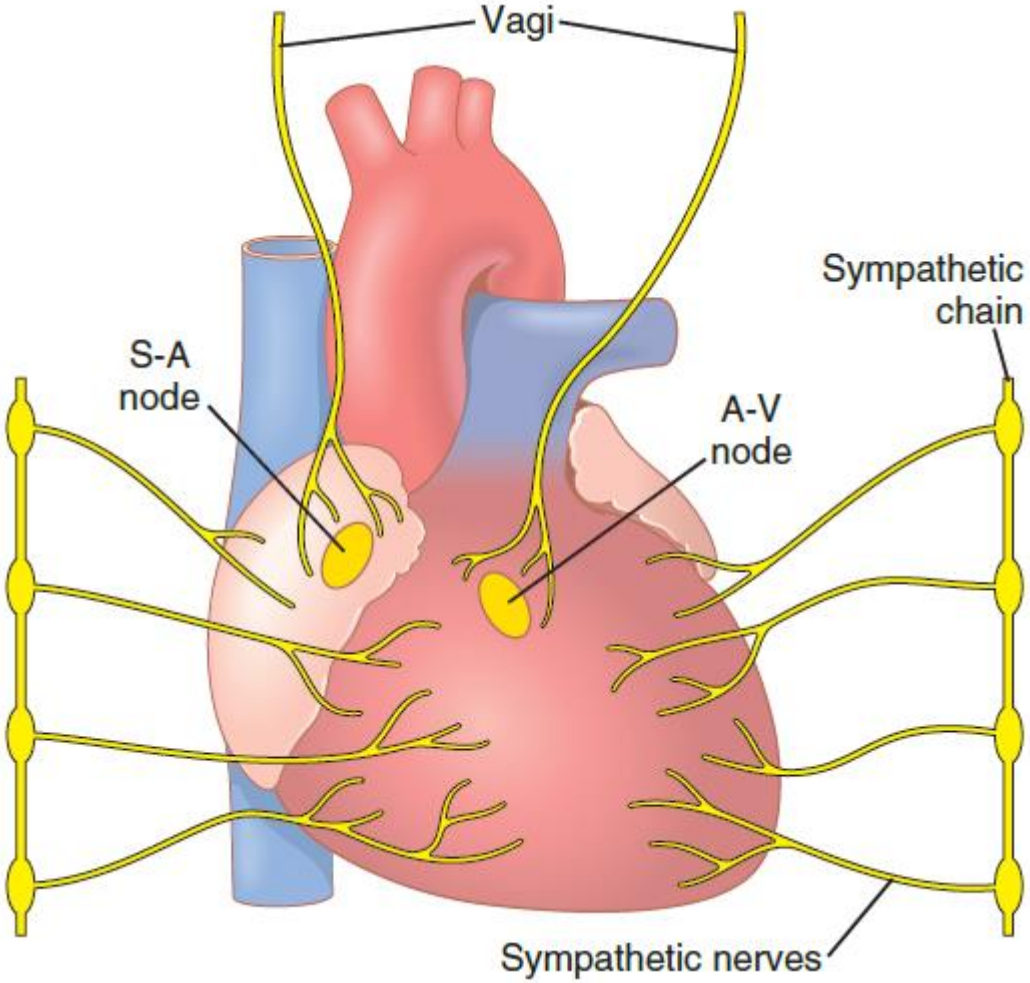
SIMPLY FINALS

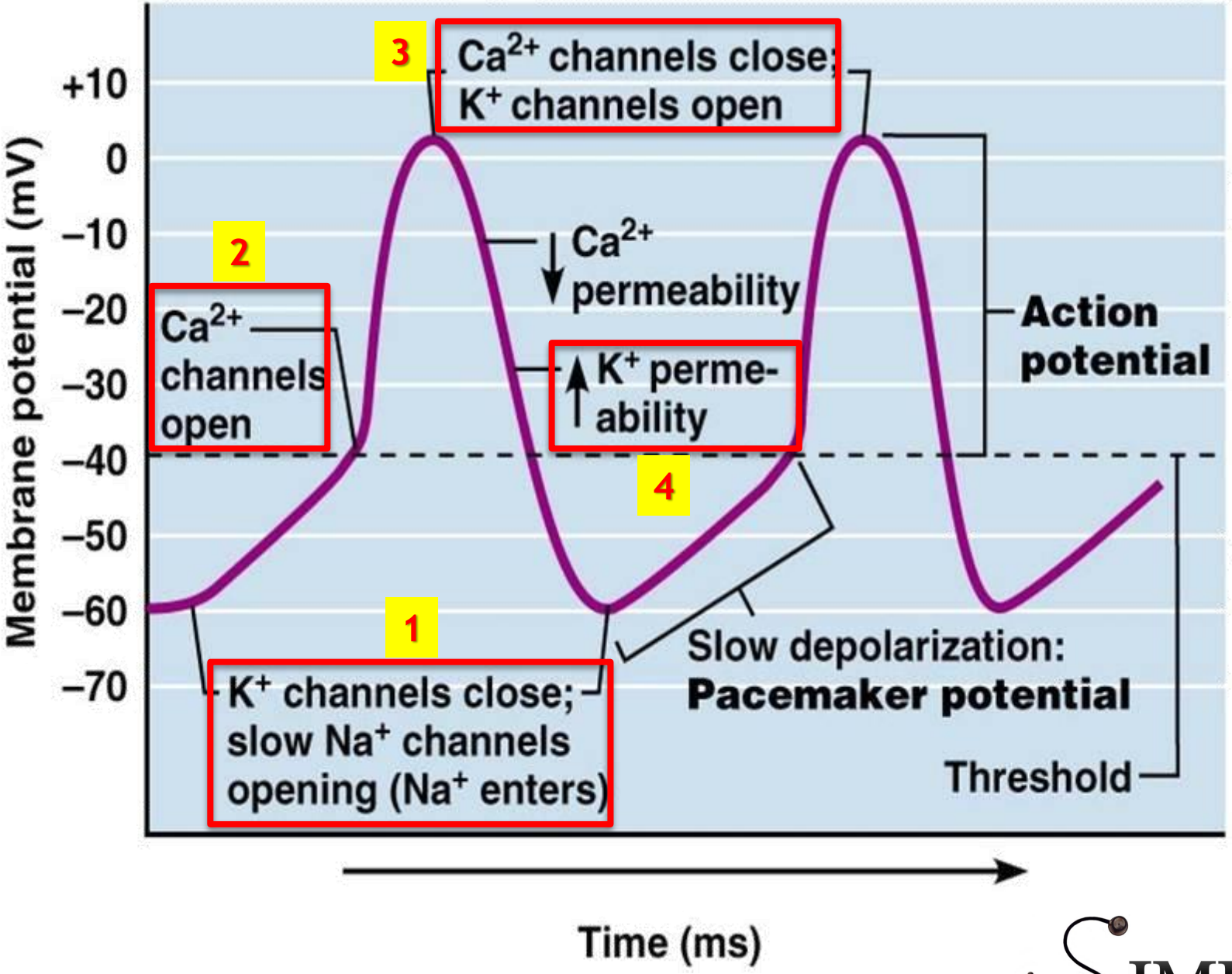
Pacemaker & myocardial potentials

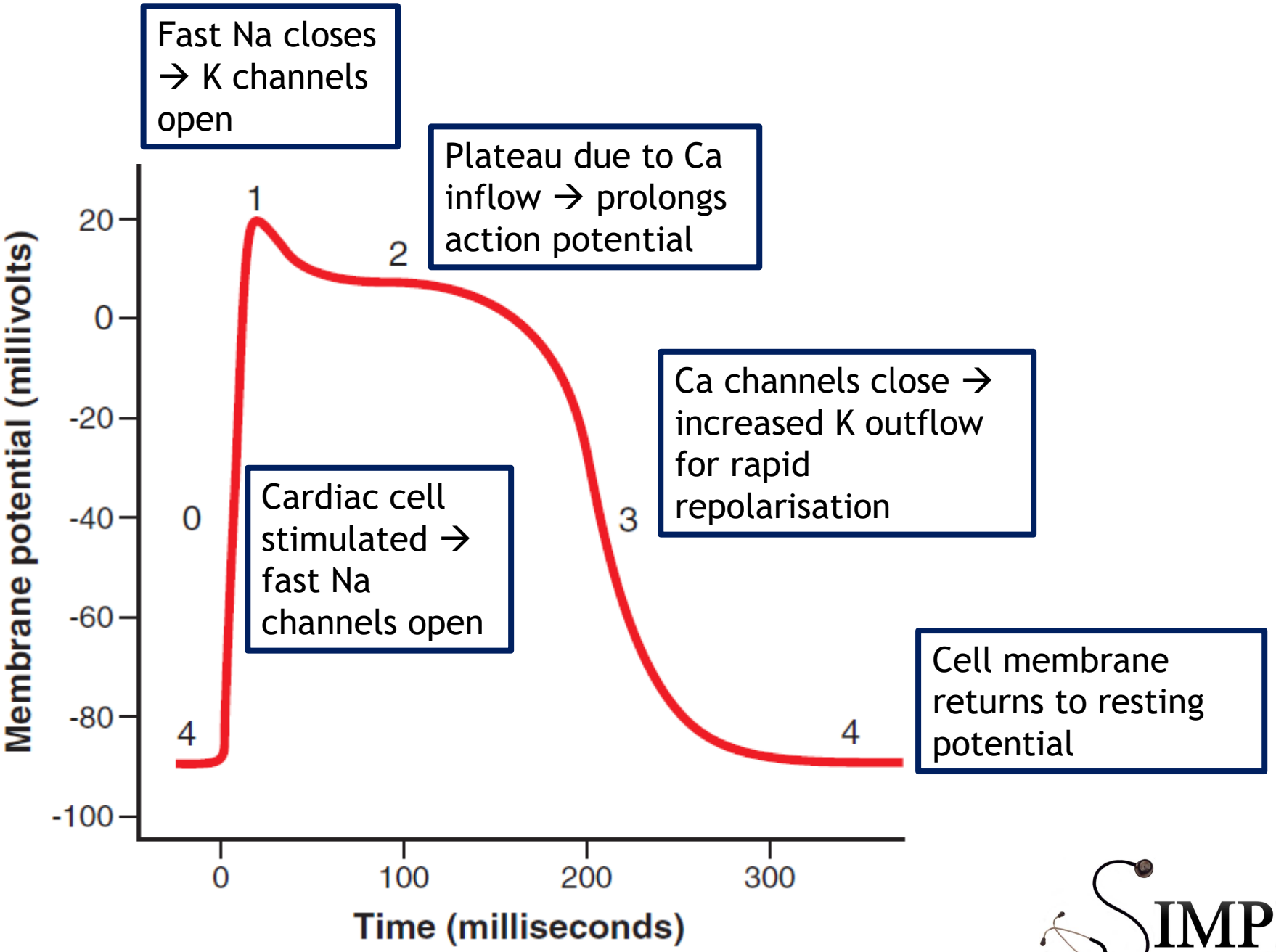
- Pacemaker potentials
  - Originate at rapidly conducting tissue
  - SAN → AVN → Bundle of His → Ventricular fibres
  - SAN ordinarily sets the pace [70-80/min]
  - Sympathetic and parasympathetic input

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







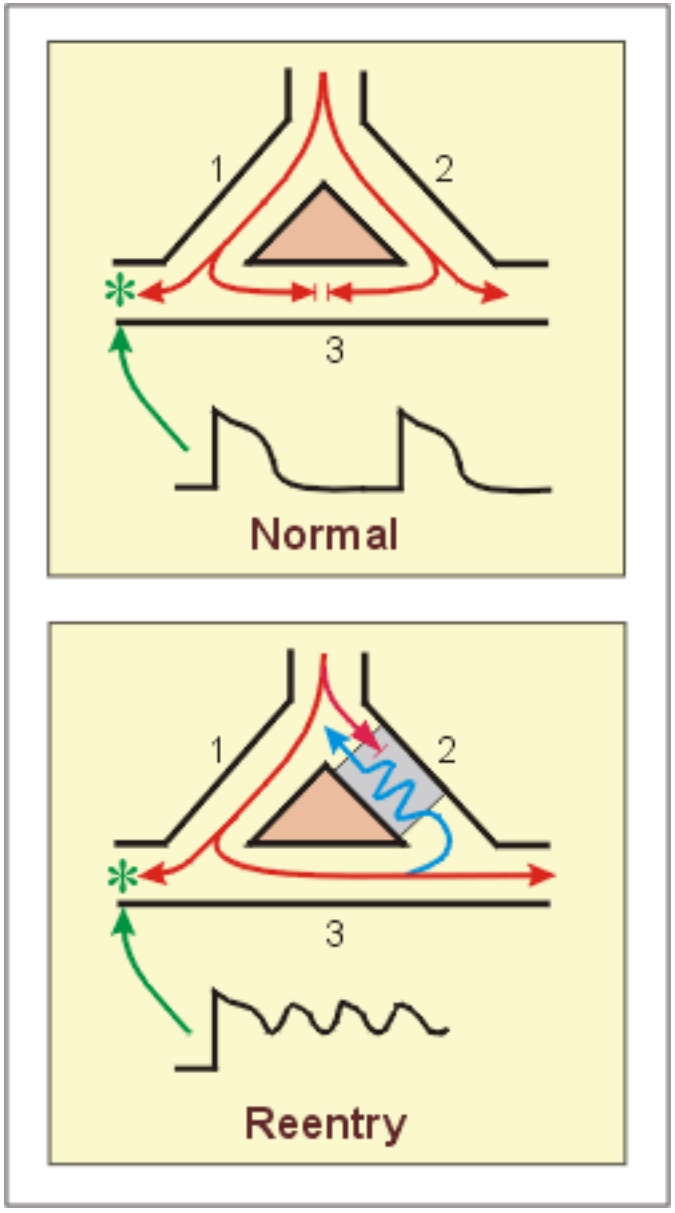


Anti-arrhythmics

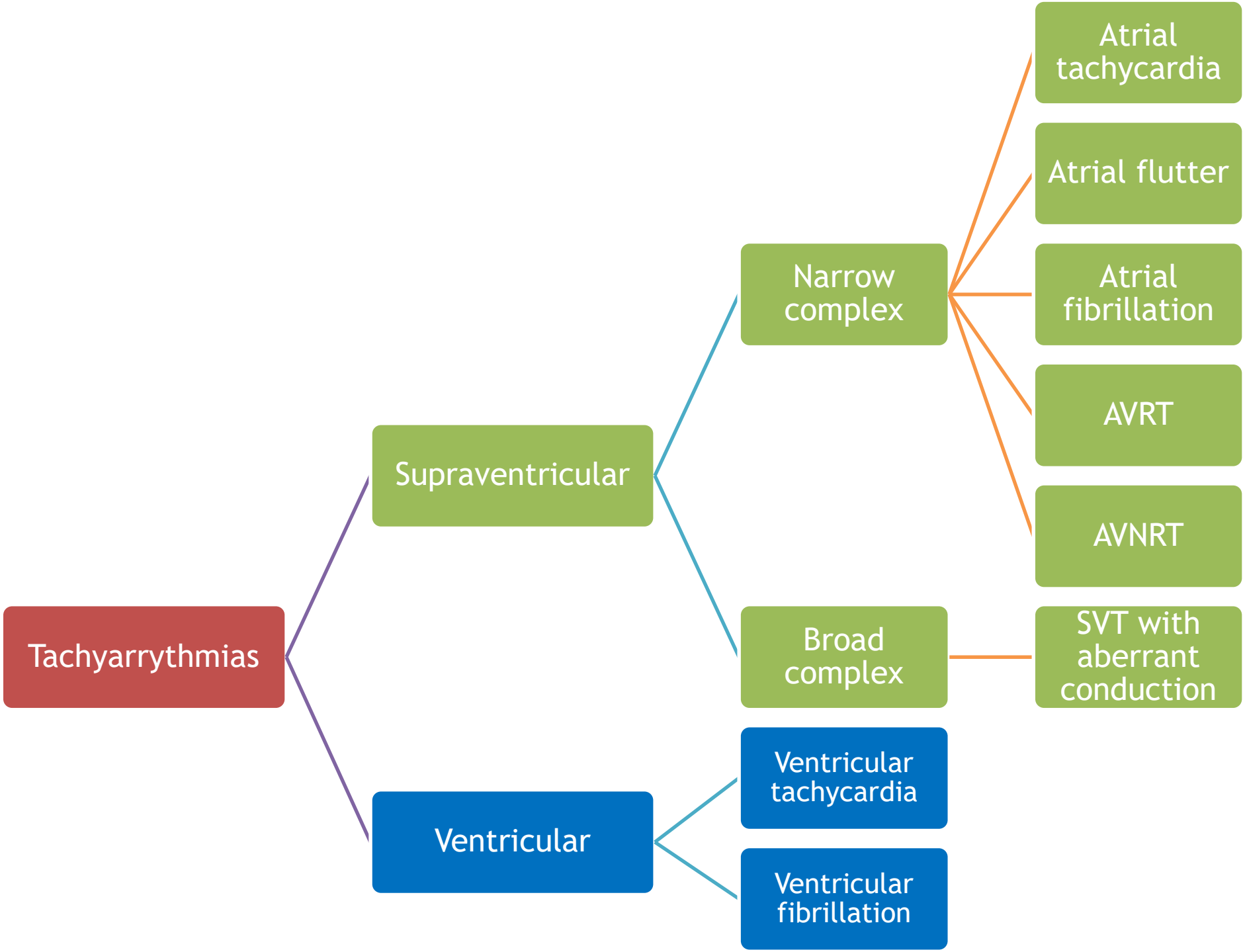
- Vaughan-Williams classification
  - According to predominant mechanism of action
- 4 classes
- Amiodarone; digoxin; adenosine
- Rx for tachyarrhythmias
- [Atropine]

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

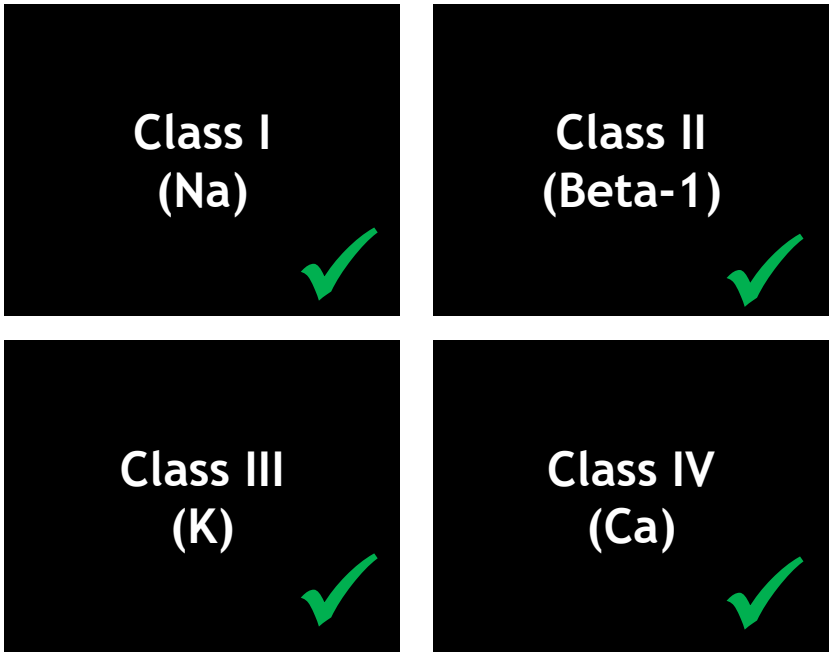


Class	Site	Mechanism	Example
I [Ia; Ib; Ic]			
II			
III			
IV			


Tachyarrythmias
Supraventricular
Ventricular
Narrow complex
Broad complex
Atrial tachycardia
Atrial flutter
Atrial fibrillation
AVRT
AVNRT
SVT with aberrant conduction
Ventricular tachycardia
Ventricular fibrillation

Atrial fibrillation

- Multiple re-entry mechanisms



Atrial fibrillation

- Rate vs rhythm control

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

Atrial fibrillation

- Rate vs rhythm control

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

A

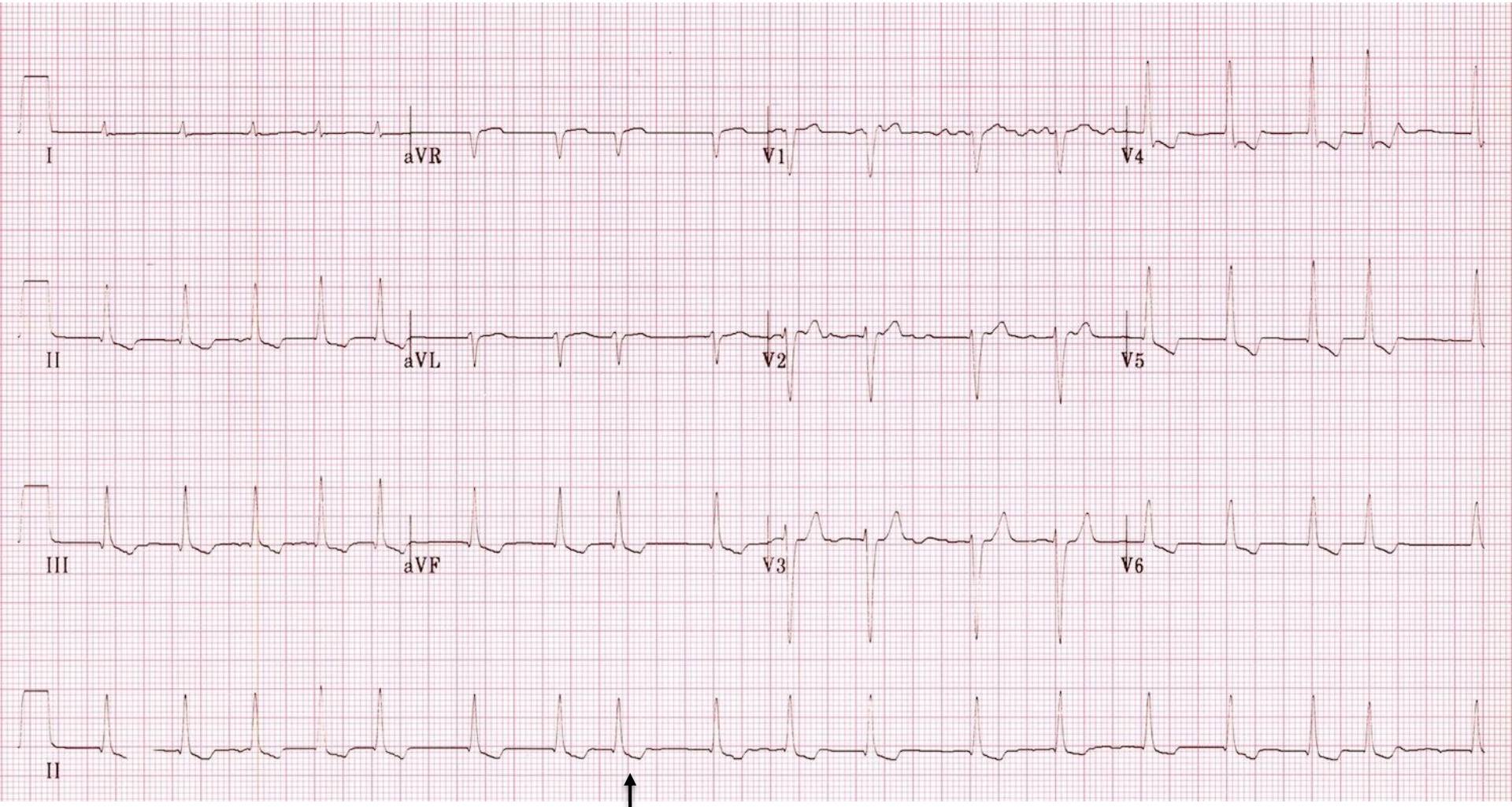
B

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

Digoxin effect – therapeutic doses



Reverse-tick ST depression

SIMPLY FINALS

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

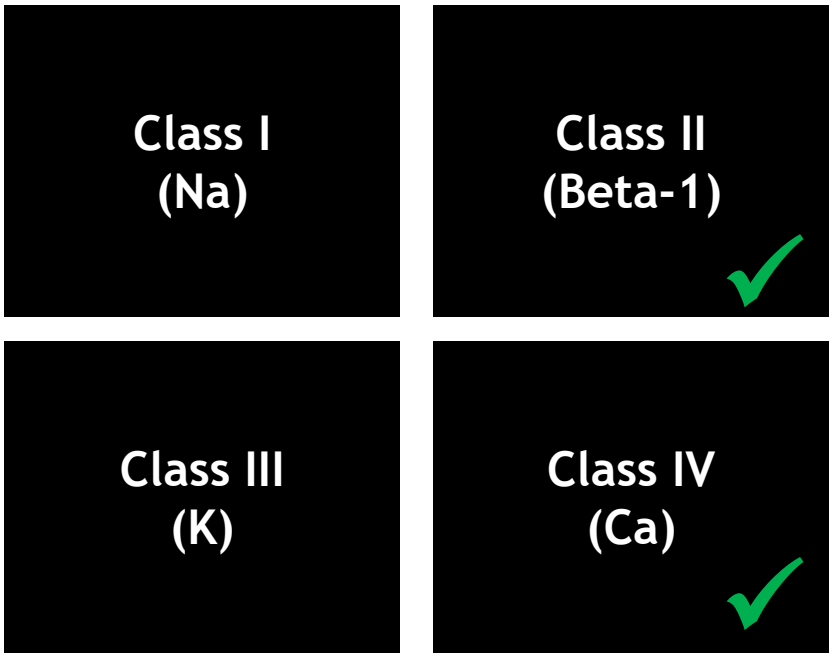
- Hyperkalaemia
- [renal dysfunction]
- Serum digoxin level

Management

- Digifab (digoxin-specific antibody fragments)

AVNRT

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



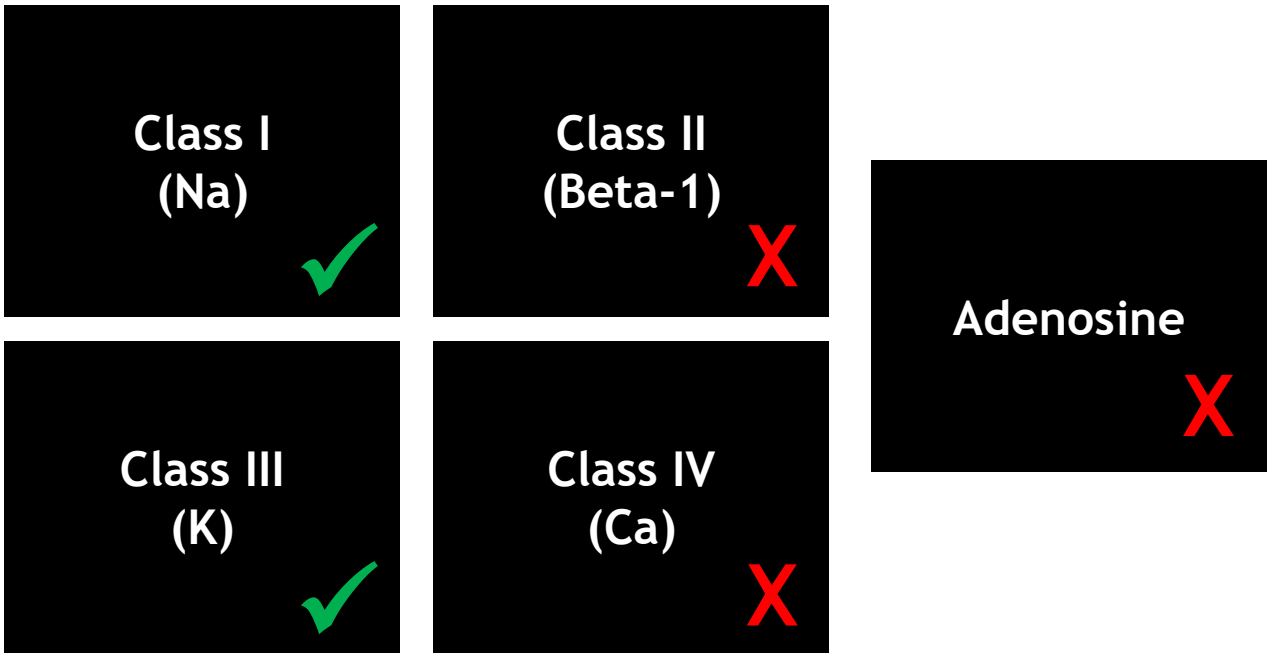
AVNRT

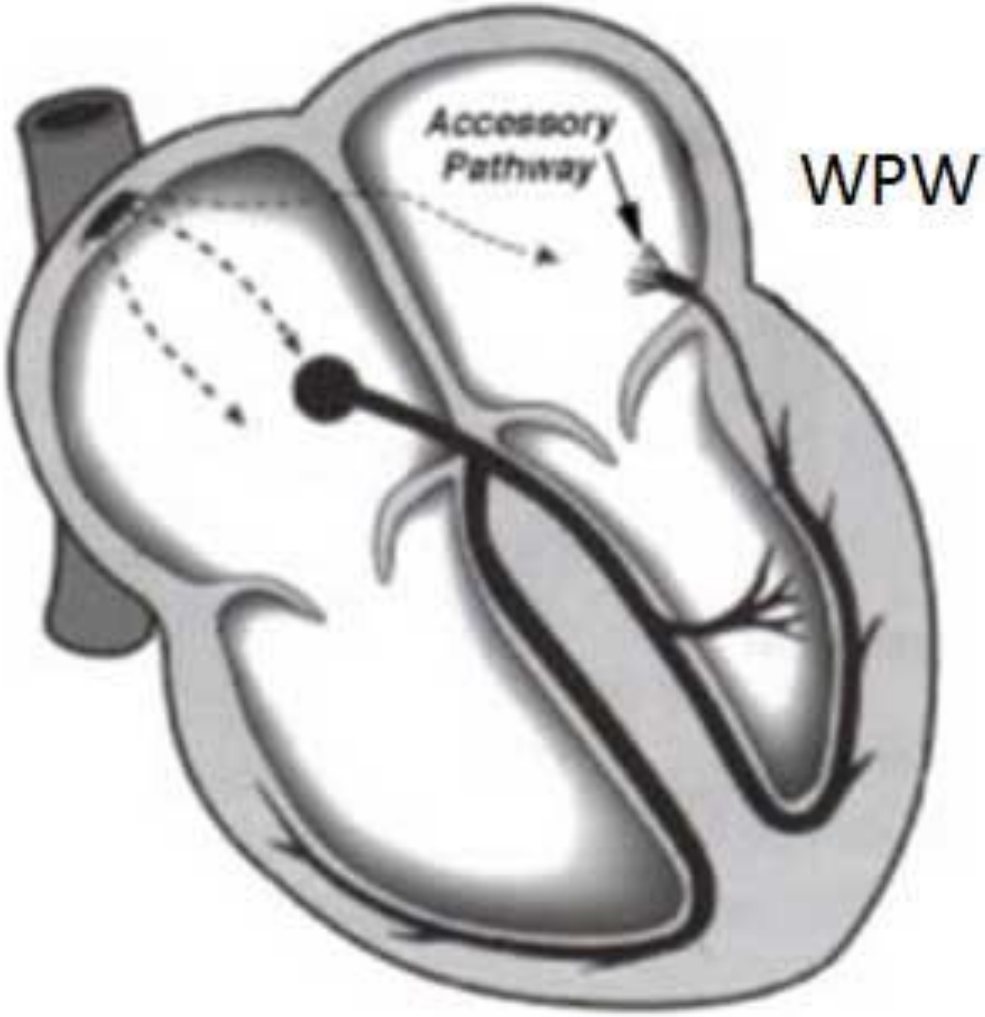
- Vagal maneuvers → adenosine → BB/CaCB/dig

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

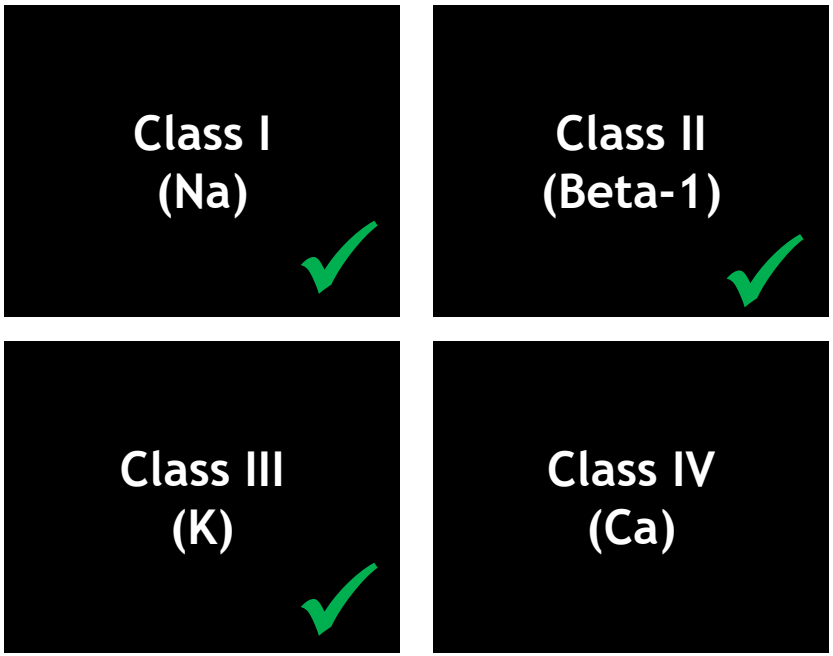




WPW

VT

- Usually secondary to structural heart disease



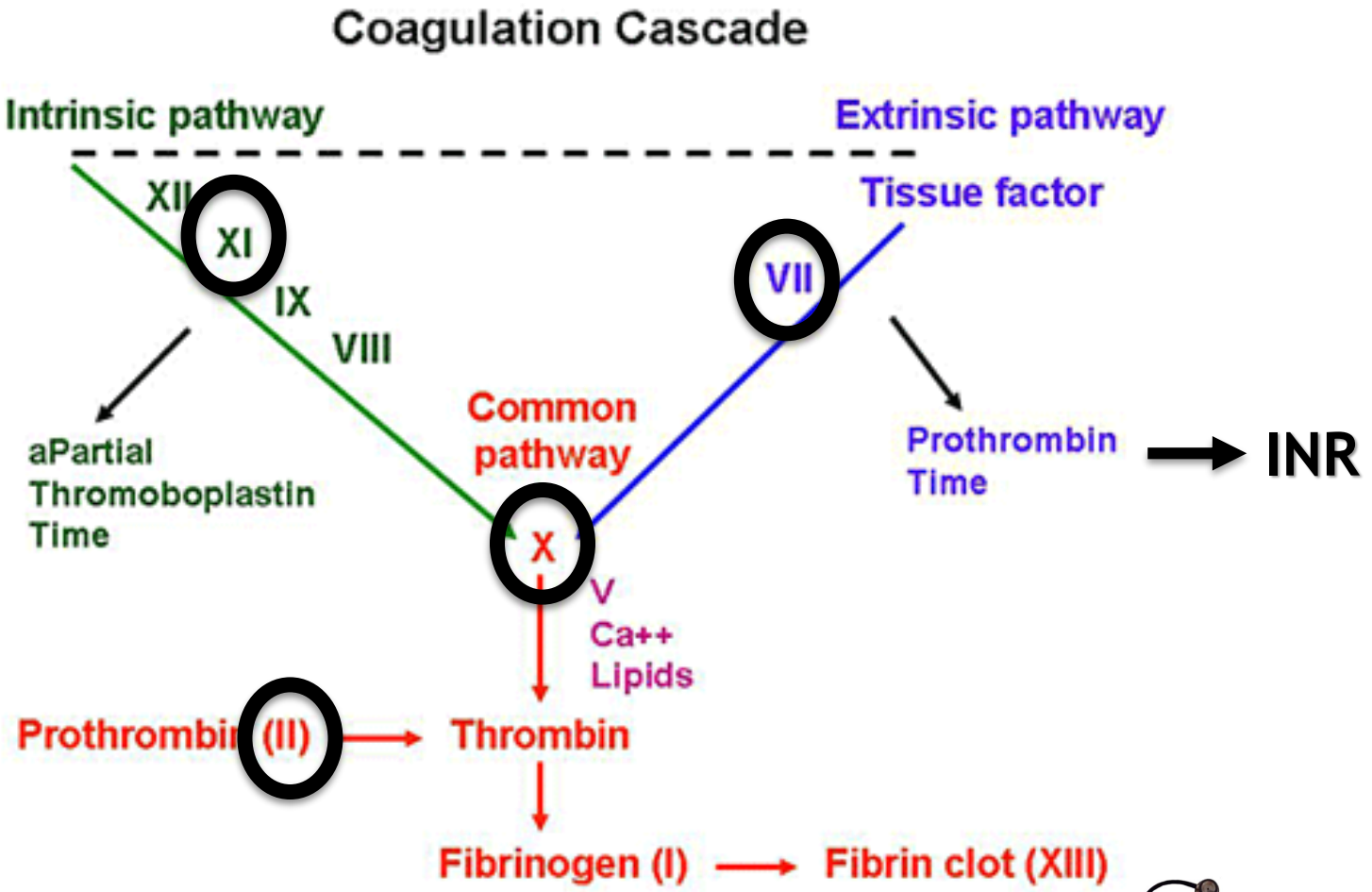
VT

- 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



SIMPLY FINALS

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 - 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	- 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_2DS_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 CHA_2DS_2-VASc risk score

CHA_2DS_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 βmol/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?