Cardiac Glycosides and drugs for heart failure

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Contents

Introduction

- Heart fails to pump blood to the body for normal functions
- Systolic/diastolic dysfunction
- Produces congestive symptoms like
  - Venous engorgement, edema, enlargement of liver, dyspnoea, oliguria

- Glycosides: by improving CO,
  reduces cardiac work and O2 demand

- Other newer drugs added

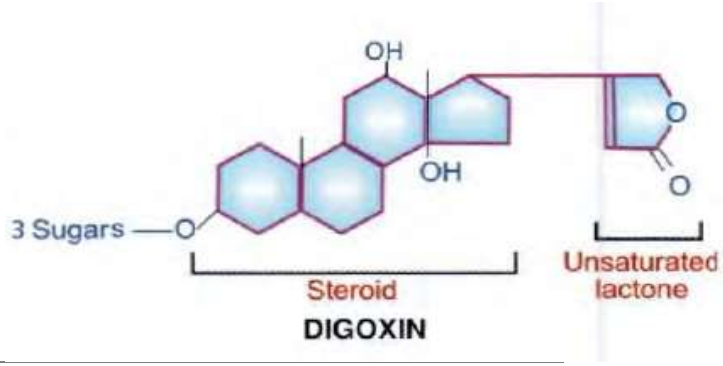
Cardiac glycosides

- William withering

- Foxglove (digitalis)

- Sources of cardiac glycosides:
  - Digitalis lanata=digoxin
  - Digitalis purpurea=digitoxin; not useful

Chemical structure



- Aglycone along with sugar moieties
- Aglycone:- pharmacological activity
- Sugar:- modify solubility and permeability

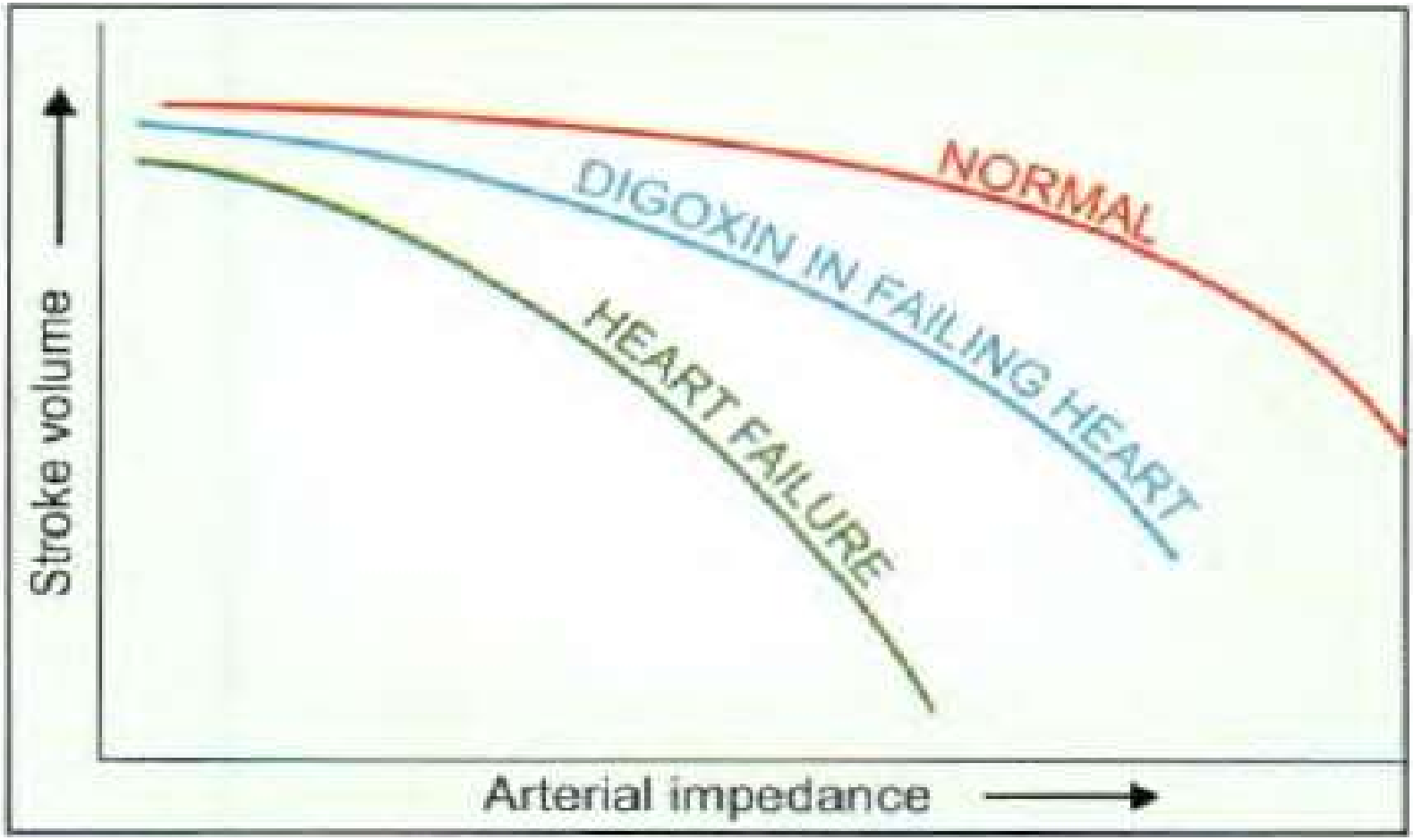
Pharmacological actions

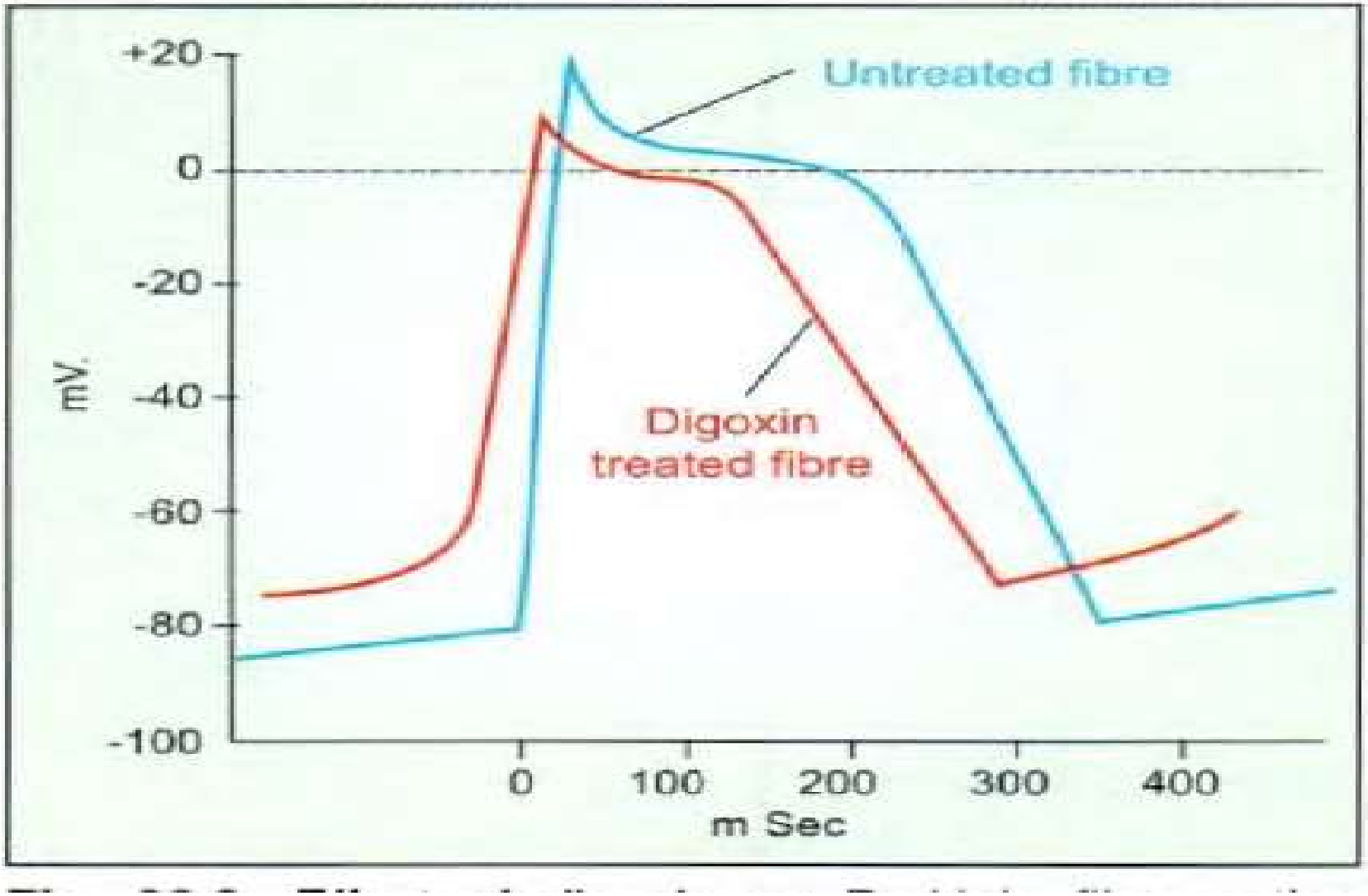
Digoxin is prototype drug

1. Heart:-
   - Force of contraction:- increase dose dependent inotropic effect

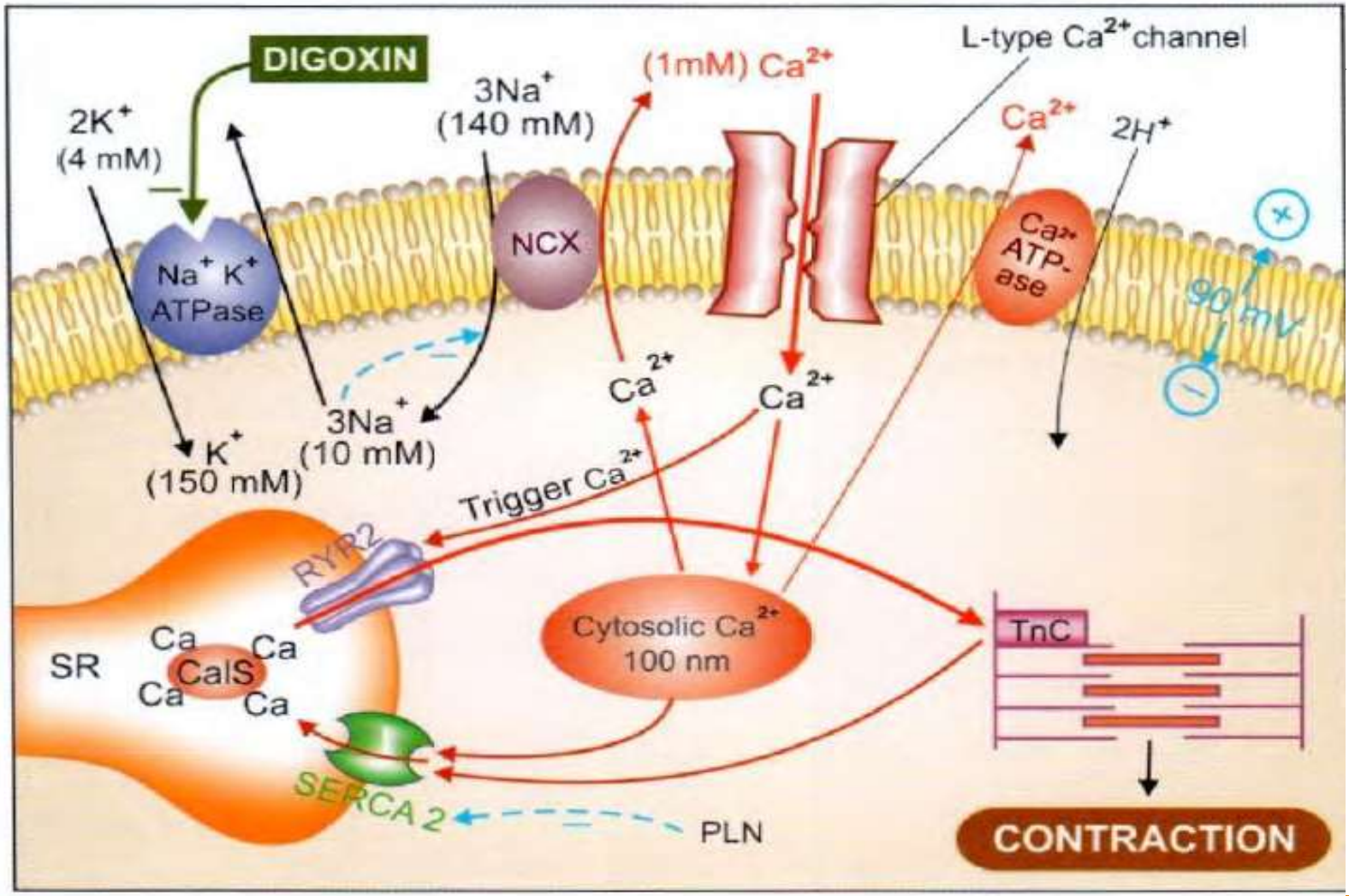
   Cardiac output:- increases
   - Heart rate:- decreases
     - Both vagal (direct stimulation) and extra-vagal action (direct depressant on SA node and AV node)
     - Vagal action can be blocked by atropine

Stroke volume Vs Arterial Impedance




+20
0
-20
-40
-60
-80
-100
mV.
Untreated fibre
Digoxin
treated fibre
0
100
200
300
400
m Sec

Mechanism of action



2. Blood vessels
   - Constriction, but not much of effect. No significant effect on coronary circulation

3. Kidney
   - Diuresis increases due to improved circulation

4. CNS
   - Higher doses:- CTZ stimulation

Pharmacokinetics

- Lipid soluble:- digitoxin (Liver)
- Food affects both (Delays absorption)
- Common:
  - Large volume of distribution (concentrated in heart, liver, kidney, skeletal muscle)
  - T1/2: 40 hours
  - Steady state levels and full therapeutic effect after long time
  - Cumulative drug

Adverse effects

Narrow therapeutic index

Extra cardiac:

- Nausea, vomiting, abdominal pain

Due to gastric irritation, mesenteric vasoconstriction and CTZ stimulation

- Fatigue, malaise, headache, mental confusion, disorientation, psychosis
- Visual disturbances

Cardiac

- Arrhythmia:- pulsus bigeminus, ventricular extra-systole, tachycardia and fibrillation
- Partial or complete AV block

Extra cardiac symptoms generally proceed to cardiac

Treatment:- stop digitalis, nothing much in case of extra-cardiac

1) For tachyarrhythmias:-
   - Infuse IV KCl 20 mmol/hour
2) For ventricular arrhythmias:-
   - Lidocaine IV
3) For supraventricular:-
   - Propranolol
4) For A-V block
   - Atropine 0.6 to 1.2 mg IM
   - Digibind:- 38 mg vial; digoxin specific antibody; given IV

Drug drug interactions

1. Diuretics
2. Calcium
3. Quinidine, Verapamil
4. Adrenergic drugs
5. Metoclopramide, antacids
6. Propranolol, verapamil, diltiazem

Therapeutic uses

1. Congestive heart failure (CHF)
   - Dosing pattern

1) Slow digitalization:-
   - Maintenance dose 0.125-0.25 mg/day given from beginning
   - Takes one week for response
   - Gradually increase to 0.375, 0.5 mg weekly
   - Relief of symptoms
   - bradycardia:- sign to stop the drug

2) Rapid digitalization:-

- 0.5 to 1.0 mg stat followed by 0.25 mg every 6 hourly
- Takes 6-24 hours
- Not practiced now

2. Cardiac arrhythmias
   - Atrial fibrillation:- control ventricular rate
   - Atrila flutter (200-350 beats/min) less than AF
   - Paroxysmal supraventricular tachycardia (150-200/min)

Reference

Author	Result	Journal	Level
Ioana Dumitru	Out of 2891 patients, 1) 18% of whom initiated treatment with digoxin, incident digoxin use was associated with significantly higher rates of death 2) Digoxin use was not associated with a significant difference in the risk of hospitalization for heart failure	Medscape	Level 1

Thank you