**Heart Failure**

**Definition**

Syndrome characterized by inadequate COP necessary to meet the metabolic demands of the body, manifested as end-organ hypoperfusion and/or vascular congestion.

- Acute vs. Chronic
- Systolic vs. Diastolic
- Forward vs. Backward (hypoperfusion vs. congestion)
- Left-sided vs. Right-sided
- Low-output vs. High-output
- NYHA classification
- ACC/AHA classification

*Note* Most cases of CHF are of mixed type (e.g. biventricular, both systolic and diastolic, both forward and backward)

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic HF</th>
<th>Diastolic HF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left-Sided HF</strong></td>
<td>↓ ventricular contractility</td>
<td>↓ compliance and/or impaired relaxation</td>
</tr>
<tr>
<td>S3 sound</td>
<td>S4 sound</td>
<td></td>
</tr>
<tr>
<td>↑ heart size</td>
<td>↑ heart size</td>
<td></td>
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<tr>
<td>EF</td>
<td>EF</td>
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</tbody>
</table>

**Etiology**

- Ischemic CM, valvular HD, DCM
- IHD, HTN, HCM, RCM, AS

<table>
<thead>
<tr>
<th>Hemodynamic profiles in patients with acute HF.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most patients can be categorized into one of the four hemodynamic profiles by performing a brief bedside examination that includes examination of the neck veins, lungs, and peripheral extremities.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Etiologies</th>
<th>The Five most common causes of CHF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nb</td>
<td>Consider predisposing, precipitating and perpetuating factors</td>
</tr>
<tr>
<td></td>
<td>1. CAD (60-70%)</td>
</tr>
<tr>
<td></td>
<td>2. HTN</td>
</tr>
<tr>
<td></td>
<td>3. Valvular (AS, AR and MR)</td>
</tr>
<tr>
<td></td>
<td>4. Idiopathic (often in the form of DCM)</td>
</tr>
<tr>
<td></td>
<td>5. Alcohol (may cause DCM)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Nb</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Toxic - anthracyclines, radiation, uremia, catecholamines</td>
</tr>
<tr>
<td>2.</td>
<td>Infectious - Chagas’ disease (South America), Coxsackie virus, HIV</td>
</tr>
<tr>
<td>3.</td>
<td>Endocrine - hyperthyroidism, DM, acromegaly</td>
</tr>
<tr>
<td>4.</td>
<td>Metabolic - thiamine deficiency, selenium deficiency</td>
</tr>
<tr>
<td>5.</td>
<td>Infiltrative - sarcoidosis, amyloidosis, hemochromatosis</td>
</tr>
<tr>
<td>6.</td>
<td>Genetic - HCM, Friedreich’s Ataxia, muscular dystrophy</td>
</tr>
<tr>
<td>7.</td>
<td>Congenital heart disease</td>
</tr>
<tr>
<td>8.</td>
<td>Peripartum</td>
</tr>
</tbody>
</table>

**NYHA (New-York Heart Association) Classification of HF**

- **Class 1**: No limitation of physical activity
- **Class 2**: Comfortable at rest + mild limitation of physical activity
- **Class 3**: Comfortable at rest + marked limitation of physical activity
- **Class 4**: Uncomfortable at rest + marked limitation of physical activity

**ACC/AHA (American College of Cardiology/American Heart Association) Classification of HF**

- **Stage A**: Patients at high risk for developing CHF in the future but NO functional or SHD
- **Stage B**: SHD but NO symptoms of CHF
- **Stage C**: SHD WITH current and/or prior symptoms of CHF
- **Stage D**: Refractory CHF despite medical therapy

**ETiology**

- IHD, HTN, HCM, RCM, AS
- Ischemic CM, valvular HD, DCM
- Low-output HF (demand for ↑COP)
- High-output HF

**C/P of pulm congestion (e.g. pulm edema)**

**C/P of systemic congestion (e.g. pedal edema, hepatic congestion)**

**Etiology**

- Ischemic CM, valvular HD, DCM
- IHD, HTN, HCM, RCM, AS
Precipitating factors

- Usually REVERSIBLE
- Sudden decompensation (1st episode of CHF and/or clinical deterioration)
- Important to differentiate from disease progression
- Common precipitants include:
  1. Life-style changes: ↑ salt / fluid intake, ↑ alcohol (most common)
  2. Non-compliance with treatment
  3. Uncontrolled HTN
  4. Ischemia/infarction
  5. Arrhythmias, especially A.Fib
  6. Infections, especially pneumonia
  7. Anemia
  8. Hyperthyroidism
  9. Other: PE, renal failure, sleep apnea, NSAIDs
- Routine tests to order: CXR and EKG ± cardiac enzymes (to R/O pneumonia, arrhythmias and/or ischemia/infarction)

Pathogenesis

1. HF is PROGRESSIVE DISORDER that is initiated after INDEX EVENT either
   a) Damages heart muscle, with resultant loss of cardiac myocytes, or,
   b) Disrupts ability of the myocardium to generate force, thereby preventing the heart from contracting normally.

2. Patients may remain ASYMPOTOMATIC due to activation of ADAPTIVE MECHANISMS (LV remodeling) in response to cardiac injury and/or LV dysfunction.
   a) Activation of RAAS & SNS → maintaining COP (↑ salt and water retention).
   b) Activation of VD molecules [atrial and brain natriuretic peptides (ANP and BNP), PG (PGE2 and PGJ2), and NO] → offsets excessive peripheral VC.

These adaptive mechanisms initially modulate LV function so that functional capacity of the patient is preserved; however, LATER ON patients become OVERTLY SYMPTOMATIC, with resultant increase in morbidity and mortality rates.

Activation of neurohormonal systems in HF

1. ↑ COP → "UNLOADING" of high-pressure baroreceptors (circles) in the LV, carotid sinus, and aortic arch → LOSS of inhibitory parasympathetic tone to the CNS → INCREASE in efferent sympathetic tone, and non-osmotic release of AVP from the pituitary.
   a) AVP [or ADH] is powerful VC that increases the permeability of the renal collecting ducts → water reabsorption.
   b) Activation of efferent SNS pathways to heart, vasculature, kidney and skeletal muscles.
   1. SNS stimulation of the kidney leads to the release of renin → ↑ AT II and Ald. The activation of the RAAS → salt and water retention, peripheral VC, myocyte hypertrophy, myocyte cell death, and myocardial fibrosis.

2. Although these neurohormonal mechanisms facilitate short-term adaptation by maintaining BP, and hence perfusion to vital organs, the same neurohormonal mechanisms contribute to EOD in heart and circulation and to excessive salt and water retention in advanced HF.

<table>
<thead>
<tr>
<th>Compensatory / pathophysiology</th>
<th>Compensatory mechanism</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAAS activation</td>
<td>↑ BP</td>
<td>Volume overload (congestion)</td>
<td>PVR</td>
</tr>
<tr>
<td></td>
<td>↑ SV &amp; CO (↑ preload)</td>
<td></td>
<td>Cardiac Remodeling</td>
</tr>
<tr>
<td>SNS activation</td>
<td>↑ BP</td>
<td></td>
<td>↑ 02 demand</td>
</tr>
<tr>
<td></td>
<td>↑ HR</td>
<td></td>
<td>PVR</td>
</tr>
<tr>
<td></td>
<td>↑ SV &amp; CO (↑ contractility)</td>
<td></td>
<td>Cardiac Remodeling</td>
</tr>
<tr>
<td>Frank-Starling mechanism</td>
<td>↑ SV &amp; CO (↑ preload)</td>
<td>Volume overload (congestion)</td>
<td></td>
</tr>
<tr>
<td>Ventricular Hyper trophy</td>
<td>↑ SV &amp; CO (↑ contractility)</td>
<td></td>
<td>↑ 02 demand</td>
</tr>
</tbody>
</table>
### Measuring NT-pro BNP

**Measuring NT-pro BNP**

- **B TYPE NATRIURETIC PEPTIDE (B-NP)** precursor is secreted by ventricles due to LV stretch and wall tension that is cleaved into proBNP. After secretion into ventricles, proBNP is cleaved into the active C-terminal portion and the inactive N-terminal-proBNP portion.
- Most useful for excluding CHF as a contributing factor to clinical presentation. **>150 pg/ml** had a sensitivity and specificity of 85% and 83% and LR (+) of 5.3, LR (-) 0.18 for the diagnosis of HF

<table>
<thead>
<tr>
<th>NT-proBNP levels (pg/ml)</th>
<th>Age</th>
<th>HF very likely</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;50</td>
<td>&gt;450</td>
</tr>
<tr>
<td></td>
<td>50–75</td>
<td>&gt;900</td>
</tr>
<tr>
<td></td>
<td>&gt;75</td>
<td>&gt;1800</td>
</tr>
</tbody>
</table>

### Framingham criteria for diagnosis of HF

<table>
<thead>
<tr>
<th>Major criteria</th>
<th>Minor criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>PND</td>
<td>Bilateral ankle edema</td>
</tr>
<tr>
<td>JVD distension (↑ JVP)</td>
<td>Nocturnal cough</td>
</tr>
<tr>
<td>Cracks in lung fields</td>
<td>DOE</td>
</tr>
<tr>
<td>Cardiomegaly on CXR</td>
<td>HR</td>
</tr>
<tr>
<td>Acute pulmonary edema</td>
<td>Pleural effusion</td>
</tr>
<tr>
<td>S3</td>
<td>HR &gt;120/min</td>
</tr>
<tr>
<td>Hepato-Jugular Reflux</td>
<td>Decrease in VC by 1/3</td>
</tr>
<tr>
<td>Wt loss &gt;4.5 kg in 5 days with Rx</td>
<td></td>
</tr>
</tbody>
</table>

### Evidence of LV:

- Apex: shifted out and down, localized
- Retraction of the apex parasternal space with each apical bulge (LV rocking)

### Evidence of RVE:

- Apex: shifted out, diffuse + Lt parasternal pulsations
- Retraction of the apex with each parasternal bulge (RV rocking)
- Precordial bulge: If RVE occurs during childhood
- Dullness to the RT sternum if RAE

### Investigations

1. Identify and assess precipitating factors and treatable causes of CHF
2. **Blood work:** CBC, electrolytes (Ca / Mg), BUN, creatinine, Fbg, Hba 1c, lipid profile, LFT, TFT, t ferritin, BNP, uric acid (associated with prognosis of HF)
3. **ECG:** chamber enlargement, arrhythmia, ischemia/infarction
4. **CXR:** cardiomegaly, pleural effusion, vascular redistribution, Kerley B-lines, bronchio-alveolar cuffing
5. **ECHO:** LVEF, cardiac-dimensions, SWMA, valvular disease, pericardial effusion
6. **Radionuclide angiography (MUGA):** LVEF
7. **Myocardial perfusion scintigraphy (thallium or sestamibi SPECT)**

### Symptoms of systemic congestion:

- **Dyspepsia:** anorexia, nausea, vomiting and malabsorption in severe cases
- Pain in the RUQ and epigastrum
- LL swelling and abdominal distension

### Symptoms of pulmonary congestion:

- **Dyspnea:** orthopnea, PND, chronic/nightly cough ± wheezing, hemoptysis
- Recurrent chest infection

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### Symptoms of pulmonary congestion:

- **Dyspnea:** orthopnea, PND, chronic/nightly cough ± wheezing, hemoptysis
- Recurrent chest infection

### Local signs

- **General signs**
  - JVP
  - Age
  - Kidney
  - Pulse
  - BP
  - Ratio

- **Palpitation, symptoms of cause, symptoms of complication**
  - Bilateral basal rales
  - Pleural effusion
  - JVD ± HJR
  - Enlarged tender liver
  - LL edema and ascites

- **Coldness, peripheral cyanosis, signs of cause, signs of complications**
  - Evidence of LVE:
  - Evidence of RVE:

- **Pericardial exam**
  - Evidence of LVE:
  - Evidence of RVE:

- **Auscultation**
  - S3 over the apex
  - Functional MR due to LVD
  - Evidence of the cause eg murmurs of valvular lesions

- **Investigations**
  - Blood work: CBC, electrolytes (Ca / Mg), BUN, creatinine, Fbg, Hba 1c, lipid profile, LFT, TFT, t ferritin, BNP, uric acid (associated with prognosis of HF)
  - ECG: chamber enlargement, arrhythmia, ischemia/infarction
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- **Framingham criteria for diagnosis of HF**

- **Major criteria**
  - PND
  - JVD distension (↑ JVP)
  - Cracks in lung fields
  - Cardiomegaly on CXR
  - Acute pulmonary edema
  - S3
  - Hepato-Jugular Reflux
  - Wt loss >4.5 kg in 5 days with Rx

- **Minor criteria**
  - Bilateral ankle edema
  - Nocturnal cough
  - DOE
  - HR
  - Pleural effusion
  - HR >120/min
  - Decrease in VC by 1/3

### Backward symptoms

1. Fatigue, weakness
2. CNS: dizziness, giddiness, and syncope
3. CV: angina
4. Kidney: oliguria, nocturia
5. LL: intermittent claudication

### Forward symptoms

1. Fatigue, weakness
2. CNS: dizziness, giddiness, and syncope
3. CV: angina
4. Kidney: oliguria, nocturia
5. LL: intermittent claudication

### LSHF vs RSHF

- **General signs**
  - JVP
  - Age
  - Kidney
  - Pulse
  - BP
  - Ratio

- **Palpitation, symptoms of cause, symptoms of complication**
  - Bilateral basal rales
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- Dullness to the RT sternum if RAE

### Limitations

- Age
- Renal function
- PE
### Medications in CHF

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE-I / ARBs*</td>
<td>All asymptomatic patients FC II-IV</td>
</tr>
<tr>
<td>Beta blockers (carvedilol, metoprolol and bisoprolol)</td>
<td>± Antiarrhythmic</td>
</tr>
<tr>
<td>Ald antagonists* (if severe CHF)</td>
<td>± Anticoagulant</td>
</tr>
<tr>
<td>Combination of hydralazine + nitrates*</td>
<td>= Mortality Benefit</td>
</tr>
<tr>
<td>Diuretic</td>
<td></td>
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</tbody>
</table>

### General Goals
1. Identify and treat the underlying condition.
2. Eliminate any precipitating factors.
3. Treat the symptoms (optimize preload, minimize afterload).
4. Improve survival.

### Lifestyle measures
- Diet: <30% calories from fat, <5% calories from saturated fat, <10% calories from cholesterol.
- Alcohol: <2 drinks/day for men, <1 drink/day for women.
- Smoking: Quit.
- Exercise: 30 minutes/day, 5 days/week.
- DM control: Tight glycemic control, lipid management.
- Patient education: sodium and fluid restriction.

### Vasodilator

- ACE-I: Standard of care - slow progression and improve survival
  - All asymptomatic patients FC II-IV
  - All asymptomatic patients with LV EF <40%
  - Post-MI
  - Maximum tolerated dose

### B - blocker

- Slow progression and improve survival
- Class I-III with LV EF <40%
- Class IV stable patients
- Notes: Should be used cautiously, titrate slowly because may initially worsen CHF

### Diuretics

- Furosemide: (40-500 mg OD) for potent diuresis
- Metolazone: May be used as adjunct to furosemide to increase diuresis
- Spironolactone: For class III/IV CHF already on ACEI and loop diuretic

### Ald antagonists

- Spironolactone (up to 250 mg/day)

### Inotropes

- Intravenous: Dopamine, Dobutamine
- Oral: Milrinone, Esmolol

### Nesiritide

- Intravenous: May be considered if intolerable endocrine side effects

### Anticoagulant

- Warfarin: Standard of care
- Low molecular weight heparin: For symptom control (IVfluid overload)

### CCB

- CCBS: (equivocal effect on survival): not currently recommended

### MOA

<table>
<thead>
<tr>
<th>Clinical uses</th>
<th>MOA</th>
<th>MOA</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHF and/or AF</td>
<td>Na/K-ATPase</td>
<td>Na/Ca – exchange</td>
</tr>
<tr>
<td></td>
<td>intracellular Ca</td>
<td>Other actions</td>
</tr>
<tr>
<td></td>
<td>parasympathetic NS activation</td>
<td></td>
</tr>
</tbody>
</table>

### Factors that increase digoxin toxicity ± levels

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiazide and/or loop diuretics (hydropenia)</td>
<td>± age</td>
</tr>
<tr>
<td>Spironolactone (± renal excretion)</td>
<td>± renal insufficiency</td>
</tr>
<tr>
<td>Quinidine (± renal excretion)</td>
<td>± hypokalemia, hypercalcemia, hypomagnesemia</td>
</tr>
<tr>
<td>Verapamil (± renal excretion)</td>
<td></td>
</tr>
</tbody>
</table>

### Side effects

- GI distress: anorexia, nausea, vomiting, diarrhea
- Visual disturbances: yellow-green halos, blurry vision
- CNS effects: confusion, drowsiness, psychosis/depression
- Arrhythmias: any type of brady- and/or tachyarrhythmia; “PAT with block” (pathognomonic for digoxin toxicity)
- Hyperkalemia
- Gynecomastia

### Management of digoxin toxicity

1. Hemodynamic instability
2. Hyperkalemia
3. Altered LOC
4. Accidental/intentional overdose (>10 mg)

### Other cardiac glycosides

- NSAIDs - may increase BP
- Class I/III antiarrhythmics
- Metformin: C/I in severe HF
- Thia-zoline-diones - increase edema
- Cyclic GMP phosphodiesterase inhibitors (sildenafil) with baseline low BP
### Procedural interventions

- **Cardiac Resynchronization Therapy (CRT):** symptomatic improvement with biventricular pacemaker
  - QRS > 130 msec + LVEF < 35% + severe symptoms despite optimal therapy
  - Greatest benefit likely with QRS > 150 msec, marked LVE ± MR, high diuretic requirement
- **ICD:** mortality benefit in 1st and 2nd prevention of SCD
  - Prior MI, optimal medical therapy, LVEF < 30%, clinically stable
  - Prior MI, Nonsustained VT, LVEF 30-40%, EPS inducible VT
- **LVAD/RVAD**
- **Cardiac transplantation**
- **Valve repair** if patient has significant valve disease contributing to CHF
- **Revascularization Therapy**

### ACC / AHA task force

| Stage | Life-style modification (✔ alcohol, smoking cessation) Correction of any underlying abnormalities (HTN, HPL) ±
|-------|---------------------------------------------------------------------------------------------------------------|
| Stage A | as for Stage A + ACE-Is ±
| Stage B | as for Stage A + ACE-Is ±
| Stage C | as for Stage B + Diuretics ±
| Stage D | as for Stage C + Extraordinary measures

- **Indications for ACE-I therapy:**
  1. Symptomatic CHF
  2. Asymptomatic CHF + DM
  3. Asymptomatic CHF + EF < 40%
  4. Post-MI (especially anterior MI) if EF < 40% and/or manifestations of CHF
- **Manifestations of systemic and/or pulm congestion** ➤ add diuretics
- **CHF stabilized with ACE-Is + diuretics** ➤ β-blockers
  - NOT use β-blockers in decompensated CHF and/or NYHA Class IV CHF
- **Symptomatic despite standard therapy (ACE-Is + diuretics ± β-blockers)** ➤ add ALD ANT (especially beneficial in NYHA class III/IV patients)
  - Intolerance to ACE-Is (e.g. chronic cough) ➤ ARBs
  - Intolerance and/or CIs to ACE-Is and/or ARBs ➤ hydralazine/nitrates (especially beneficial in African-American patients)
- **CHF + A.Fib** ➤ start digoxin (although β-blockers can also be used)
- **Diastolic dysfunction** ➤ β-blockers ± CCBs (verapamil, diltiazem) ± diuretics
- **Severely symptomatic despite all available therapy** ➤ 48-hr infusion of inotropic agents (dobutamine, milrinone); may ➤ mortality

### Selecting the initial optimal therapies for the management of HF.

<table>
<thead>
<tr>
<th>Congestion?</th>
<th>Low perfusion?</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>Warm &amp; Dry OutPt Rx</td>
</tr>
<tr>
<td>Yes</td>
<td>Warm &amp; Wet Diuresis = vasodilator</td>
</tr>
<tr>
<td>Cold &amp; Dry</td>
<td>Cold &amp; Wet Tailored Rx CCU</td>
</tr>
</tbody>
</table>

Left out notes on slide 36, 38, 39