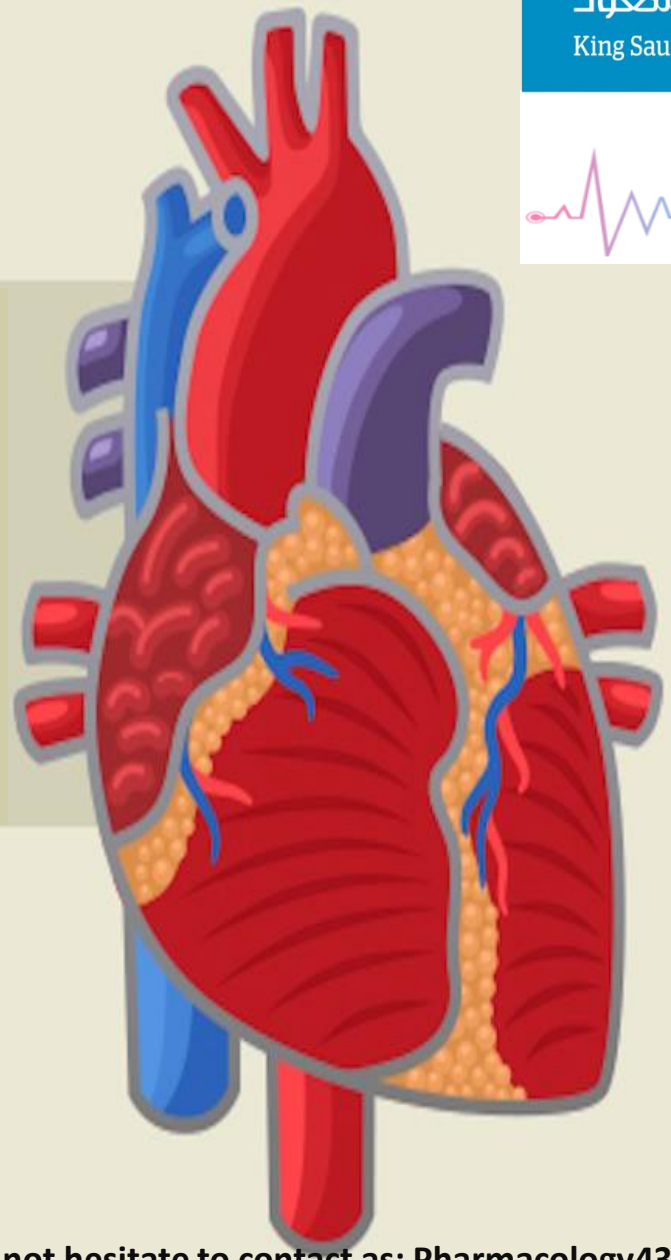
5&6

Drug treatment of heart failure.



Cardiovascular Block.

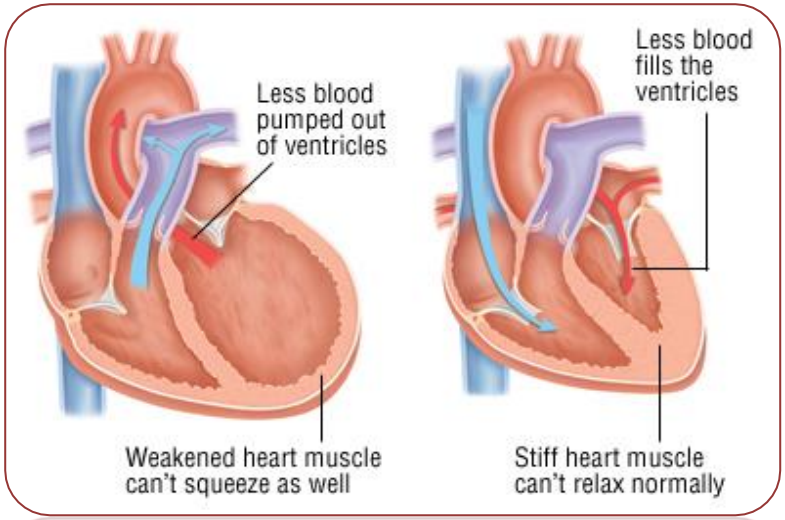
For any correction, suggestions or any useful information do not hesitate to contact as: Pharmacology434@gmail.com

Drug Treatment of HF

Learning Objective:

- ***Describe the different classes of drugs used for treatment of acute & chronic heart failure and their mechanism of action.***

- **Understand their pharmacological effects, clinical uses, adverse effects and their interactions with other drugs.**



CAUSES OF HEART FAILURE:

High blood pressure-
abnormal heart rhythm-
heart valve disorder-
cardiomyopathy-
disorder of coronary arteries

HEART FAILURE:

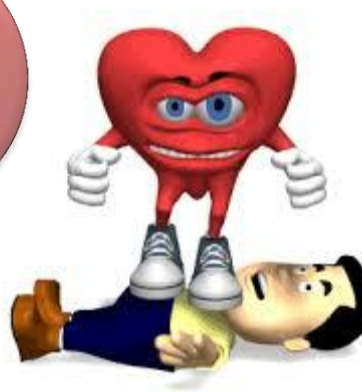
Inability of the heart to maintain an adequate cardiac output to meet the metabolic demands of the body.

Heart failure symptoms

- Tachycardia
- Decreased exercise tolerance (rapid fatigue)
- Cardiomegaly (dilated in the heart)
- Dyspnea (pulmonary congestion)
- Peripheral edema

Factors affecting cardiac output and Heart Failure:

- Cardiac contractility
- Preload (high in HF patients)
- Afterload (high in HF patients)
- Heart rate.



Drugs used in the treatment of heart failure

***Drugs that increase contractility**

- Cardiac glycosides
- Phosphodiesterase inhibitors
- β- adrenoceptor agonists

Drugs that decrease preload

- Diuretics(decreases the blood volume)
- Venodilators (decreases the venous pressure)

Drugs that decrease afterload

- Arteriolodilators

Drugs that decrease preload & afterload

- Angiotensin converting enzyme (ACE) inhibitors
- Angiotensin receptor antagonists
- Directly-acting vasodilators
- α1-adrenoceptor antagonists

* These drugs increase the myocardial contractility, also these drugs have + inotropic action. - Heart rate is involved in the processes above.

Group	Cardiac glycosides	Phosphodiesterase inhibitors	β – adrenocepters agonists
Action	Increase contractility (+ve inotropic)		
Drugs	Digoxin / Digitoxin / Oabain Source: (from digitalis latana plant)	Bipyridines : Amrinone / Milirone	Dobutamine: β1 agonist
Mechanism of action	Inhibit NA/K ATPase enzyme : 1-inhibit Na/K pump directly ↓ 2-indirect inhibition of Na/Ca exchange 3- facilitate Ca influx 4- ↑ Ca release from ER & T tubules	Inhibit Phosphodiesterase isoenzyme 3 in cardiac cycle & smooth muscles → ↑cAMP: ↓ 1- in heart: ↑ Ca → ↑ contraction 2- in peripheral vessels: dilatation → ↓ after-pre load	-
Pharmacolo-gical action	↑ inotropy + ↓ heart size → ↓ venous P →edema ↓ chronotropy by vagal stimulation (inhibition of SAN by ↑ parasympathetic effect)	-	-
Therapeutic uses	Congestive heart failure Atrial arrhythmias : Atrial flutter / Atrial fibrillation / Supraventricular tachycardia	Treatment of acute heart failure (I.V)	Treatment of acute heart failure (Cardiogenic shock / I.V in severe cases)
Pharmaco-kinetics	Digoxin : - narrow therapeutic index - 40-8-% absorbed orally → variable bioavailability - I.V → act within 15min – 3hrs - 25% protein bound - 85% excreted unchanged in urine	-	-
Adverse effects	*Digitalis – induced arrhythmia (any type): - extrasystoles , - A.V.block, - coupled beats (Bigeminal rhythms - ventricular tachycardia or fibrillation - cardiac arrest. *GIT : early sign of toxicity - *CNS Headache , visual disturbances, drowsiness	* GIT upsets (Nausea ,vomiting) * arrhythmias (less than digitalis) * thrombocytopenia * live toxicity (Milrinone has LESS hepatotoxic and less bone marrow depression than amrinone)	-

Factors that increase digitalis toxicity :

- Renal diseases
- Small Lean body mass
- Hypothyroidism
- Hypomagnesemia
- Hypercalemia
- Hypokalemia

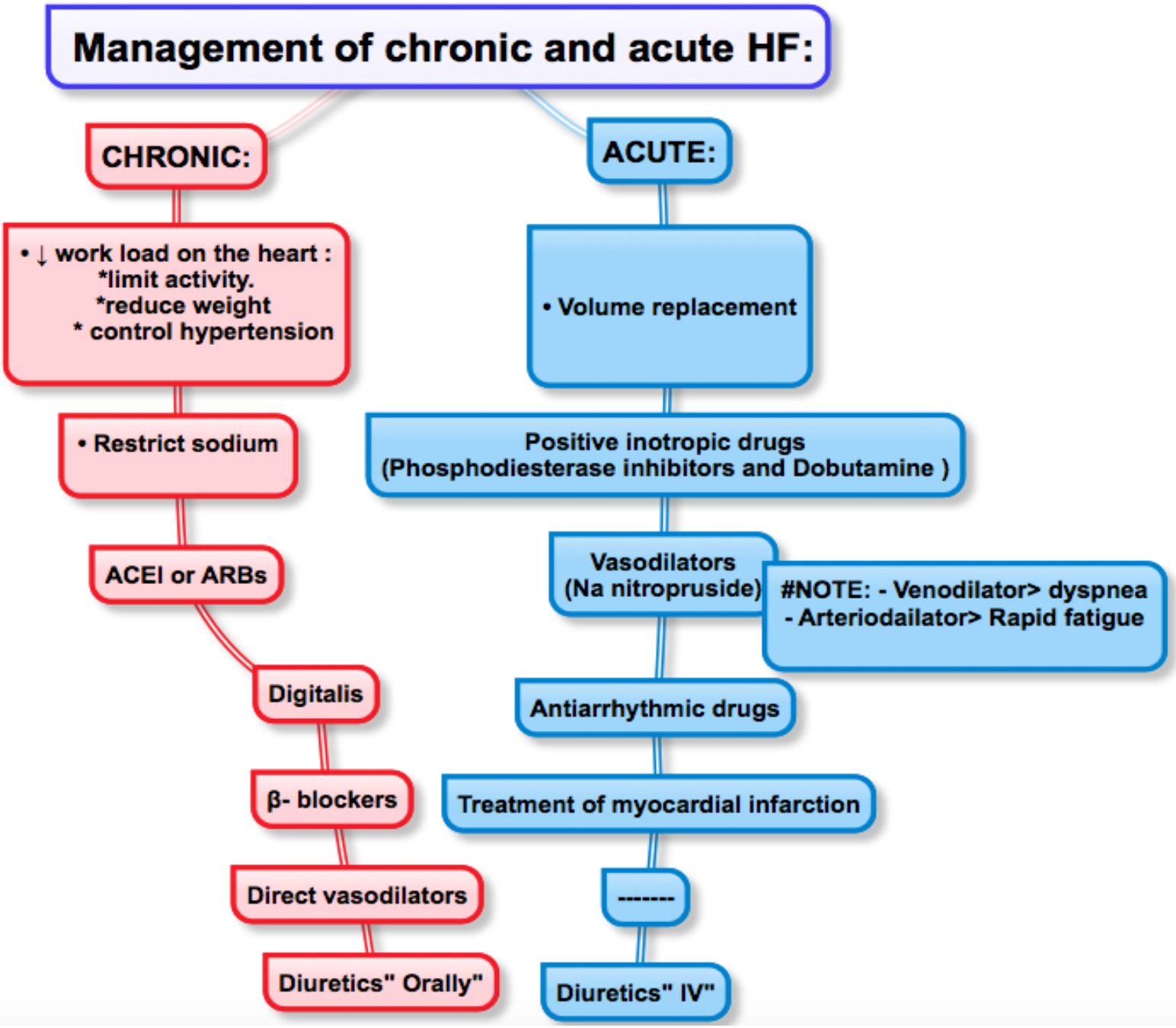
Stop Digoxin

switch to diuretics

- **give K supplements / antiarrhythmic drugs (lidocaine or procainamide) / FAB fragment (Ab to stop digoxin)**

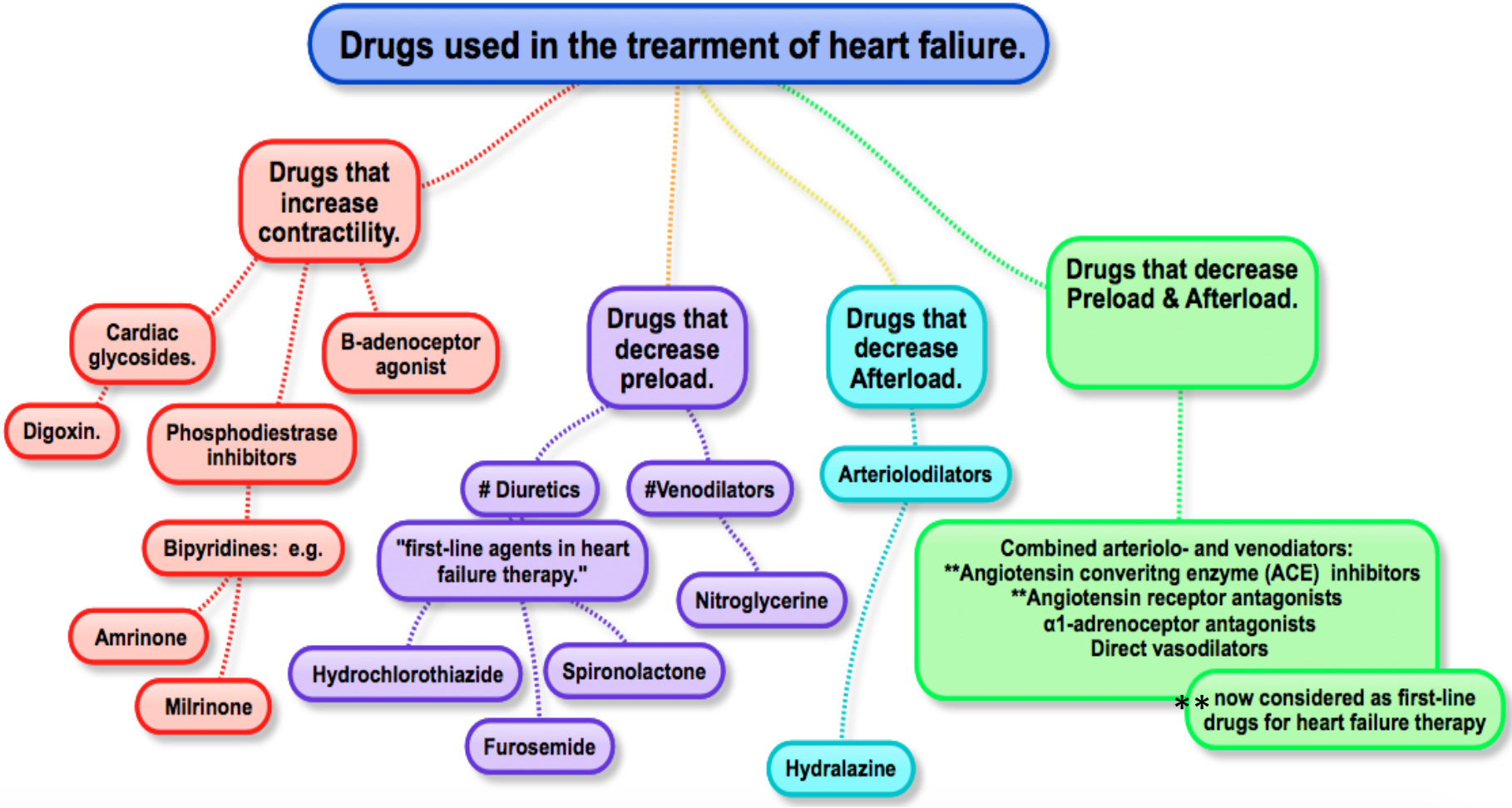
Group	Diuretics	Venodialators	Arteriolodialators
Action	**Decrease preload (VR) (EDV)**		**Decrease afterload (resistance)**
General	*1st line in heart failure therapy * used to treat the signs and symptoms of volume overload (pulmonary and/ or peripheral edema)	We give Venodilators or Arteriolodilators according to the patient main symptom:	
Mechanism of action	↓ salt & water retention → ↓ ventricular preload / venous pressure → ↓ cardiac size → improve cardiac performance	Dilate venous blood vessels & ↓ preload	↓ peripheral vascular resistance
Drugs	**1- Hydrochlorothiazide**: used in mild congestive HF ➔ side effect **(hypokalemia so→ give K supplements)** **2- Spironolactone:** used in congestive HF ➔K sparing diuretic - **↓ Remodeling** **3-Furosemide:** Potent diuretic Used for immediate reduction of pulmonary congestion & severe edema associated with : - Acute HF - Moderate & sever Chronic failure	**Nitroglycerine:** I.V → used in severe HF when main symptom is **Dyspnea** due to pulmonary congestion	**Hydralazine:** Used when the main symptom is **Rapid fatigue** due **low** cardiac output

Group	Angiotensin converting enzyme inhibitors	Angiotensin receptor Blockers	β adrenocepters antagonists	Direct vasodilators
Action	Decrease both (preload & afterload) / arteriolo-veno dialators			
General	*1st line in heart failure therapy with diuretics		-	-
Mechanism of action	↓ ACE → reduce/inhibit synthesis of AgII → activation of Bradykinin system which is potent vasodilation → ↓ preload & afterload	Blocks AT1 receptors → block the action of AgII (more potent effect than ACE)	-↓ mitogenic activity of catecolamines (E/NE) →↓ Remodeling -↓ mortality rate of hypertrophic cardiomyopathy -↓ H.R / Renin release	-
Drugs	Captopril / Enalapril / Rampril (Oral) Rapidly absorbed from GIT Food reduce their bioavailability -Short duration of action -no prodrug -Prodrugs converted to their active metabolites in the liver. -Long T1/2 - Given once daily Enalaprilat (active metabolite of Enalapril) Used I.V in hypertensive emergency	Losartan / Valsartan / Irbesartan -	2nd generation: Bisoprolol Metoprolol Cardioselective β1 antagonist	3rd generation Carvedilol Has additional vasodilator action α Blocker	Sodium nitroprusside -I.V → acute or severe refractory HF -Acts immediately -Effect lasts 1 – 5 min
Effects	↓Peripheral resistance (Afterload) ↓Venous return (Preload) ↓sympathetic activity ↓remodeling (cardiac & vascular) → ↓mortality rate		↓ progression of chronic HF Not used in acute HF (may precipitate acute decompensation of cardiac function)	


Management of chronic and acute HF:
CHRONIC:
ACUTE:
• ↓ work load on the heart :
*limit activity.
*reduce weight
* control hypertension
• Volume replacement
• Restrict sodium
Positive inotropic drugs
(Phosphodiesterase inhibitors and Dobutamine)
ACEI or ARBs
Vasodilators
(Na nitropruside)
#NOTE: - Venodilator> dyspnea
- Arteriodailator> Rapid fatigue
Digitalis
Antiarrhythmic drugs
β- blockers
Treatment of myocardial infarction
Direct vasodilators

Diuretics" Orally"
Diuretics" IV"

Summary:



Diuretics (decreases the blood volume)
Venodilators (decreases the venous pressure)

MCQs

- 1- Patient who started vomiting after taking Digoxin what is the first thing you should do :

A) taking Atropine B) taking K supplements

c) Stopping Digoxin D) Taking FAB fragment

- 2- Patient came to you and his main symptom is rapid fatigue due to low cardiac output which drug you should give him:

A) Furosemide B) Hydrochlorothiazide

C) Hydralazine D) Dobutamine

- 3- All drugs are rapidly absorbed from GIT after oral administration and Food reduce their bioavailability:

A) Enalaprilat B) Captopril, enalapril and ramipril

C) Enalapril , ramipril D) Captopril, enalapril

- 4- Used for immediate reduction of the pulmonary congestion& severe edema in association with acute heart failure, moderate & severe chronic failure:

A)Spironolactone B) Hydrochlorothiazide

C)Hydralazine D) Furosemide

- 5-Which one can cause any type of arrhythmia?

A) digitalis B) Captopril

C) Bipyridines D) Spironolactone

- 6-Treatment of acute heart failure in cardiogenic shock:

A)Bipyridines B) Dobutamine

C) Digitalis D) Furosemide

- 7- which drug causes more Thrombocytopenia and Liver toxicity:

A) Milrinone B) Amrinone

C) Bipyridines D) Valsartan

- 8) Management of acute heart failure:

A)Restrict sodium B) Diuretics

C) Digitalis D) ACEI or ARBs

- 9) Factors that increase digitalis toxicity:

A) Liver disease B) hyperkalemia

C) Hypocalcemia D) Hypothyroidism

- 10) Sodium nitroprusside is given:

A) IM B) I.V

C) SC D) orally

Answers :

1) C
2) C
3) B
4) D
5) A
6) B
7)B
8)B
9)D
10)B

Long video but it is helpful:

GOOD LUCK!

Done By Pharmacology Team

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For any correction, suggestions or any useful information do not hesitate to contact as: Pharmacology434@gmail.com