The Aging Heart

Age-Related Changes in Cardiac Structure and Function

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Why Care About Pictures of the Normal Aging Process?

Almost no resources available
Why Should You Care?

→ The % of people 65 years and older is projected to rise from 13% to 20% between 2010 and 2030.

Regardless of the field of medicine you choose, you will treat more patients who are 65 years or older than any previous generation of physicians.
Aging ≠ Disease

And disease is not inevitable with aging

However, the chance of developing some diseases increases with age...

This is a function of **HOMEOSTENOSIS**.
Homeostasis vs. Homeostenosis

**Homeostasis** = the process through which the body maintains internal equilibrium.

→ With aging, more physiologic reserves are needed to maintain homeostasis when the body is not at rest.

**Homeostenosis** = the normal decline in the body’s functional reserves.

→ With aging, homeostenosis increases the vulnerability of organs to certain disease states, but a homeostenotic organ is not necessarily diseased.
With homeostenosis, an insult that may be withstood in a younger person pushes the elderly beyond their functional capacity, causing decompensation, disease, or death.

Physiologic reserves allow us to maintain homeostasis in the presence of environmental, emotional, or physiological stress.
Homeostenosis

- Exertion requires the body to engage its physiologic reserves.
- The homeostasis line can be thought of as the state of the heart at rest.
- Think of the red arrow as representing the physiologic reserve required to carry 20 lbs. up a flight of stairs.
Consider a Case...

A normal 78 year old woman comes in for her regular check-up. She reports feeling fine at rest, and is able to do most of her activities of daily living (ADL) without any problems. Recently, however, she has noticed that when carrying things up stairs in her home she becomes short of breath, and has even had to stop and rest if her load is too heavy.

What is causing her shortness of breath?

- It is normal for the capacity for physical exertion to decline with aging.

- In the heart, normal aging brings about changes that contribute to this decreased tolerance for exertion.
Homeostenosis in the Aging Heart

In other words, a homeostenotic heart is one that has undergone the normal aging process.

Compared with a normal young heart, the aged heart has a decreased functional capacity, but is not diseased.
Homeostenosis: Visual Evidence

While homeostenosis is a physiologic phenomenon, its anatomic basis can be seen on a gross and histological level.

Let’s turn to consider this...
Quick Review:
Heart Structure & Blood Flow

Diastole
(filling)

Systole
(pumping)
Cardiac Homeostenosis: Changes with Normal Aging

1. Structural
   a. ↑ LV wall thickness, ↓ LV chamber size

2. Histologic/Cellular
   b. Aortic valve calcification
   c. Mitral annulus calcification

3. Molecular

4. Functional
Left Ventricular Structural Changes

▲ left ventricular (LV) wall thickness, ▼ LV chamber size
Valvular Changes

Normal aortic valve

Leaflet calcification

Annulus calcification

Normal mitral valve

Insert image **Normal Aortic Valve** image such as can be viewed via http://www.heart-valve-surgery.com/Images/normal-aortic-valve.jpg

Insert image **Normal Mitral Valve** image such as can be viewed via http://dx.doi.org/10.1016/j.carrev.2009.10.004

Insert image **Annulus Calcification** image such as can be viewed via http://www.heart-valve-surgery.com/Images/mitral-valve-calcification.jpg.
Cardiac Homeostenosis: Changes with Normal Aging

1. Structural
   a. ↓ # of cardiomyocytes

2. Histologic/Cellular
   b. (↑ apoptosis, necrosis)
   c. ↑ myocyte size (hypertrophy)
   d. ↑ lipid deposits
   e. ↑ lipofuscin deposition
   f. ↑ collagen deposition and fibrosis in myocardium

3. Molecular

4. Functional
   g. Thickening of arterial intima
↓ Myocyte #, ↑ Myocyte Size (Hypertrophy)

Note: Clear spaces between the muscle fibers are artifacts due to slide processing and are not present in living tissue, however there is a slight increase in inter-myocyte space in the aged heart.
Lipofuscin (black arrows) is a brownish “wear and tear” pigment that accumulates with age.

The pigment is a product of lipid oxidation, and is a sign of free radical damage.
Thickening of Arterial Intima

Normal

Aged

Advancing Geriatrics Education (AGE): A UMMS initiative funded by the Donald W. Reynolds Foundation
Cardiac Homeostenosis: Changes with Normal Aging

1. Structural

2. Histologic/Cellular

3. Molecular
   a. Altered $\text{Ca}^{2+}$ handling
   b. $\downarrow$ $\beta$-adrenergic responsiveness

4. Functional
Altered Ca\textsuperscript{2+} Handling

- At rest, intracellular Ca\textsuperscript{2+} is largely sequestered in the sarcoplasmic reticulum (SR). This is the same in the old and young heart (the figures above are mirror images of one another).

- Contraction of cardiac muscle depends on the release of Ca\textsuperscript{2+} from the SR.
Changes in Ca\(^{2+}\) Contribute to ↓ Contractility

Changes in Ca\(^{2+}\) channel activity contribute to the prolongation of APs in the aged heart.

These changes also decrease the Ca\(^{2+}\) stored in the SR, which means action potentials trigger a smaller rise in intracellular [Ca\(^{2+}\)].

This is important because the force of myocardial contraction is proportional to the amount of Ca\(^{2+}\) released.

Thus, these changes in Ca\(^{2+}\) handling contribute to the decreased contractility of the aged heart.
β-adrenergic Responsiveness

Isoproterenol is a β-agonist (it stimulates β-receptors), similar to epinephrine (think of an adrenaline rush). Isoproterenol increases calcium release, and thus the force of myocyte contraction.

The decline in β-adrenergic responsiveness means that the aged heart gets less of a boost in contractility when stimulated by the sympathetic nervous system compared to the young heart.
Cardiac Homeostenosis: Changes with Normal Aging

1. Structural

2. Histologic/Cellular

3. Molecular

4. Functional
   a. ↑ Afterload
   b. Diastolic dysfunction
   c. Decreased contractility
   d. ↓ Maximum HR
Q: What happens when a muscle is forced to work harder for an extended period?

This can contribute to LV hypertrophy (LVH). Look for it in lab!

↑ Afterload means that during systole, the LV must work harder to eject blood into the less compliant aorta.
LV Changes

↑ Afterload

↑ LV wall thickness

↑ LV Stiffness

↓ LV chamber size

RF = risk factor for heart failure
1. ↓ LV filling in early diastole

2. ↑ Importance of the LA “kick” (atrial systole) late LV filling
How would you expect decreased EDV to affect the aged heart?
Determinants of Stroke Volume

Recall Dr. Fahey’s lecture:

Any other consequences of a decreased EDV?

**Abbreviations:**
- End-diastolic Volume = EDV
- End-systolic Volume = ESV
- Stroke Volume = SV
- Ejection Fraction = EF

**Stroke volume = EDV - ESV**

A smaller EDV means a smaller SV

**Ejection fraction = (EDV-ESV)/EDV**

Or...

**SV/EDV**

Fahey-DSF-2011
Frank Starling & PV Curves

Parameters represented in the PV curve.

- **Facebook**
  - ES: Hypothetical relation
  - SV: Stroke volume
  - ESV: End-systolic volume
  - EDV: End-diastolic volume

Blood pressure (surrogate for afterload)

- \( \downarrow \) EDV
- \( \downarrow \) Preload

Fahey-DSF-2011
What about contractility?

→ Contractility decreases with age.

This is in part due to the molecular changes considered earlier:

1. Decreased $\beta$–adrenergic responsiveness
2. Impaired $Ca^{2+}$ handling
Functional Changes

So far we have seen that with normal aging, the heart can not augment $SV$ as effectively due to:

1. $↑$ Afterload
2. Diastolic dysfunction
3. $↓$ Contractility

These changes contribute to the decline in $CO_{max}$ that reduces the exercise tolerance of older adults.

$\downarrow CO = \downarrow SV \times HR$

Now let’s consider the last part of the equation
Age-Associated Decline in Exercise Tolerance: Decreased $\text{HR}_{\max}$

With aging, $\text{HR}_{\max}$ decreases progressively from age 10 by about 1 bpm per year.

$$\text{HR}_{\max} = 220 - \text{age}$$

Why?

So glad you asked! Let’s find out.
What Determines HR at Rest?

Parasympathetic Tone

- **Pacemaker cells** of the sino-atrial node (SAN) depolarize spontaneously. In the young heart, the **intrinsic heart rate** \( (HR_{int}) \) of pacemaker cell depolarization is about 100 bpm.

Then why is the average normal resting HR 70 bpm?

- The SAN is under control of the **autonomic nervous system** (ANS). At rest, **parasympathetic** input from the **vagas nerve** slows the rate of pacemaker cell depolarization from 100 to approximately 70 bpm.

\[ \text{When parasympathetic input to the SAN is removed, HR increases to } HR_{int} \]
Resting HR vs. Intrinsic HR

Evidence for a decreased intrinsic HR with age

- When vagal tone is removed from the *aged heart*, HR may only increase to 80 bpm.
- This is less than the increase to ~100 bpm seen in the young heart.

\[ \text{HR}_{\text{int}} \text{ decreases with aging.} \]

But...

The resting HR of the aged heart is the same as that of a young heart: ~60 – 70 bpm.

What does this mean?
Resting HR vs. Intrinsic HR

→ Vagal tone diminishes with aging.

- In a 20 y.o., HR_{int} is ~100 bpm.
  → At rest, vagal tone decreases HR by ~30 – 40 bpm.

- In an 80 y.o., HR_{int} may be ~70 bpm.
  → The effect of vagal tone is to decrease HR by ~5-10 bpm.

This is important because it means the aged heart gets a smaller increase in CO by removing vagal tone than the younger heart.
Maximum HR

- HR rises above HR_{int} when the SAN is stimulated by the sympathetic nervous system.

- The decreased HR_{int}, vagal tone, and adrenergic responsiveness all contribute to the decreased HR_{max} of the aged heart.

This may be a more familiar depiction of the same concept.
Back to Our Case...

Why is our 75 year old patient becoming short of breath during an activity that she used to be able to do without difficulty?

What changes have we considered that might account for her decreased tolerance for exertion?
Summary of Normal Physiological Changes During Exercise

- **Lung**
  - Increased ventilation
  - Reduction of CO₂

- **Venous return increases**

- **Muscle Pump**
  - Increase in CO₂
  - Blood flow to exercising muscles increases

- **Heart**
  - Cardiac output increases
  - Stroke volume increases due to Starling mechanism and inotropic changes
  - Heart rate increases due to increase in sympathetic activity, vagal withdrawal, and catecholamine release

- **Adjustments to peripheral circulation**
  - Overall decrease in peripheral resistance

- **Blood flow to non-exercising organs**
  - Decreases and cerebral blood flow is preserved
Age-Related Cardiac Changes that Decrease Exercise Tolerance

\[
\text{CO} = \text{SV} \times \text{HR}
\]

- \( \downarrow \) Max HR
- \( \downarrow \) Intrinsic HR
- \( \downarrow \) \( \beta \)-adrenergic Responsiveness
- Altered Myocardial Ca\(^{2+} \) Handling
- \( \downarrow \) Aortic Compliance
- \( \downarrow \) Ejection Fraction
- \( \downarrow \) Stroke Volume
- \( \downarrow \) LV Filling
- \( \uparrow \) LV Stiffness

Note: Ejection fraction is the clinically measured index of contractility.
Homeostenosis

- Any exertion requires the body to engage its physiologic reserves.
- The homeostasis line can be thought of as the state of the heart at rest.
- Think of the red arrow as representing the physiologic reserve required to carry 20 lbs. up a flight of stairs.

So, what is going on with our patient? Normal aging!
Bibliography


Bibliography


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