Author(s): Louis D’Alecy, D.M.D., Ph.D., 2009

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Pathophysiology of Heart Failure

Congestive HF = CO = Demand
= ↓ CO &/or ↑ Demand

Louis G. D’Alecy, Professor of Physiology
Heart Failure Outline

1) Normal Control of Stroke Volume
   a) Contractility
   b) Preload
   c) Afterload

2) Pathophysiology
   a) Systolic Dysfunction
   b) Diastolic Dysfunction
   c) Right-Sided Heart Failure
   d) Compensatory Mechanisms
Requirements for Effective Cardiac Pumping

1 Synchronized  
not arrhythmnic

2 Valves open fully  
not stenotic

3 Valves don't leak  
not insufficient or regurgitant

4 Forceful  
not failing

5 Must fill  
Not "dry"
Fig. 3.14
Lilly p 61

2 Pumps
-in series
-Interact
-Preload
-Afterload
Interaction RV & LV (e.g.)

If RV in failure inadequate blood gets to LV for adequate LV **preload** & LV output goes ↓.
If LV in failure inadequate blood gets removed from lungs and RV and excess **afterload** to RV ↓ output & ↑ pulmonary edema.
Lilly Table 9.1 Definitions

Preload - The ventricular wall tension at the end of diastole.

Afterload -- The ventricular wall tension during contraction; the resistance that must be overcome for the ventricle to eject its contents. Approximated by systolic ventricular or arterial pressure.

Contractility -- Property of heart muscle that accounts for changes in strength of contraction independent of preload and afterload.
Inotropic state

End-diastolic pressure

Arterial pressure

Contractility

Preload

Afterload

Heart rate

Stroke volume

CARDIAC OUTPUT

Ejection Fraction

~ 55%
Normal response: increased contractility increases stroke volume

Fig 9.5
Decreased SV with Systolic Dysfunction

**Abnormal**

Even

Because

**EDV**

**SV**

**Source Undetermined**
Normally:
Increased preload increases
stroke volume

Fig 9.5

Pressure (mm Hg)

ESV

(Preload)

Volume (ml)

1 2 3
skeletal muscle

heart muscle

Frank-Starling

Decompensation

Source Undetermined
Fig 9.3

Heart Failure

Increased contractility

Normal

Increased

Heart failure

Hypotension

Pulmonary congestion

Left ventricular end-diastolic pressure (or end-diastolic volume)

Stroke volume (or cardiac output)
Arterial pressure

Increased afterload decreases stroke volume
Fig 9.5

Increased afterload decreases stroke volume

Same for 1, 2, 3

(Preload)

Same for 1, 2, 3
Inotropic state or End-diastolic Pressure or Arterial Pressure or LV stress

Contractility

Preload

Afterload

Heart rate

Stroke volume

Heart rate

Cardiac output

LaPlace Relationship
systolic ejection. **Wall stress** (\( \sigma \)), like pressure, is expressed as force per unit area, and for the left ventricle, may be estimated from the LaPlace relation for a hollow sphere:

\[
\sigma = \frac{P \cdot r}{2h}
\]

Pressure \( X \) radius
2 \( X \) thickness

in which \( P \) is ventricular pressure, \( r \) is ventricular chamber radius, and \( h \) is ventricular wall thickness. In general, a useful mea-

Hypertrophy: not beat to beat.
Laplace Law

\[ CWS = \frac{(Pb)}{h} \left( 1 - \frac{b^2}{2a^2} - \frac{h}{2b} + \frac{h}{8a^2} \right) \]

where:
CWS = circumferential wall stress in dynes/cm² × 10³;
P = left ventricular pressure in dynes/cm²; a and b = major and minor semiaxes, respectively, in cm;
h = left ventricular wall thickness in cm
\[ T = P \times r \]

Tension = Press X radius

“COST”

LaPlace Relationship

50T = 50P \times r

2T = P \times 2r

50T = 25P \times 2r
As ventricle fills during diastole, the volume increases, tension doubles, with little increase in pressure.
T = P \times r  
Tension = \text{Press} \times \text{radius}  
“COST”

Isovolumetric contraction  
Increases T and P

2T = P \times 2r

50T = 25P \times 2r

“iso”
T = P \times r

Tension = \text{Press} \times \text{X radius}

"COST"

50T = 50P \times r

2T = P \times 2r

50T = 25P \times 2r
Left ventricle pressure-volume loop

Counter Clockwise

50P (Systolic)
25P (Diastolic)

Fig. 9.4
Pathophysiology of HF

CO fails to meet demand because:

1) SYSTOLIC DYSFUNCTION
   a) Impaired ventricular contractile function
   b) Increased afterload

2) DIASTOLIC DYSFUNCTION
   a) Impaired ventricular filling

3) COMPENSATORY MECHANISMS
   a) Frank-Starling
   b) Hypertrophy
   c) Neurohumoral
Reflexes

**Impaired Contractility**

1. Myocardial infarction
2. Transient myocardial ischemia
3. Chronic volume overload
   a. mitral regurgitation
   b. aortic regurgitation
4. Dilated cardiomyopathy

**Afterload (Pressure Overload)**

1. Aortic stenosis
2. Uncontrolled hypertension

"Contractile function"

Systolic Dysfunction

Left-sided Heart Failure

Fig 9.6 Top
Impaired Ventricular Relaxation
1. Left ventricular hypertrophy
2. Hypertrophic cardiomyopathy
3. Restrictive cardiomyopathy
4. Transient myocardial ischemia

Obstruction of Left Ventricular Filling
1. Mitral stenosis
2. Pericardial constriction or tamponade

Systolic Dysfunction

Left-sided Heart Failure

Diastolic Dysfunction

↑↑ Afterload (Pressure Overload)
1. Aortic stenosis
2. Uncontrolled hypertension

Fig. 9.6
Fig 9.6

Stiffness

↑

Impaired Ventricular Relaxation

1. Left ventricular hypertrophy
2. Hypertrophic cardiomyopathy
3. Restrictive cardiomyopathy
4. Transient myocardial ischemia

Obstruction of Left Ventricular Filling

1. Mitral stenosis
2. Pericardial constriction or tamponade

Diastolic Dysfunction

Left-sided Heart Failure

“Chronic”

Acute

Source Undetermined
Decreased SV with Diastolic Dysfunction

Increased stiffness
Decreased Compliance

Figure 9.7 B

Pressure (mm Hg)

EDP

Volume (ml)

SV

EDV

Diastolic pressure-volume curve
Right-Sided Heart Failure

**TABLE 9.2. Examples of Conditions That Cause Right-Sided Heart Failure**

**Cardiac causes**
- Left-sided heart failure
- Pulmonic valve stenosis
- Right ventricular infarction

**Parenchymal pulmonary disease**
- Chronic obstructive pulmonary disease
- Interstitial lung disease (e.g., sarcoidosis)
- Adult respiratory distress syndrome
- Chronic lung infection or bronchiectasis

**Pulmonary vascular disease**
- Pulmonary embolism
- Primary pulmonary hypertension
**limited**

Graph showing the relationship between cardiac output and preload, with arrows indicating the effects of afterload, contractility, and heart rate.
Heart Failure

COMPENSATORY MECHANISMS
or failing compensatory mechanisms!

Frank-Starling
Hypertrophy
Neurohumoral
Fig. 9.8

Backwards failure

- ↓ Stroke Volume
- Hypertrophy
- Frank-Starling

Initial compensation

- ↑ Ventricular end-diastolic volume
- ↑ Ventricular mass

↑ atrial pressure
Fig. 9.9

Decreased Cardiac Output

↑ Sympathetic nervous system

↑ Heart rate

↑ Contractility

↑ Renin-angiotensin system

Vasoconstriction

↑ Circulating volume

↑ Antidiuretic hormone

Maintain Blood Pressure

Cardiac Output

↑ Venous return to heart (↑ preload)

↑ Stroke volume

Peripheral edema and pulmonary congestion
Decreased CO ..decreased MAP…Baroreceptor Reflex !!!
Baroreceptor Reflex

\[
\uparrow \text{Sympathetic nervous system} \quad \uparrow \text{Renin-angiotensin system} \quad \uparrow \text{Antidiuretic hormone}
\]

\[
\begin{align*}
\uparrow \text{Contractility} & \quad \uparrow \text{Heart rate} & \quad \uparrow \text{Vasoconstriction} & \quad \uparrow \text{Circulating volume}
\end{align*}
\]

\[
\begin{align*}
\text{+ Ino} & \quad \text{+ Chron} & \quad \text{VC + Veno C} & \quad \text{Fluid retention}
\end{align*}
\]
Fig. 9.9

Decreased Cardiac Output

↑ Sympathetic nervous system

↑ Heart rate

↑ Contractility

↑ Renin-angiotensin system

Vasoconstriction

↑ Circulating volume

↑ Antidiuretic hormone

Maintain Blood Pressure

Arteriolar Venous

↑ Venous return to heart (∆ preload)

Cardiac Output

↑ Stroke volume

↑ Stroke volume

Peripheral edema and pulmonary congestion

Source Undetermined
TABLE 9-4 COMPARISON OF CARDIOVASCULAR FUNCTION IN A NORMAL PERSON AND A PATIENT WITH MODERATE-TO-SEVERE CONGESTIVE HEART FAILURE (CHF) AT REST AND AT MAXIMAL (MAX) EXERCISE

<table>
<thead>
<tr>
<th></th>
<th>CO (LITERS/MIN)</th>
<th>HR (BEATS/MIN)</th>
<th>SV (ML)</th>
<th>MAP (MM HG)</th>
<th>VO₂ (ML O₂/MIN)</th>
<th>A–VO₂ (ML O₂/100 ML)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (Rest)</td>
<td>5.6</td>
<td>70</td>
<td>80</td>
<td>95</td>
<td>220</td>
<td>4.0</td>
</tr>
<tr>
<td>Normal (Max)</td>
<td>18.0</td>
<td>170</td>
<td>106</td>
<td>120</td>
<td>2500</td>
<td>13.9</td>
</tr>
<tr>
<td>CHF (Rest)</td>
<td>4.0</td>
<td>80</td>
<td>50</td>
<td>90</td>
<td>220</td>
<td>5.5</td>
</tr>
<tr>
<td>CHF (Max)</td>
<td>6.0</td>
<td>120</td>
<td>50</td>
<td>85</td>
<td>780</td>
<td>13.0</td>
</tr>
</tbody>
</table>

CO, cardiac output; HR, heart rate; SV, stroke volume; MAP, mean arterial pressure; VO₂, whole-body oxygen consumption; A–VO₂, arterial–venous oxygen difference. VO₂ is calculated from the product of CO and A–VO₂, after the units for CO are converted to mL/min and the units for A–VO₂ are converted to mL O₂/mL blood.
TABLE 9.3. Factors that may Precipitate Symptoms in Compensated Heart Failure

- Increased metabolic demands
- Fever
- Infection
- Anemia
- Tachycardia
- Hyperthyroidism
- Pregnancy

Things that require an increase in cardiac output.
## TABLE 9.3. Factors that may Precipitate Symptoms in Compensated Heart Failure

| Increased circulating volume (increased preload) |
| Excessive sodium content in diet |
| Excessive fluid administration |
| Renal failure |
| Conditions that increase afterload |
| Uncontrolled hypertension |
| Pulmonary embolism (increased right ventricular afterload) |
| Conditions that impair contractility |
| Negative inotropic medications |
| Myocardial ischemia or infarction |
| Ethanol ingestion |
| Failure to take prescribed heart failure medications |
| Excessively slow heart rate |

- e.g. Beta blk.
- Isoflurane
- Thiopental
Coming Attractions: what to do!

Fig 9.10
HF-Evidence Based Therapies

1) ACE inhibitors
2) ARB’s (angiotensin receptor blockers)
3) Beta-blockers
4) Aldosterone antagonists
5) Anticoagulants for Atrial fibrillation
6) Implantable cardioverter (ICD)
7) Cardiac resynchronization (CRT)
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