Medicine TEAM 437

MED437 KING SAUD UNIVERSITY

Heart Failure

Objectives :

- Different classifications of heart failure.
- Causes and precipitating factors for heart failure decompensation.
- Pathophysiology, therapies that improve survival, and prognosis.
- Diagnostic tests of HF.
- Different treatment of HF.
- Side effects of medication of HF.
- Management of cardiac risk factors for HF.
- Role of devices and lifestyle in HF treatment.

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Resources :

437 slides, 436 team, Davidson.

Introduction

★ General principles: (watch this)

- **(Only this was mentioned in the slides) Ejection Fraction (EF)** is a measurement of how much blood the left ventricle pumps out with each contraction, Normally between 50% and 70%. (EF= SV/EDV) An ejection fraction of 60 percent means that 60 percent of the total amount of blood in the left ventricle is pushed out with each heartbeat.

EXTRA

Preload is the end-diastolic volume (EDV) at the beginning of systole. It's The amount of ventricular stretch at the end of diastole.

- **Afterload is the ventricular pressure at the end of systole (ESP)**. The amount of resistance the heart must overcome to open the aortic valve and push the blood volume out into the systemic Circulation.
- **Cardiac output** is simply the amount of blood pumped by the heart per minute. Necessarily, the cardiac output is the product of the **heart rate**, which is the number of beats per minute, and the **stroke volume**, which is amount pumped per beat: **CO = HR X SV** (Note : SV = EDV - ESV). Cardiac output at rest is about 5 liters/minute (4900 ml/min). Cardiac output is determined by preload (the volume and pressure of blood in the ventricles at the end of diastole), afterload (the volume and pressure of blood in the ventricles during systole) and myocardial contractility; this is the basis of *Starling's Law.*

★ Heart Failure:

Heart failure is bad , and its prognosis is bad. Even as worse as cancers. You have to treat probably. Heart failure age among Saudis is lower 10-15 years in comparison to Europe because of DM, HT, poor lifestyle and other comorbidities.

- ➔ Heart failure is **a complex syndrome** [1] that can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood (and profuse tissues).
- ➔ The initial manifestations of hemodynamic dysfunction are a reduction in stroke volume and a rise in ventricular filling pressures under conditions of increased systemic demand for blood flow. This stimulates a variety of interdependent compensatory responses involving the cardiovascular system, neurohormonal systems, and alterations in renal physiology
- ➔ Heart failure describes the state that develops when the heart cannot maintain an adequate cardiac output or can do so only at the expense of elevated filling pressures.
- ➔ In mild to moderate forms of heart failure, cardiac output is normal at rest and only becomes impaired when the metabolic demand increases during exercise or some other form of stress.
- ➔ Almost all forms of heart disease can lead to heart failure. An accurate aetiological diagnosis is important because treatment of the underlying cause may reverse heart failure or prevent its progression. Approximately 50% of patients are dead within 5 years.

1 HF is a syndrome as a result of many diseases of the heart. Complex clinical syndrome: because there are many mechanisms that will result in HF signs and Sx.

★Etiology:

The common cause differs regionally as in Asia ,Middle East and etc.
The common cause in SA is IHD but in Africa is Hypertension.

Main causes Focus mainly on these four major groups	★ **First: Ischemic heart disease[5], most common cause** (35–40%) ★ **Second: Cardiomyopathy (dilated)** Such as in Peripartum Cardiomyopathy (30–34%) ★ **Third: Hypertension** (15–20%) ★ **Valvular heart disease (mitral, aortic, tricuspid).**
Other causes	• Cardiomyopathies (other than dilated): hypertrophic, restrictive (amyloidosis, sarcoidosis) • Congenital heart disease (Atrial septal defect, ventricular septal defect). • Drugs (chemotherapy – trastuzumab, imatinib, Doxorubicin[2]). • Hyperdynamic circulation (anaemia*, sepsis, thyrotoxicosis*, pregnancy* and Paget's disease[3] AV fistula, Beriberi (alcohol abuse causes it)) —High output status^‖ • Hypervolemic state (Renal failure; Iatrogenic) • Haemochromatosis[4], radiation. • Right heart failure (Cor pulmonale, right ventricular infarct, pulmonary hypertension, pulmonary embolism, COPD, Pneumonia, Interstitial lung disease). • Tricuspid incompetence. • Obesity* Any factor that increases myocardial work (*) may aggravate existing HF or initiate failure. • Arrhythmias* (atrial fibrillation, AV block, bradycardia (complete heart block, sick sinus syndrome)) • Pericardial disease (constrictive pericarditis, pericardial effusion) if the pericardium is calcified there will be impaired filling which in turn lead to HF. • Infections (e.g. myocarditis due to Chagas' disease), (Coxsackieviruses). • Sleep apnea.

(not in slides)
HF could be caused by:

1. **Loss of muscles:**
Post-MI (decreased blood supply), chronic ischemia, connective tissue diseases, infections, poisons (alcohol,cobalt and drugs).

2. **Inappropriate workload:**
- ***Volume overload:*** Regurgitate valve (Aortic, mitral), High output status (mentioned above^).
- ***Pressure overload:*** Systemic HTN, Outflow obstruction (Aortic stenosis).

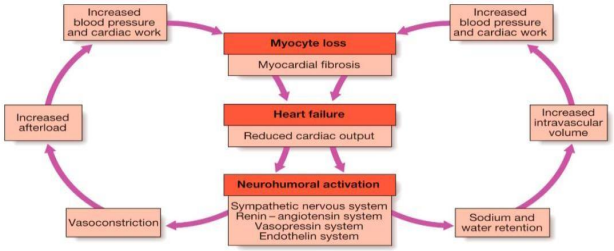
3. **Restricted filling:**
Pericardial diseases, Restrictive cardiomyopathy, tachyarrhythmias.

[2] Echo is required before and during the treatment.
[3] Paget disease is a cause of HF.
[4] Storage disorder causes restrictive cardiomyopathies.
5 As IHD is the most common cause in SA, you have to know its risk factors: DM, HT, Hyperlipidemia, smoking and family history.

Pathophysiology of Heart Failure:

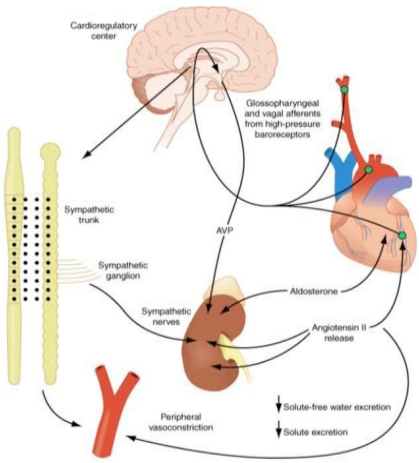
In patients without a valvular disease, the primary abnormality is *impairment of ventricular myocardial function*, leading to a fall in cardiac output. This can occur because of ***impaired systolic contraction, impaired diastolic relaxation, or both***. This activates counter-regulatory neurohumoral mechanisms that, in normal physiological circumstances, would support cardiac function but, in the setting of impaired ventricular function, can lead to a deleterious increase in both afterload and preload . A vicious circle may be established because any additional fall in cardiac output will cause further neurohumoral activation and increasing peripheral vascular resistance.

In acute heart failure, this body's response(Activation of RAS & SNS)is essential for survival but for chronic heart failure it would harmful, so we block RAS and SNS in management.



- ***Stimulation of the renin–angiotensin–aldosterone system*** *(mediated by* ***angiotensin II****, a potent constrictor of arterioles, in both the kidney and the systemic circulation)* ***leads to:***

  1) **Vasoconstriction**
  2) **Sodium and water retention.**
  3) **Sympathetic nervous system activation.**



After MI, cardiac contractility is impaired and neurohumoral activation causes hypertrophy of non-infarcted segments, with thinning, dilatation and expansion of the infarcted segment (remodelling). This leads to further deterioration in ventricular function and worsening heart failure.

Initially:

Activation of the sympathetic nervous system may *initially sustain cardiac output* through increased myocardial contractility (inotropy) and heart rate (chronotropy).

Prolonged Sympathetic Stimulation:

Negative effects :

- Cardiac myocyte apoptosis
- Hypertrophy and focal myocardial necrosis.
- **Peripheral vasoconstriction**
- arrhythmias

Activation of SNS

Sodium and water retention [5]

Promoted By:

- **Aldosterone**
- **Endothelin-1** (a potent vasoconstrictor peptide produced by the vascular endothelium with marked effects on the renal vasculature).
- Antidiuretic hormone **(ADH)** **"in severe HF".**

ADH = AVP = Vasopressin

Results in:

Pulmonary and peripheral oedema occurs because of high left and right atrial pressures.

Cellular Changes:

Last thing to happen, irreversible.

Changes in Ca^{+2} handling

(In heart failure, there is a prolongation of the calcium current in association with prolongation of contraction and relaxation).

Changes in adrenergic receptors:

- Slight ↑ in α1 receptors
- β1 receptors desensitization → followed by down regulation
- Changes in contractile proteins.
- Program cell death (Apoptosis).
- Increase amount of fibrous tissue.

★ Neurohormonal Changes:

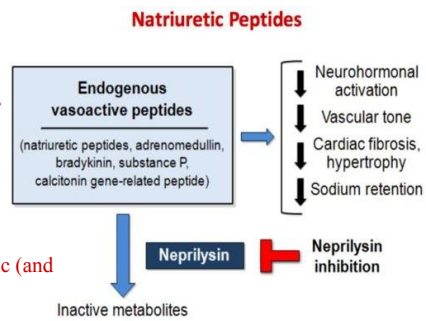
Neurohormonal changes	Favorable effect	Unfavorable effect
↑ **Increased sympathetic activity**	• ↑ HR and contractility • Vasoconstriction→ ↑ Venous return, ↑ filling	↑ Arteriolar constriction → After load → ↑ workload → ↑ O 2 consumption
↑ **Renin-Angiotensin-Aldosterone**	Salt & water retention → ↑ Venous return (preload).	•Angiotensin-II will lead to Arteriolar constriction ↑ Afterload. •Increased salt & water retention → peripheral and pulmonary edema.
↑ **Vasopressin**	Same effect	Same effect
↑ **Interleukins & TNFα**	May have roles in myocyte hypertrophy	Apoptosis
↑ **Endothelin**	Vasoconstriction→ ↑ Venous return	↑ Afterload

★ **Natriuretic peptides** are released from the atria in response to atrial stretch, and act as physiological ***antagonists*** ***to the fluid-conserving effect of aldosterone***. There are four different groups NPs identified till date [atrial natriuretic peptide (ANP), B-type natriuretic peptide (BNP), C-type natriuretic peptide (CNP) and dendroaspis natriuretic peptide, a D-type natriuretic peptide (DNP)].

➔ *Atrial natriuretic peptide (ANP) is released from atrial myocytes in response to stretch. ANP induces diuresis, natriuresis, vasodilatation and suppression of the renin–angiotensin system.*

Levels of circulating ANP are increased in congestive cardiac failure and correlate with functional class, prognosis and haemodynamic state.

➔ Administration of synthetic natriuretic peptides has not improved outcomes in acute HF but modulation of the natriuretic system through inhibition of the enzyme that degrades natriuretic (and other vasoactive) peptides, ***neprilysin***, has proven to be successful (ARN-is)



Classifications of Heart Failure

[6] reduced
[7] preserved

★ Diastolic/Systolic Failure: (MOST IMP. CLASS.)

HFrEF and HFpEF are the most and uptodate classification for heart failure. The prognosis for each is different. You cannot differentiate between them by clinical symptoms. You have to do an echo.

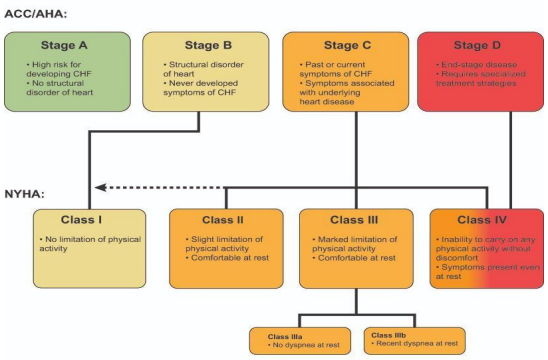
Systolic Dysfunction (HFr[6]EF)	Diastolic Dysfunction (HFp[7]EF)
Owing to impaired contractility • The abnormality is decreased EF • Causes include: 1. **Ischemic heart disease** or after a recent MI—infarcted cardiac muscle does not pump blood (decreased EF) 2. HTN resulting in cardiomyopathy 3. Valvular heart disease 4. Myocarditis (postviral) 5. Less common causes: Alcohol abuse, radiation, hemochromatosis, thyroid disease	Owing to impaired ventricular filling during diastole, because of either: 1. Impaired relaxation 2. Increased stiffness of ventricle or both - EF is preserved - Diastolic dysfunction is less common than systolic dysfunction. - HTN leading to myocardial hypertrophy is the most common cause of diastolic dysfunction. - **All-cause mortality:** similar to that of heart failure with reduced LVEF. Mortality is mostly due to non-cardiac causes - **Risk factors:** Age; female; HTN; LVH; ischemia; DM; Obesity; RCM; HCM. - **Factors associated with decompensation:** uncontrolled / labile HTN; AF; ischemia; volume overload; extracardiac cause. whom have HFrEF will end up with HFpEF but not usually the other way around.
• Usually both systolic and diastolic dysfunctions present simultaneously • Around 20-33% of HF cases have normal EF	

★ High/Low Output Heart Failure:

High Output Heart Failure[8]	Low Output Heart Failure[9]
Certain medical conditions **increase demands on cardiac output**, causing a clinical picture of heart failure due to an excessively high cardiac output. (**ex; severe anemia, thyrotoxicosis or pregnancy**)	Cardiac output is inadequate to perfuse the body (ie ejection fraction <40%), or can only be adequate with high filling pressures.

★ New York Heart Association Classification (VERY Important):

Class I	No limitation during ordinary activity. Normal physical exercise doesn't cause symptoms (fatigue,dyspnea or palpitations).
Class II	Slight/Mild limitation during ordinary activity. Comfortable at rest but normal physical exercise causes symptoms
Class III	Marked limitation. Comfortable at rest but gentle physical activity produces symptoms
Class IV	Symptoms of heart failure occur at rest, and exacerbated by any physical activity.

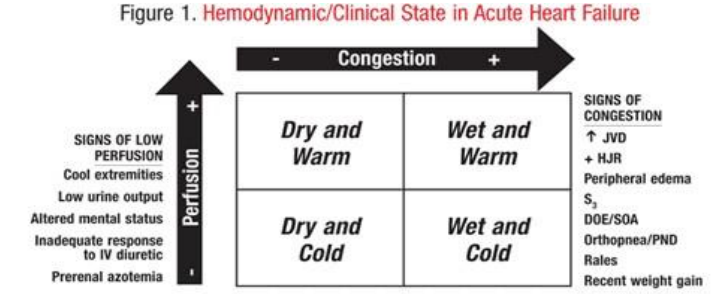


★ Acute/Chronic Heart Failure:

Acute heart failure (Acute Pulmonary edema)		Chronic heart failure (More Common)
This usually presents with sudden-onset dyspnoea at rest with acute respiratory distress, orthopnoea . A precipitant (e.g. acute MI, valvular disease, myocarditis, and cardiogenic shock) may be apparent from the history. The peripheries are cool to the touch, the pulse is rapid and there is JVD. The apex is not displaced, as there has been no time for ventricular dilatation. Auscultation may reveal S3 _gallop' and crepitations are heard at the lung bases.		This commonly follows a relapsing and remitting course, with periods of stability interrupted by episodes of decompensation. A low cardiac output causes fatigue, listlessness and a poor effort tolerance; the peripheries are cold and BP is low Clinical picture depends on: 1. The underlying heart disease 2. Type of heart failure 3. Neurohormonal changes that developed. Sometimes associated with: - Weight loss (cardiac cachexia) - Poor tissue perfusion - Skeletal muscle atrophy
Management of Acute Decompensated Heart Failure	**A. Oxygen** **B. Loop diuretics** (furosemide): Most important drug that decreases the preload[10] **C. Nitrate (IV)** : that decrease the afterload **D. Morphine** can be used Note: If pulmonary edema continuous despite these 4 > dobutamine is added (increased contractility & decrease afterload) *ACE inhibitors and β-Blockers are not used in acute settings.	

★ Forrester Classification:

Figure 1. Hemodynamic/Clinical State in Acute Heart Failure



↑: increased; +: positive; -: negative; DOE: dyspnea on exertion; HJR: hepatojugular reflux; JVD: jugular venous distention; PND: paroxysmal nocturnal dyspnea; S_3: ventricular filling murmur; SOA: shortness of air.
Source: References 10, 11.

Tx of Cold & Dry: Vasodilators/+ve inotropes (eg dobutamine)
Warm & Wet most common presentation + tx w/diuretics
You never give HF pt IV Fluids.

Dry and cold worse prognosis.

★ Dry: no congestion.
★ Wet: congestion.
★ Warm: no decrease in perfusion.
★ Cold: decrease in perfusion.

★ Left, right and biventricular heart failure:

The left side of the heart comprises the functional unit of the LA and LV, together with the mitral and aortic valves; the right heart comprises the RA, RV, and tricuspid and pulmonary valves

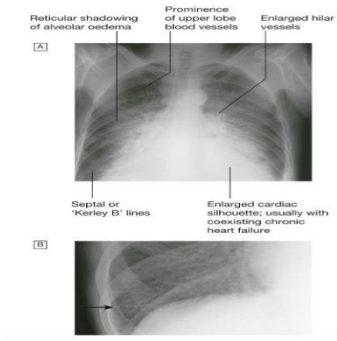
[10] Best initial therapy

Left-sided Heart Failure (reduction in LV output)		Right-sided Heart Failure (reduction in RV output)[11]
***Left-sided heart failure*:** There is a reduction in left ventricular output and an increase in left atrial and pulmonary venous pressure. An acute increase in left atrial pressure causes *pulmonary congestion or pulmonary oedema*; a more gradual increase in left atrial pressure, as occurs with mitral stenosis, leads to reflex pulmonary vasoconstriction, which protects the patient from pulmonary oedema. This increases pulmonary vascular resistance and causes pulmonary hypertension, which can, in turn, impair right ventricular function.		***Right-sided heart failure*:** There is a reduction in right ventricular output and an increase in right atrial and systemic venous pressure. Causes of isolated right heart failure include chronic lung disease (cor pulmonale), pulmonary embolism and pulmonary valvular stenosis.
Symptoms:	❖ **Dyspnea**: Difficulty breathing secondary to pulmonary congestion/edema ❖ **Orthopnea**: Difficulty breathing in the recumbent position; relieved by elevation of the head with pillows" the severity can be determined by number of the pillows" ❖ **Paroxysmal nocturnal dyspnea (PND)**: awakening after 1 to 2 hours of sleep due to acute shortness of breath (SOB) ❖ **Nocturnal cough (nonproductive)**: worse in recumbent position (same pathophysiology as orthopnea) ❖ **Confusion and memory impairment:** occur in advanced CHF as a result of inadequate brain perfusion ❖ **Diaphoresis and cool extremities at rest**: Occur in desperately ill patients (NYHA class IV)	❖ **Peripheral pitting edema**: Pedal edema lacks specificity as an isolated finding. In the elderly, it is more likely to be secondary to venous insufficiency ❖ **Nocturia**: Due to increased venous return with elevation of legs
Signs	❖ **Displaced PMI** (usually to the left) due to cardiomegaly ❖ **Pathologic S3 (ventricular gallop)** *"low pitched sound that is heard during rapid filling of ventricle"* ❖ S4 gallop ❖ Crackles/rales at lung bases [12]	❖ **Jugular venous distention (JVD)** ❖ **Painful Hepatomegaly/hepatojugular reflux** ❖ **Ascites** ❖ Right ventricular heave
Biventricular failure (Both sides)		
Example: dilated cardiomyopathy or ischaemic heart disease, affects both ventricles or because disease of the left heart leads → chronic elevation of the left atrial pressure→ pulmonary hypertension → right heart failure		

11 Most common cause of Right-sided HF is left-sided HF.

12 Because of Pulmonary Edema

★Diagnosis of CHF:

Test:	Findings:
Transthoracic Echocardiogram	★ **Initial test of choice:** should be performed whenever CHF is suspected based on history, examination, or CXR. - Useful in determining whether systolic or diastolic dysfunction predominates, and determines whether the cause of CHF is due to a pericardial, myocardial, or valvular process. - **Estimates EF (very important)**: Patients with systolic dysfunction (EF <40%) should be distinguished from patients with preserved left ventricular function (EF >40%). - Shows chamber dilation and/or hypertrophy. - Identify patients who will benefit from long-term drug therapy, e.g. ACE inhibitors.
Chest X ray (CXR)	High pulmonary venous pressure in left-sided heart failure first shows on the chest X-ray as an abnormal distension of the upper lobe pulmonary veins (with the patient in the erect position). The vascularity of the lung fields becomes more prominent, and the right and left pulmonary arteries dilate. Subsequently, interstitial oedema causes thickened interlobular septa and dilated lymphatics. These are evident as horizontal lines in the costophrenic angles (septal or _Kerley B‘ lines). More advanced changes due to alveolar oedema cause a hazy opacification spreading from the hilar regions, and pleural effusions.  - **Cardiomegaly** - ***Kerley B lines*** are short horizontal lines near periphery of the lung near the costophrenic angles, and indicate pulmonary congestion secondary to dilation of pulmonary lymphatic vessels - **Pleural effusion**
ECG	- **Nonspecific**, but can be useful for detecting chamber enlargement and presence of ischemic heart disease or prior MI. Recommended to determine rhythm, heart rate, QRS and to detect relevant abnormalities. A completly normal ECG makes systolic hf unlikely
Catheter	- Precise valve diameter, septal defects (when CAD or valvular suspected or if heart transplant is indicated)
Blood tests	- CBC for→ anemia. --Blood glucose; HbA1c - -Creatinine. -Urinalysis. -Lipids - -If necessary: CK, Iron assessment, HIV, ANA, RF, Urine metanephrines, SPEP-UPEP, Uric acid, CRP, troponin, polysomnography - Liver biochemistry(may be altered do to hepatic congestion) - Brain natriuretic peptide (BNP) or (Pro BNP), if normal(<100pg/mL) exclude heart failure (particularly pulmonary edema). - T4 & TSH - Electrolytes imbalance(including Ca / Mg)→ Chronic renal insufficiency
Others (Selected patients)	-Radionuclide ventriculography, -Cardiac MRI, - Coronary Angiography, stress test / 6MWT / VO2 Max , -Biopsy

★Management of CHF:

What are the classes and what are the options to treat HF. No need to memorize doses.

Management of any disease we think in three categories: 1- life modification. 2- Medical management. 3- Surgical intervention.

Systolic Failure Management

General lifestyle modification

Aim of management?
1.Improve quality of life:
-Reduce symptoms
-Reduce hospitalization
-Improve functional class
-Prevent disease progression
2.improve quantity:
Improve survival.

- Sodium restriction (2 gram Na = 5 gram NaCl)
- Fluid restriction (1.5 Liter = 6-8 cups)
- Weight loss
- Daily weight (tailor therapy). (diuretics) ةعرجنا دوز داز هتفش اذا كوزو بقار ضيرمهن لوقTo check whether the diuretics are effective or not.
- Smoking cessation
- Restrict alcohol use
- Exercise program (to increase heart contractility function)" Cardiac Rehab"
- Annual influenza vaccine and pneumococcal vaccine recommended because influenza virus has mortality in chronic diseases one of them chronic heart failure.

Diuretics

- Most effective means of providing symptomatic relief to patients with moderate to severe CHF
- Recommended for patients with systolic failure and volume overload
- Have not been shown to reduce mortality or improve prognosis, ***just for symptom control.*** Goal is relief of signs and symptoms of volume overload (dyspnea, peripheral edema)
- Loop diuretics: **Furosemide (Lasix)**—most potent (Most common use. Sometimes we use (furosemide + metolazone (thiazide[13]) _work in distal convoluted tubule')
- Thiazide diuretics: **Hydrochlorothiazide**—modest potency
- Side effect of these drugs: Pre-renal azotemia, Skin rashes, Neutropenia, Thrombocytopenia, Hyperglycemia, ↑Uric Acid, Hepatic dysfunction, ototoxicity" Single high dose"
  - High stage of heart failure needed high dose comparison to early stage of heart failure.

β-Blockers[14]

Has been traditionally contraindicated in pts with CHF .Now they are the main stay in treatment on CHF & may be the only medication that shows substantial improvement in LV function

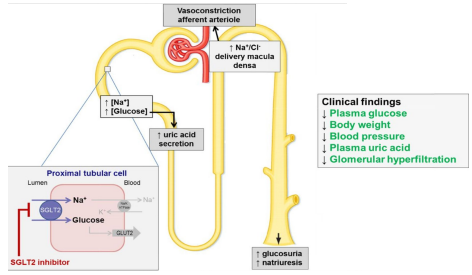
- The combination of B blockers and an ACE inhibitors required for patient with LVEF less than 40% either **symptomatic or asymptomatic**
- Proven to decrease mortality in patients with post-MI heart failure.
- β-Blockers also have antiarrhythmic and anti-ischemic effect.
- Reported to improve symptoms of CHF; may slow progression of heart failure by slowing down tissue remodeling. The decrease in heart rate(antiarrhythmic) ar leads to decreased oxygen consumption (anti ischemic effect)
- Should be given to stable patients with mild to moderate CHF (class I, II, and III) unless there is a noncardiac contraindication.
- Not all β-blockers are equal. There is evidence only for metoprolol, bisoprolol, and carvedilo
- It is contraindicated in acute HF or in case of pulmonary edema.

Spironolactone (aldosterone antagonist)

- It reduces mortality
- Monitor serum potassium and renal function
- **Prolong survival** in CHF patients with subsequent effect on myocardial remodeling and fibrosis.
- Monitor serum potassium and renal function
- Spironolactone is proven effective only for more advanced stages of CHF (classes III and IV)
- Eplerenone is an alternative to spironolactone (does not cause gynecomastia). If the patient developed gynecomastia, impotence (cause its structurally similar to progesterone) switch to eplerenone.

[13] Not effective with GFR < 30/min

[14] When a patient comes to ER with very high HR don't give him beta-blocker! Because you're blocking the mechanism that increase his cardiac output! Think, why he is having tachycardia? because of activation of sympathetic NS, now you want him to relax so give him oxygen or diuretics > HF will improve > HR back to normal. (YOU DON'T TREAT NUMBERS! YOU DEAL WITH PATHOPHYSIOLOGY).

ACE Inhibitors (Benazepril, Captopril, Enalapril, Fosinopril. Lisinopril)	Cause venous and arterial dilation, decreasing preload and afterload. ❖ **The combination of a diuretic and an ACE inhibitor should be the initial treatment in most symptomatic patients.** ❖ ACE inhibitors reduce mortality, prolong survival, and alleviate symptoms in mild, moderate, and severe CHF. ❖ Indicated for left ventricular systolic dysfunction (LV ejection fraction less than 40%). ❖ All patients with systolic dysfunction should be on an ACE inhibitor **even if they are asymptomatic.** ❖ Side effects of ACE inhibitors: Angioedema"most serious" (rare occurring but when it happen it is scary we should stop this medication and start alternative one which is ARBs and give patient steroid), Hypotension, Renal insufficiency (afferent arteriole constriction), Rash , Cough"most common"(increase in Bradykinin) ❖ If patient developed hyperkalemia or renal impairment or is pregnant→ **switch from ACEI to Hydralazine** (arterial dilator)(decrease afterload) with isosorbide dinitrate (Venodilator)(decrease preload). Always start at a low dose to prevent hypotension, Monitor BP, potassium, BUN, and creatinine.
Angiotensin II receptor blockers (ARBs)	Used in patients unable to take ACE inhibitors due to side effects (eg, angioneurotic edema, cough) **but do not replace ACE inhibitors if patient tolerates an ACE inhibitor.**
Angiotensin Receptor-Neprilysin inhibitor (ARNi)	❖ Recent FDA approval (2015). ❖ The only product available (valsartan/sacubitril). Not used alone, it needs to be combined ARBs. ❖ Valsartan = ARB. ❖ Sacubitril = prodrug for sacubitrilat. ❖ Inhibit neprilysin which breakdown the vasoactive peptides. ❖ Used if patient LVEF <= 35% and still symptomatic with ACE/ARB. In this specific group of patients it improves mortality and morbidity. "HFrEF only"
If - Channel blocker[15]:	❖ Ivabradine; Inhibit the Na inflow during the SA node action potential phase 4. ❖ Decrease the heart rate. ❖ Only use it if HR not controlled by B-blocker and remains > 70 bpm and the patient has sinus rhythm. In this group if patients it improve Morbidity and Mortality. Restrictive criteria for prescription.
SGLT2 Inhibitors (Dapagliflozin)	Diabetic medication used in Heart Failure. Blocks SGLT2 transporter in the proximal renal tubule and reduces glucose and Na+ reabsorption. It promotes diuresis, naturieses, HbA1c, weight loss. How does it promote diuresis and naturieses? During the reabsorption of of Na+ and glucose, **water** is absorbed with them. By blocking the transporter you are promoting water and sodium loss, thus reducing fluid retention. 

[15] Funnel channel Na in SA node.

Digitalis **We avoid digitalis because of its narrow therapeutic index and mostly HF patients have renal failure.**	❖ Positive inotropic[16] agent. Has vagotonic[17] & arrhythmatic effects. ❖ Useful in patients with EF <40%, who continue to have symptoms despite optimal therapy (with ACE inhibitor, β-blocker, aldosterone antagonist, and a diuretic), severe CHF, or severe AFib. ❖ Provides short-term symptomatic relief (used to control dyspnea and will decrease frequency of hospitalizations) but has not been shown to improve mortality. ❖ **Serum levels should be monitored (digoxin toxicity: yellow vision, nausea, vomiting)** ❖ Neither works on RAAS nor improves patient survival. Potassium level has to be monitored because digitalis can cause hypokalemia.

Diastolic Failure Management

Notes	Few therapeutic options available; patients are treated symptomatically (NO medications have proven mortality benefit) 1.β-Blockers have clear benefit and should be used 2.Diuretics are used for symptom control (volume overload) 3.ACE inhibitors and ARBs (Digoxin and spironolactone should NOT be used).
➔ **The standard treatment of systolic dysfunction is:**	Diuretics + ACE inhibitor + β blockers.
➔ **The initial treatment for symptomatic patient is:**	Diuretics + Vasodilatation (ACEI, ARB or Hydralazine with isosorbide[18]).

★The following medications are contraindicated in patients with CHF:

1. Metformin—may cause potentially fatal lactic acidosis.
2. Thiazolidinediones—causes fluid retention.
3. NSAIDs may increase risk of CHF exacerbation.,
4. COX-2 inhibitors because they cause water sodium retention, worsening renal function

Some antiarrhythmic agents that have negative inotropic effect.

5.CCB except amlodipine and felodipine(negative inotropic)

6. Addition of an ARB or renin inhibitor is not recommended to ACE combo also mineralocorticoids antagonist bc of risk of renal failure

★Medications that have been shown to lower mortality in systolic heart failure: (imp.)

1. ACE inhibitors and ARBs β-Blockers
2. Aldosterone antagonists (spironolactone) Hydralazine and
3. nitrate (Nitroglycerin)

★ The following devices have been shown to reduce mortality in selected patients: "after you consider all the treatment options"

1. **An ICD[19]** lowers mortality by helping prevent sudden cardiac death (which is the most common cause of death in CHF). It is indicated for patients at least 40 days post-MI, EF <35%, and class II or III symptoms despite optimal medical treatment.
2. **Cardiac resynchronization therapy (CRT):** This is biventricular pacemaker indications are similar to ICD except these patients also have prolonged QRS duration >120 msec. Most patients who meet criteria for CRT are also candidates for ICD and receive a combined device.
3. **Revascularization.**

★ Cardiac transplantation is the last alternative if the above do not control symptoms.

Advance stage of heart failure (stage D) management Cardiac Transplant (best)

There are criteria to be accepted as a candidate for Cardiac Transplantation such as young and no organs failure

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[16] Affect the strength of contraction of heart muscle (myocardial contractility).

[17] Overactivity or irritability of the vagus nerve, adversely affecting function of the blood vessels, stomach, and muscles.

[18] is in the class of drugs called nitrates that are used for treating and preventing angina.

[19] An implantable cardioverter-defibrillator (ICD) or automated implantable cardioverter defibrillator (AICD) is a device implantable inside the body, able to perform cardioversion, defibrillation, and (in modern versions) pacing of the heart

Precipitating Factors for Acute Decompensated HF

Events usually leading to rapid deterioration
• Rapid arrhythmia or severe bradycardia/conduction disturbance ★
• Acute coronary syndrome ★
• Mechanical complication of acute coronary syndrome (e.g. rupture of interventricular septum, mitral valve chordal rupture, right ventricular infarction)
• Acute pulmonary embolism
• Hypertensive crisis
• Cardiac tamponade
• Aortic dissection
• Surgery and perioperative problems
• Peripartum cardiomyopathy
Events usually leading to less rapid deterioration
• Infection (including infective endocarditis) ★
• Exacerbation of COPD/asthma ★
• Anaemia
• Kidney dysfunction
• Non-adherence to diet/drug therapy ★ Very common in our region
• Iatrogenic causes (e.g. prescription of an NSAID or corticosteroid; drug interactions) ★
• Arrhythmias, bradycardia, and conduction disturbances not leading to sudden, severe change in heart rate
• Uncontrolled hypertension
• Hypothyroidism or hyperthyroidism
• Alcohol and drug abuse

Management Of Heart Failure

1. Whether patient is symptomatic / asymptomatic, give Beta Blockers +ACE-i

↓ *Patient still symptomatic and LVEF<35%?*

2. Add Mineralocorticoid Receptor Antagonist

↓ *Patient still symptomatic and LVEF<35%?*

3. Add Neprilysin inhibitor (ARN-i)

↓ *Patient still symptomatic and LVEF<35%?*

4. Add SGLT2 inhibitor

↓ *Patient still symptomatic and LVEF<35%?*

5. Surgical Intervention (ICD/heart transplant)

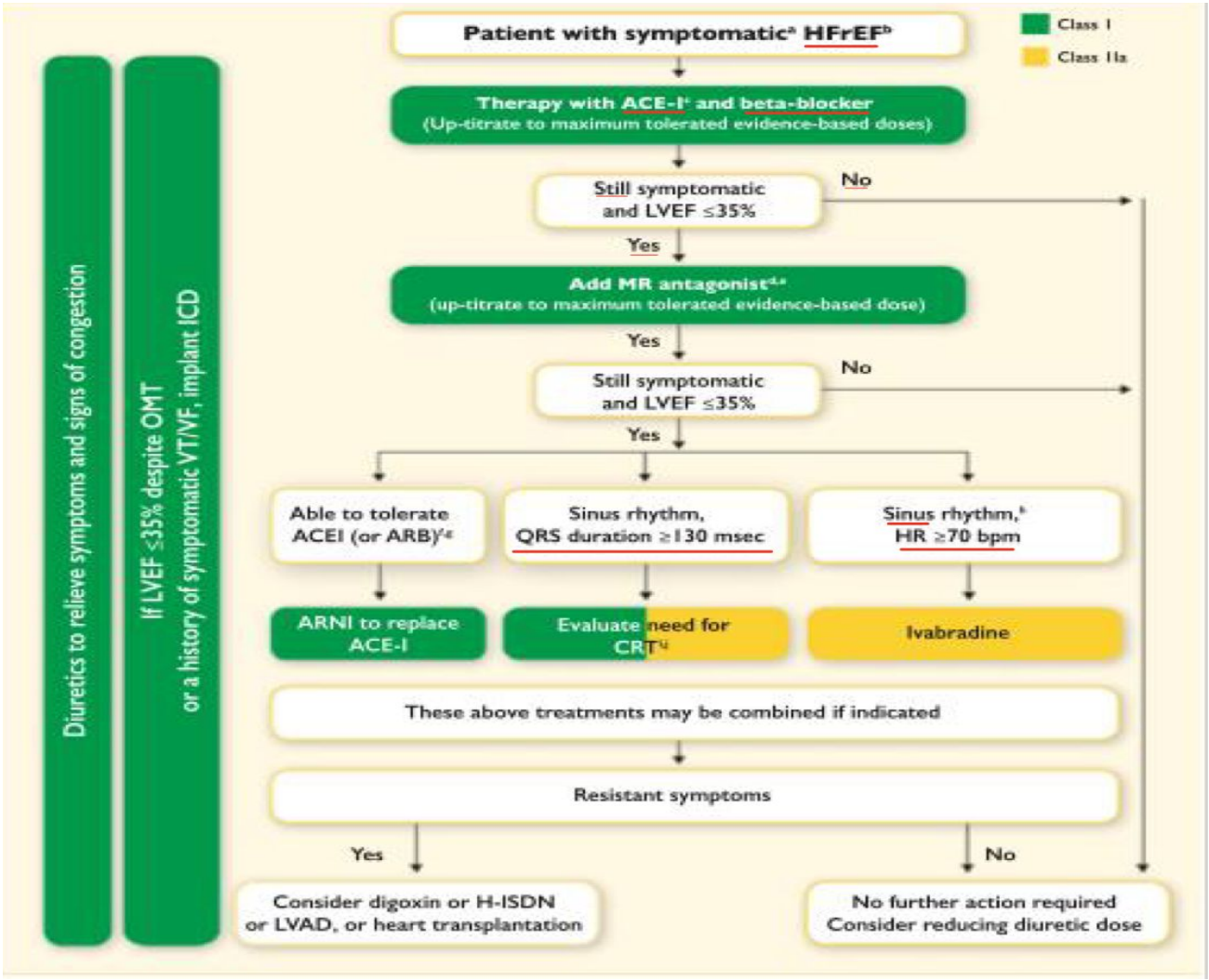
Doctors` notes IMPORTANT

1st Lecture

- Cases of HF are very important
- When we don't have s4 in patient with HF? patient with AF and atrial flutter b/c we lose atrial kick
- Ca blocker is CI in patient with HF
- Investigation / you should start by cbc , electrolyte and creatinine electrolyte= k and ca b\c you will treat patient with acei + mra-> hyperkalemia
- Creatinine =b\c you will treat patient with acei + mra
- How do we know if symptoms b/c Respiratory or cardio problem by detect bnp in blood to if it is cardio
- Acei is CI in angioedema ,pregnancy and bilateral renal artery stenosis
- In patient who can not tolerate acei and arb -> use hydralazine and isosorbide dinitrate as combo
- Depagliflozin -> new drug for HF

2nd Lecture

- Dilated cardiomyopathy ,valvular heart disease and alcohol are most in young
- We could not actually differentiate between Right side and left side HF by symptoms only but in case of acute HF we can
- In case of HHpEF the management is risk factor management
- SGLT 2 inhibitors slide is missing.
- SGLT 2 inhibitors Are used only for diabetic population.
- Positive inotropic agent slide is missing
- Anticoagulants were traditionally used for treating HF but currently is not a part of HF management and used only for specific indications.
- Anticoagulation slides are missing.
- Most common cause of death in HF patients is arrhythmia.
- recurrent hospitalization due to HF is poor prognostic factor



Diuretics are not shown here because from the beginning it would be prescribed. Is unethical to argue on diuretics because it is the most effective treatment in relieving patients' symptoms.

Mortality Benefit in Systolic Dysfunction

- ACEIs/ARBs
- Beta blockers
- Spironolactone or eplerenone
- Hydralazine/nitrates
- Implantable defibrillator
- Sacubitril

Diuretics, digoxin or positive inotropic agents(milrinone,amrinone and dobutamine) haven't been proven to lower or benefit mortality.

Summary

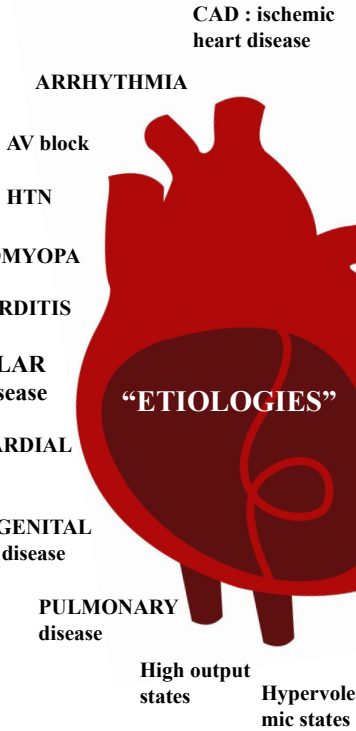
Definition: Complex clinical syndrome secondary to a functional or structural abnormality of the heart which impairs the capacity of the ventricles to eject blood or to be adequately filled.

Signs and symptoms include:

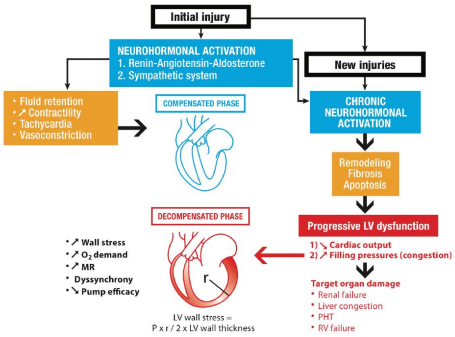
- Orthopnoea
- PND
- Decreased exercise tolerance
- Peripheral edema
- Nocturnal cough
- Tachycardia
- JVD
- S3 sound
- Crackles
- Signs of pleural effusion
- Hepatomegaly
- Peripheral edema

NYHA class:

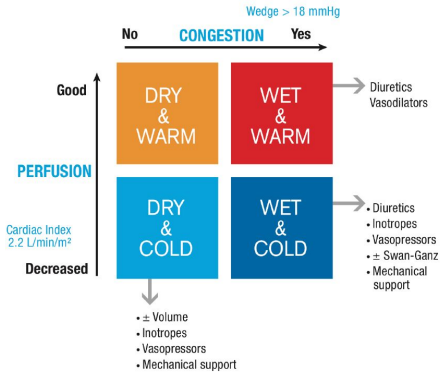
Heart failure	Symptoms
Class I	No limitation of physical activities. Ordinary physical activities do not cause any symptom
Class II	Slight limitation of physical activities. Comfortable at rest. Ordinary physical activities may cause symptoms like fatigue, palpitation, dyspnea
Class III	Marked limitation of physical activities. Comfortable at rest. Less than ordinary activities may cause symptoms like fatigue, palpitation, dyspnea
Class IV	Inability to carry out any physical activities without discomfort. Symptoms of heart failure present even at rest



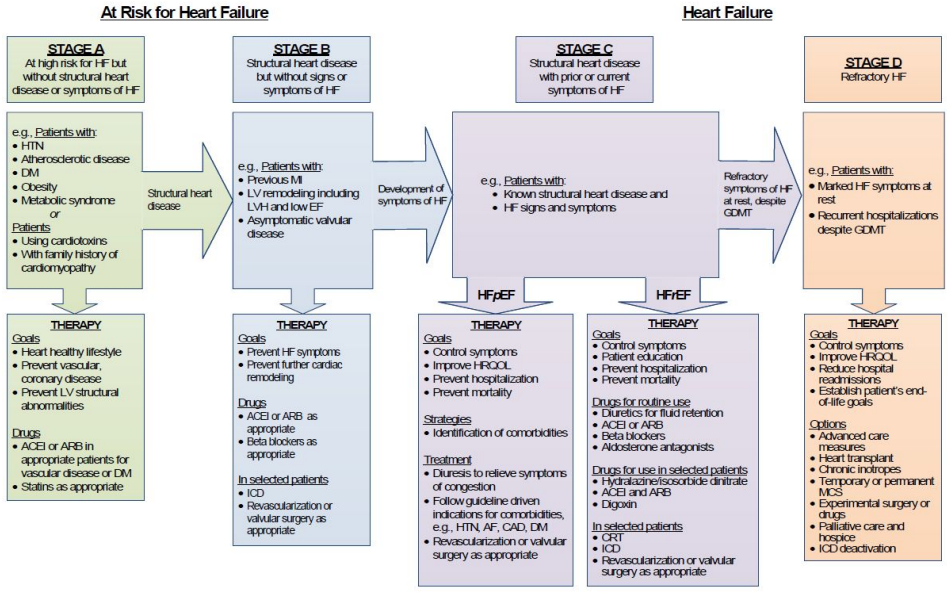
pathophysiology



Evaluation



Stages, phenotypes and treatment of HF



Summary

★ Heart Failure:

Any cardiac disorder that causes the heart to fail in ejection of blood or failure to adequately fill with blood (low cardiac output).

★ Main Pathophysiologies:

1Sympathetic nervous system: makes cardiac output better at first, but then later causes vasoconstriction.
2RAS, Aldosterone (& vasopressin): cause sodium and water retention which eventually cause peripheral and pulmonary edema. 3- Atrial Natriuretic Peptides: released from the atria to antagonize aldosterone, therefor decrease sodium and water retention.

4- Cellular changes: Changes in calcium, adrenergic receptors, and contractile proteins.

★ Classifications:

1 Systolic or Diastolic:

a. Systolic dysfunction: impaired contractility, ejection fraction is decreased. (more common)
b. Diastolic dysfunction: impaired ventricular filling, ejection fraction is preserved.

2 High or Low Output:

a. High Output: increase in demands cause excessively high cardiac output
b. Low Output: inadequate tissue perfusion, unless there is high filling pressure.

3 Class I to IV of New York Heart Association:

Depends on whether the symptoms occur at rest, or at different intensities of physical activities.

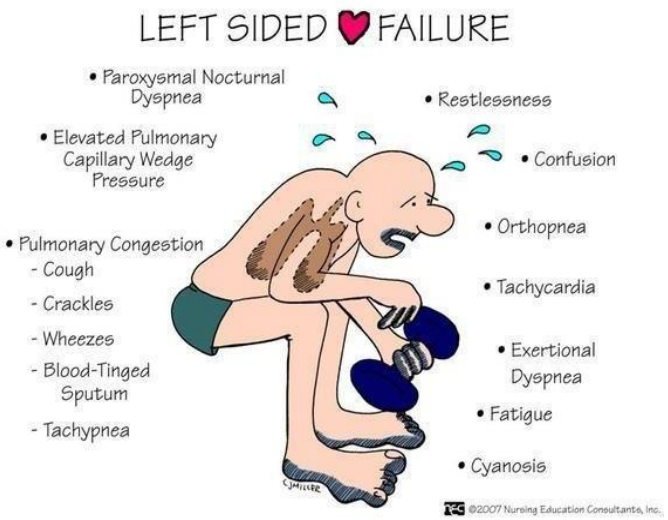
4 Acute or Chronic:

b. Acute pulmonary edema: Usually a sudden presentation of SOB and orthopnea, with Jugular Venous Distention, an S3 Gallop, but without apex beat displacement.

c. Chronic heart failure: Usually has a relapsing and remitting course, the signs and symptoms vary depending on the underlying pathologies.

5 Left sided or Right Sided or Biventricular:

b. Left sided heart failure: Reduction in Left Ventricle output, either with a sudden increase in Left Atrial (pulmonary) venous pressure which causes pulmonary edema, or gradual increase in Left Atrial pressure which protects from it. But still, this gradual increase causes pulmonary vasoconstriction which can eventually lead to Right Ventricular failure. It presents with the same signs of acute pulmonary edema, but the PMI here is displaced without JVD.



b. Right sided heart failure: Reduction in Right Ventricle output and increase in Right atrial (systemic) venous pressure. It presents with JVD, painful hepatomegaly, and ascites.

c. Biventricular heart failure: either due to a disease that affects both ventricles, or a disease of the left heart which eventually affects the right.

★ **Diagnosis:**

1- Transthoracic Echocardiogram: Determines whether systolic or diastolic (& determining EF). 2- Chest X Ray: Shows the important signs of pulmonary edema such as Kerley B Lines.

3- ECG 4- Catheter 5- Blood tests: the levels of BNP can exclude the diagnosis of heart failure.

★ **Management (main differences between systolic and diastolic):**

- Systolic: Drugs that decrease mortality (B-Blockers, ACE Inhibitors, ARBs, Spironolactone) and to improve symptoms (Diuretics, Digitalis).
- Diastolic: the drugs do not decrease mortality, they just treat the symptoms. (B-Blockers, ACE Inhibitors, ARBs, Diuretics).

Questions:

1The term „orthopnoea" refers to breathlessness (dyspnoea) in a particular situation. Which answer below describes that situation?

A. After several hours of sleep
B. Due to asthma
C. Immediately on lying flat
D. On exertion
E. On sitting upright

2Which of the following physical signs is associated with left ventricular failure?

A. A gallop rhythm with a fourth heart sound
B. A gallop rhythm with a third heart sound
C. A loud second heart sound
D. A quiet first heart sound
E. Fixed splitting of the second heart sound

3What relationship does Starling‟s Law of the heart describe?

A. Between blood pressure and cardiac output
B. Between cardiac filling and blood pressure
C. Between cardiac filling and cardiac output
D. Between heart rate and blood pressure
E. Between heart rate and cardiac output

4What underlying pathophysiological changes is chronic cardiac failure associated with?

A. Activation of the renin–angiotensin– aldosterone system (RAAS)
B. Inhibition of the RAAS
C. Inhibition of the sympathetic nervous system
D. Reduced production of brain natriuretic peptide (BNP)
E. Systemic vasodilatation

5Neuroendocrine system activation is a feature of heart failure. Abnormalities of which hormone can cause heart failure rather than result from heart failure?

A. Aldosterone
B. Angiotensin II
C. Catecholamines
D. Thyroxine
E. Vasopressin (antidiuretic hormone, ADH)

6A 78-year-old woman is admitted with heart failure. The underlying cause is determined to be aortic stenosis. Which sign is most likely to be present?

A. Pleural effusion on chest x-ray
B. Raised jugular venous pressure (JVP)
C. Bilateral pedal oedema
D. Bibasal crepitations
E. Atrial fibrillation

7A 78-year-old woman is admitted to your ward following a 3-day history of shortness of breath and a productive cough of white frothy sputum. On auscultation of the lungs, you hear bilateral basal coarse inspiratory crackles. You suspect that the patient is in congestive cardiac failure. You request a chest x-ray. Which of the following signs is not typically seen on chest x-ray in patients with congestive cardiac failure?

A. Lower lobe diversion
B. Cardiomegaly
C. Pleural effusions
D. Alveolar oedema
E. Kerley B lines

8A 70 years old female presented to the ER with SOBOE, LL swelling for 2 weeks. BP 180/100. JVP high. LL oedema. Chest crackles. ECO was done, EF = 55%. What is the patient expected to have?

A. HfpEF
B. HfrEF
C. LSHF
D. RSHF

9. A 42 English man presented to the ER with shortness of breath, fatigue, lower limb swilling. A climical dignosis of HF. on examination the patient was found to have hip pain, deafness, LL numbness, varus. What is the expected underlying cause?

A. ASD
B. Pericarditis
C. Paget‘s disease
D. Anemia.

10A patient presented with dyspnea, fatigue, palpitations at rest. He is NYHA class..

A. I
B. II
C. IV
D. III

1150 year old man is note to have severe congestive heart failure what drug of the following can prolong survival:

A. Furosemide
B. Hydrochlorothyzide
C. Spironolactone.
D. Digitalis.

12What is the initial treatment for asymptomatic patients with systolic dysfunction?

A. β blockers and Diuretics
B. Diuretics + vasodilatation (ACEI or ARBs) + β blockers
C. Diuretics + vasodilatation (ACEI or ARBs)
D. β blockers and vasodilatation (ACEI or ARBs)

13What is the standard treatment for patients with diastolic dysfunction?

A. β blockers and Diuretics
B. Diuretics + vasodilatation (ACEI or ARBs) + β blockers
C. Diuretics + vasodilation (ACEI or ARBs)
D. β blockers and vasodilatation (ACEI or ARBs)

1445 years old known CHF, he‟s on (Diuretics, ACE inhibitors, beta blockers) Recently he develops a dry cough. Which one of the following drugs caused this side effect?

A. Carvedilol (beta-blockers)
B. Enalapril (ACE inhibitors)
C. Losartan (AIIR blockers)
D. Furosemide (loop diuretic)

15Which one of the following drugs reduce the morbidity rate (hospitalization, HF symptoms) but does not affect the mortality rate?

A. Ivabradine
B. Spironolactone
C. Digoxin
D. Captopril

16. 55-year-old patient presents to you after a 3-day hospital stay for gradually increasing shortness of breath and leg swelling while away on a business trip. He was told that he had congestive heart failure, but is asymptomatic now, with normal vital signs and physical examination. An echocardiogram shows an estimated ejection fraction of 38%. The patient likes to keep medications to a minimum. He is currently on aspirin and simvastatin. Which would be the most appropriate additional treatment?

A. Begin an ACE inhibitor and then add a beta-blocker on a scheduled basis.
B. Begin digoxin plus furosemide on a scheduled basis.
C. Begin spironolactone on a scheduled basis.
D. Begin furosemide plus nitroglycerin.

17.56-year-old man, diagnosed with dilated cardiomyopathy with ejection fraction less than 25%, NYHA class II dyspnea, BP: 112/68, HR:82, JVP: 7cm water [normal], soft S3 and grade 2 pansystolic murmur, chest is clear, no lower limb edema, warm extremities.

1. According to perfusion and congestion, how do we classify this patient?

A. Warm and dry
B. Cold and dry
C. Warm and wet
D. Cold and wet

2. How do we treat this patient?

A. Diuretics
B. ACEI and beta-blockers
C. Inotropes
D. No treatment

18.You are caring for a 72-year-old man admitted to the hospital with an exacerbation of congestive heart failure. Two weeks prior to admission, he was able to ambulate two blocks before stopping because of dyspnea. He has now returned to baseline and is ready for discharge. His preadmission medications include aspirin, metoprolol, and furosemide. Systolic blood pressure has ranged from 110 to 128 mm Hg over the course of his hospitalization. Heart rate was in 120s at the time of presentation, but has been consistently around 70/minute over the past 24 hours. An echocardiogram performed during this hospitalization revealed global hypokinesis with an ejection fraction of 30%. Which of the following medications, when added to his preadmission regimen, would be most likely to decrease his risk of subsequent mortality?

A. Digoxin
B. Enalapril
C. Hydrochlorothiazide
D. Propranolol

19. A 75 year-old male presents to you with a gradual onset of symptoms suggestive of heart failure and sinus rhythm and examination confirms the presence of biventricular failure. Following confirmation of the diagnosis by chest x-ray and electrocardiography you should take the following steps:

a. Treat the heart failure with diuretics and ACE inhibitors
b. Treat the heart failure with digoxin and diuretics
c. Treat he patient with diuretics, ACE inhibitors and anticoagulants
d. Try to establish the cause of the heart failure with echocardiography, cardiac catheterisation and whatever other investigations are appropriate
e. Use ACE inhibitor, vasodilator therapy and diuretic

20-A 68-year-old man with a history of hypertension, diabetes, and urinary retention awoke feeling nauseated and light-headed. He did not respond to questions from his wife. When the emergency medical technicians arrived, his blood pressure was 60 by palpation. IV fluids and oxygen were administered. Vital signs obtained in the ER were blood pressure 60, heart rate 120 and regular, temperature 38.9C (102F), and respiratory rate 30. A brief physical examination revealed coarse rales approximately halfway up in the chest bilaterally and inaudible heart sounds. An indwelling urinary catheter was placed with drainage of 10 to 20 mL of dark urine. Chest x-ray revealed bilateral interstitial infiltrates; ECG was unremarkable except for sinus tachycardia. Antibiotics were administered, and the patient was transferred to the ICU, where a right heart catheterization was performed. Pulmonary capillary wedge pressure was 28 mmHg. Cardiac output was 1.9 L/min. Right atrial mean pressure was 10 mmHg. The most likely cause of this man's hypotension was:

(A) left ventricular dysfunction
(B) right ventricular infarction
(C) gram-negative sepsis
(D)gastrointestinal bleeding

21-A 65-year-old man with a long history of untreated hypertension complains of recurrent shortness of breath on minimal exertion. Examination of the cardiovascular system is normal except for a prominent precordial impulse. Chest x-ray is normal except for a prominent left ventricular shadow. An exercise tolerance test with thallium scanning reveals no evidence of myocardial ischemia. Two-dimensional echocardiography reveals left ventricular hypertrophy. Radionuclide ventriculography reveals normal right and left ventricular ejection fractions. What is the most likely explanation for the patient's symptoms?
(A) Chronic obstructive pulmonary disease
(B) Reactive airways disease
(C) Systolic congestive heart failure
(D) Diastolic congestive heart failure
(E) Myocardial ischemia

1-C 2-B 3-C 4-A 5-D 6-D 7-A 8-A 9-C 10-C 11-C 12-D 13-C 14-B 15-C 16-A 17(1)-A 17(2)-B 18-B 19- d 20-A 21- D