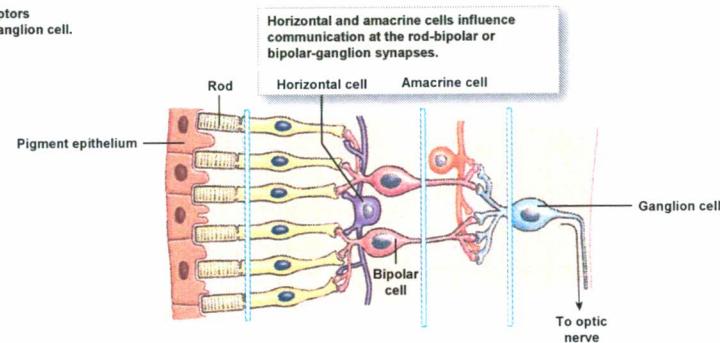


# Retina

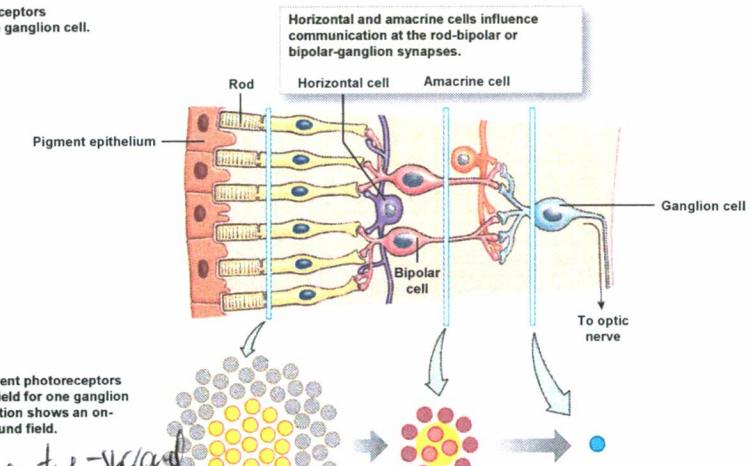
(a) Multiple photoreceptors converge on one ganglion cell.



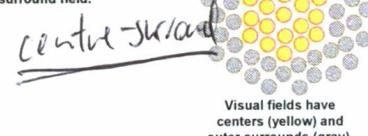
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Figure 10.33a-b (1 of 4)

(a) Multiple photoreceptors converge on one ganglion cell.



(b) A group of adjacent photoreceptors form the visual field for one ganglion cell. This illustration shows an on-center, off-surround field.



Ganglion cells respond most strongly when there is good contrast of light intensity between the center and the surround.

*1/1 correspondence of ganglion cells: visual field.*

# Receptive Fields

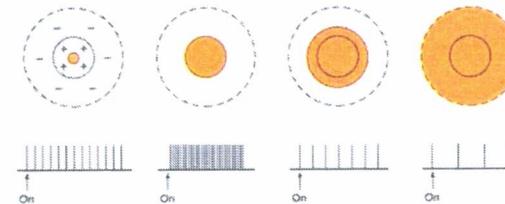
(c) The retina uses contrast rather than absolute light intensity for better detection of weak stimuli.

Visual field type	Field is on-center/off-surround	Field is off-center/on-surround
On-center, off-surround	Ganglion cell is excited by light in the center of the visual field.	Ganglion cell is inhibited by light in the center of the visual field.
Off-center, on-surround	Ganglion cell is inhibited by light on the surround of the visual field.	Ganglion cell is excited by light on the surround of the visual field.
Both field types	Ganglion cell responds weakly.	Ganglion cell responds weakly.
Diffuse light on both center and surround		

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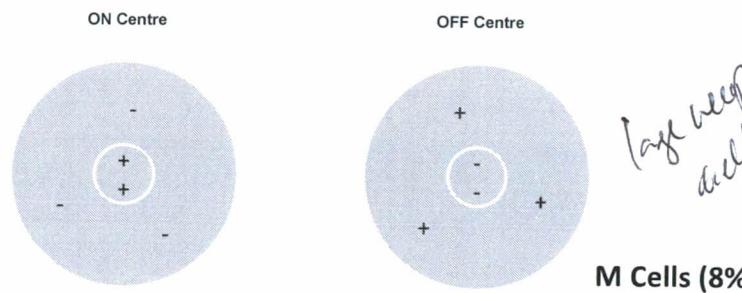
# Receptive Fields

*center surround aspect allows for*



Adapted from Hubel and Wiesel, 1961

## Receptive Fields



M Cells (8%)

↳ large  
→ contrast  
movement

P cell

↳ smaller  
→ color opponency

retinal ganglion cells.

large receptive fields.

## Colour Opponent Cells

Color opponent ganglion cells



red ON/green OFF red OFF/green ON



green ON/red OFF green OFF/red ON  
Gouras, 1968



blue ON/yellow OFF

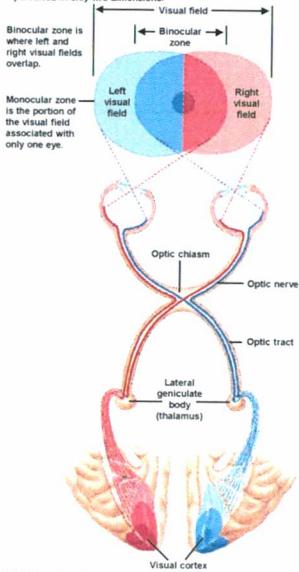


blue OFF/yellow ON

P Cells (80%)

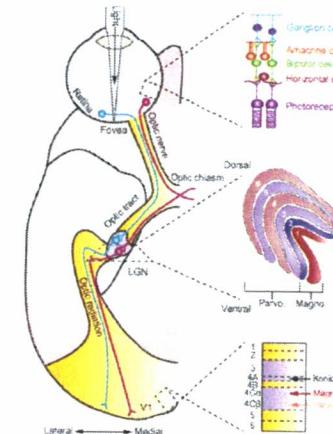
### BINOCULAR VISION

The left visual field of each eye is projected to the visual cortex on the right side of the brain, and the right visual field is projected to the left visual cortex. Objects seen by both eyes fall within the binocular zone and are perceived in three dimensions. Objects seen with only one eye fall outside the binocular zone and are perceived in only two dimensions.



into several of  
wedge of LGN  
Integrate D  
V1.

## Visual Pathway



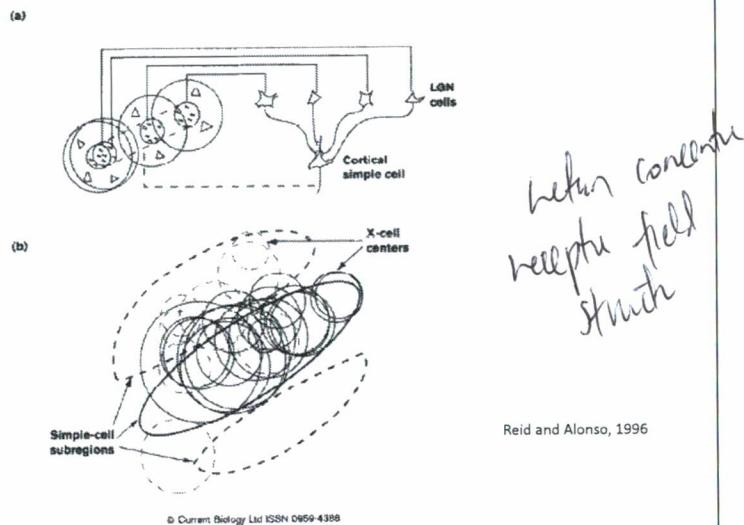
Ailsa M. Jeffries, Nathaniel J. Killian, John S. Pezaris

Mapping the primate lateral geniculate nucleus: A review of experiments and methods

Journal of Physiology-Paris, Volume 108, Issue 1, 2014, 3 - 10

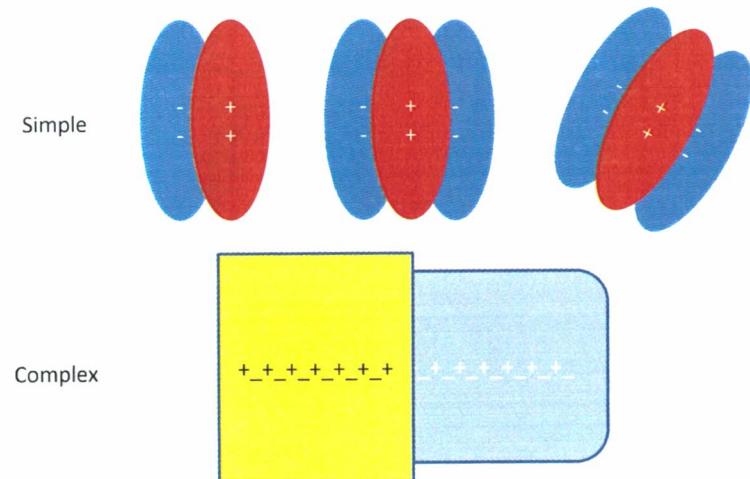
<http://dx.doi.org/10.1016/j.jphysparis.2013.10.001>

## Receptive Fields: dLGN to V1

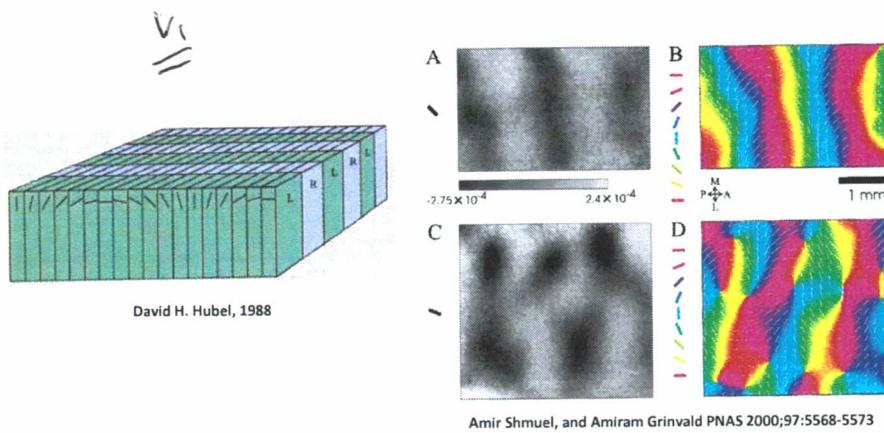


oriental selectivity  
versus.

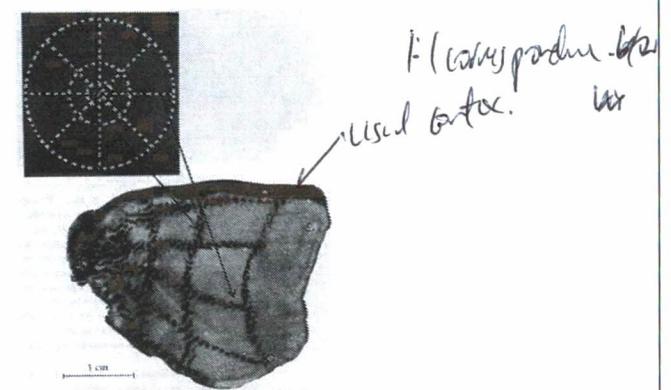
## Receptive Fields: V2



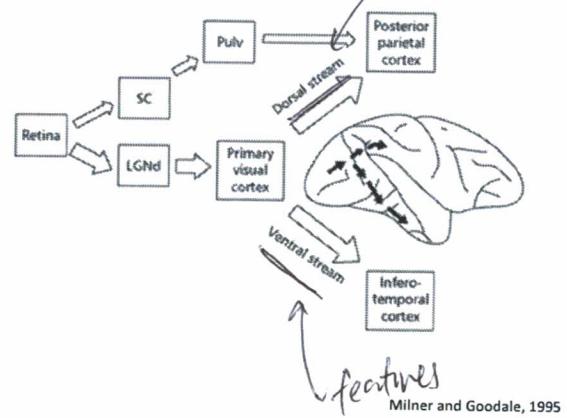
## Columnar Organization



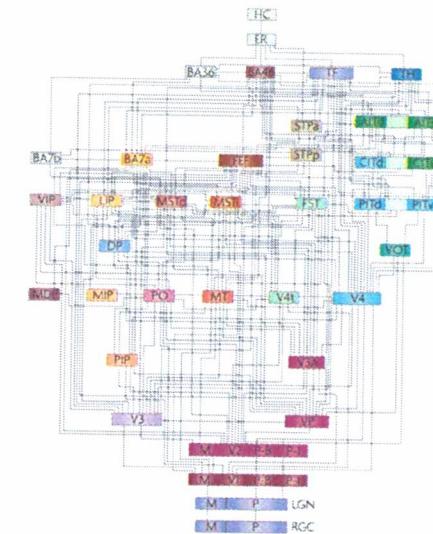
## Topography



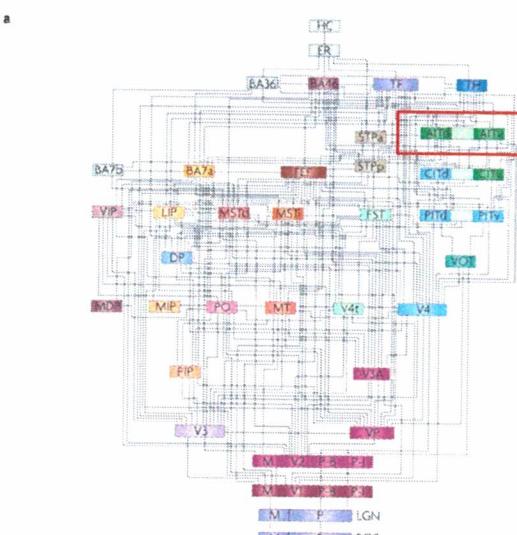
## Dorsal vs. Ventral Streams



Milner and Goodale, 1995



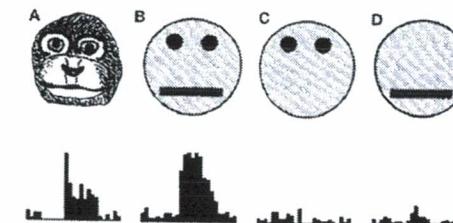
Nature Reviews Neuroscience



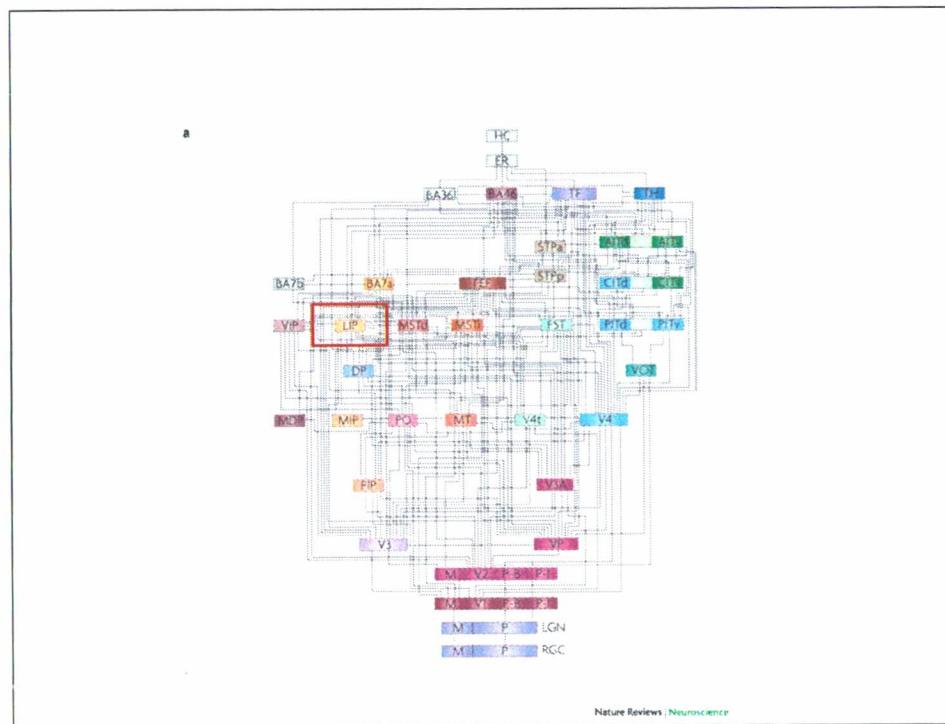
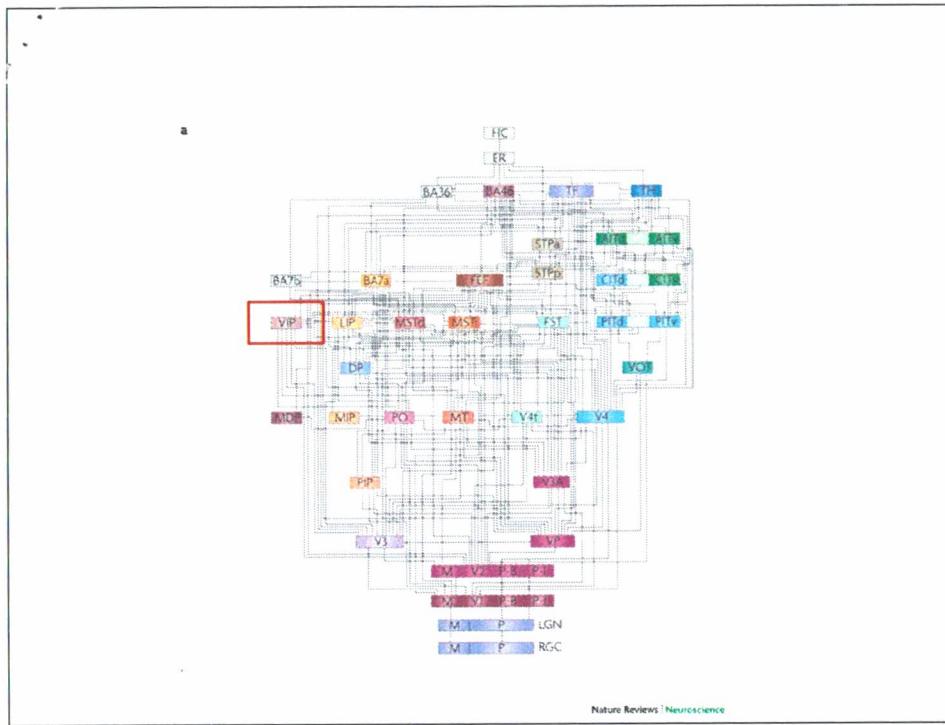
Nature Reviews | Neuroscience

## Ventral Stream: “Face” Selectivity

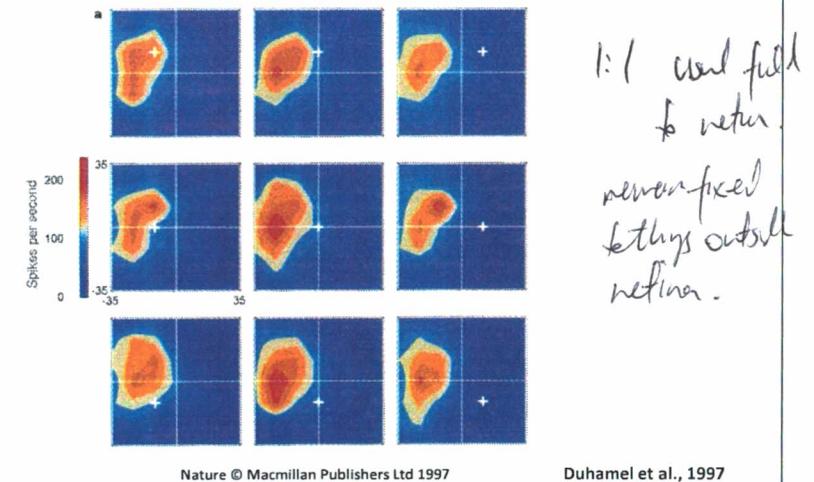
fusiform gyrus



Kobatake and Tanaka, 1994



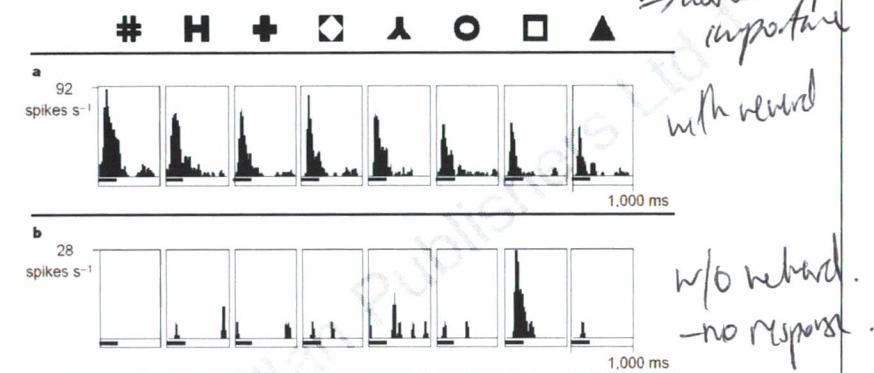
## Dorsal Stream: “Fixed” Receptive Fields



1:1 word field  
to retin.  
never fixed  
ethys outside  
retina.

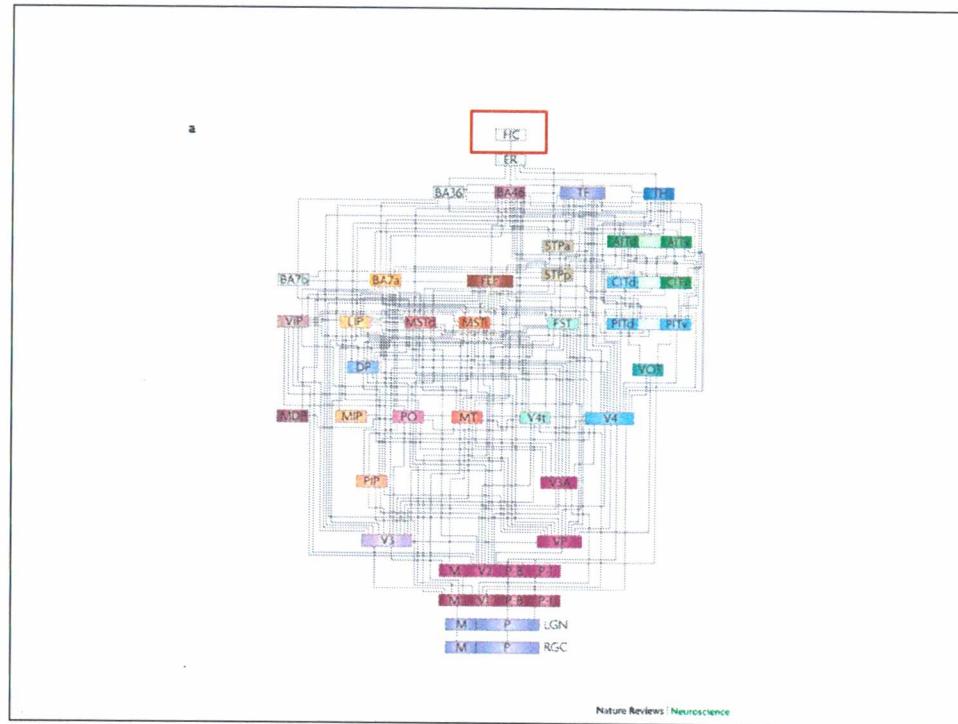
## LIP: A Dorsal Area Responsive to Shapes

*- only of meaningful shapes*  
*→ causes object importance with reward*



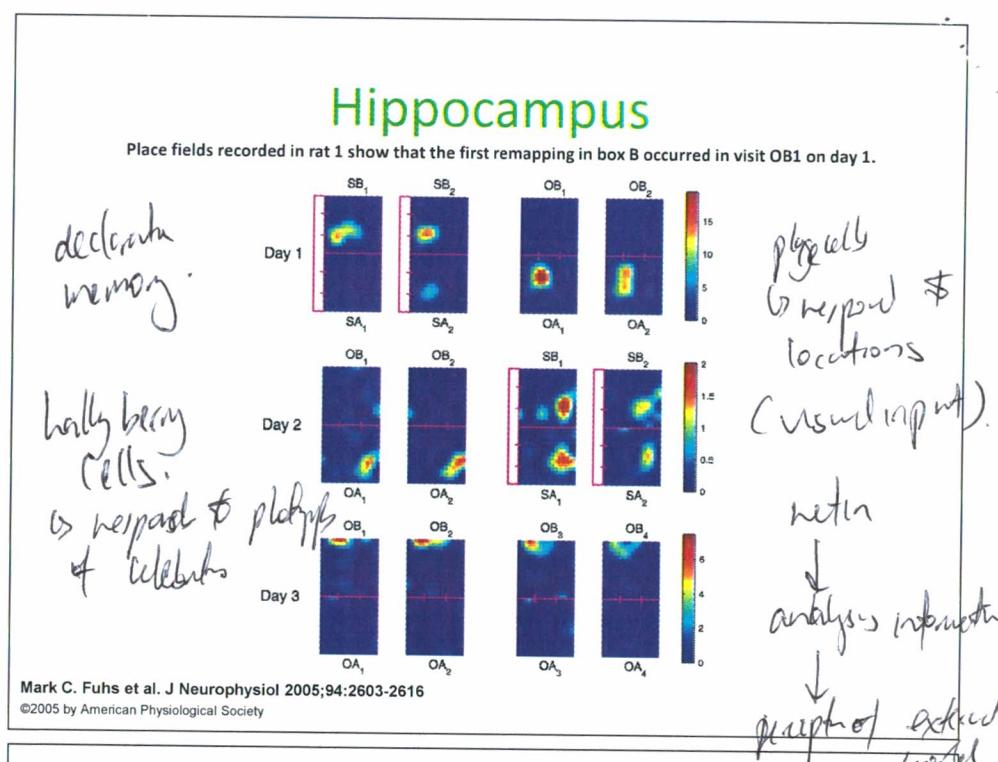
Sereno and Maunsell, 1998

w/o reward.  
no response



## Learning Objectives

- Describe the function of the fovea and relate resolving power to receptor density
  - Describe the electrical responses of retinal ganglion cells and their receptive field features
  - Describe the central visual pathway, understanding its retinotopic organisation
  - Discuss a proposed function of the visual thalamus
  - Contrast the receptive field properties of visual cortical cells with those of retinal ganglion cells and interpret the neural connections that could account for the differences



Vision Research at Sydney Uni

- Retina
    - Dario Protti
    - Ulrike Grunert
  - dLGN
    - Paul Martin
  - Visual Cortex/Visual Function
    - Paul Martin
    - Bogdan Dreher
    - Catherine Leamey
    - Atomu Sawatari

## Review Questions

Which of the following statements about the parasympathetic nervous system is INCORRECT?

- A. Ganglia are located close to their target organs
- B. Promotes digestion
- C. Nicotinic receptors mediate its effects in target organs
- D. All post-ganglionic neurons release acetylcholine

Which of the following statements regarding differences between the somatic motor and autonomic nervous systems is CORRECT ?

- A. The somatic motor system innervates skeletal and smooth muscle whereas the autonomic system controls glands and cardiac muscle
- B. The transmitter that communicates between nerve and muscle is always acetylcholine in the somatic motor system and is always noradrenaline in the autonomic nervous system
- C. Somatic motor neurons originate from the ventral horn of the spinal cord whereas autonomic pre-ganglionic neurons have their cell bodies in the dorsal horn of the spinal cord
- D. A single neuron links the CNS and muscle in the somatic system whereas there is always a 2 neuron chain in the autonomic nervous system

Which of the following statements regarding the sympathetic and parasympathetic nervous systems is correct:

- A. The sympathetic nervous system is voluntary whereas the parasympathetic is involuntary
- B. The sympathetic nervous system regulates heart rate and blood pressure whereas the parasympathetic regulates digestion
- C. The sympathetic nervous system has long postganglionic fibres whereas the parasympathetic has long preganglionic fibres
- D. Preganglionic sympathetic fibres are of craniosacral origin whereas preganglionic parasympathetic fibres are of thoracolumbar origin

The Edinger-Westphal (E-W) nucleus exerts an important influence over pupil diameter via which of the following mechanisms:

- A. An increase in light intensity causes increased firing in the E-W nucleus which causes the pupillary constrictor muscle to contract
- B. A decrease in light intensity causes increased firing in the E-W nucleus which causes the pupillary constrictor muscle to contract
- C. A decrease in light intensity causes decreased firing in the E-W nucleus which causes the pupillary dilator muscle to contract
- D. An increase in light intensity causes decreased firing in the E-W nucleus which causes the pupillary dilator muscle to relax

The addition of a muscarinic antagonist to the eye under ambient (normal) light conditions is would be expected to cause which of the following and why?

- A. Dilation due to the activation of cholinergic receptors in the pupillary dilator muscle
- B. Dilation due to the blockade of muscarinic receptors in the pupillary constrictor muscle
- C. Constriction due to the blockade of cholinergic receptors in the pupillary dilator muscle
- D. Constriction due to blockade of nicotinic receptors in the ciliary ganglion

Which of the following is true?

- A. Divergent connections from primary to secondary sensory neurons help to consolidate input onto a single larger receptive field
- B. Small receptive fields tend to have low spatial acuity due to high levels of convergent connections from primary to secondary sensory neurons
- C. Lateral inhibition contributes to decreased contrast between central and surround regions of receptive fields
- D. None of the above

The retina

- A. Is the main sensory element of the visual system
- B. Consists of multiple cellular layers
- C. Provides the first stage of visual processing
- D. All of the above

- A) Photoreceptors
- B) Bipolar cells
- C) Retinal ganglion cells

- Can respond by providing an “On” or “Off” signal to downstream RGCs
- Provide decreased glutamatergic output upon direct excitation by light
- Come in four different varieties in humans: 3 wavelength sensitive “cones” and one “rod” for scotopic vision
- Send their axonal projections out of the retina to thalamic and brain stem targets via the optic disk

## Phototransduction

- A. is characterized by a light induced increase in glutamate release from photoreceptors
- B. acts via the activation of transducin which ultimately reduces cGMP levels
- C. leads to an increase in “On” bipolar cell activity via activation of ionotropic glutamate receptors
- D. None of the above

## The fovea

- A. is a retinal specialization mainly associated with scotopic vision
- B. has a high degree of convergence between photoreceptors and RGCs
- C. is primarily important for the processing of peripheral, monocular information
- D. Receives input almost exclusively from cone type photoreceptors

## Which of the following about retinal receptive fields is TRUE?

- A. The majority of M-type cells exhibit colour opponency
- B. M-cells tend to have higher spatial, but lower temporal resolution compared to P-cells
- C. P-cells tend to have higher spatial, but lower temporal resolution compared to M-cells
- D. P-cells only make up 8% of all RGCs found in the primate retina

Which of the following statements about the dorsal lateral geniculate nucleus is FALSE?

- A. is where the input from both eyes converge and are massively integrated
- B. primarily contain cells with receptive fields that have a centre-surround structure similar to those of RGCs
- C. consist of separate M and P cell recipient layers
- D. output projects to primary visual cortex

Which of the following is FALSE about the primary visual cortex?

- A. is organized retinotopically
- B. is the first location within the early visual pathway where massive binocular integration takes place
- C. consists of processing units that are thought to be organized along rows of nearest neighbor cells
- D. is characterized by a huge foveal representation

In Hubel and Wiesel's model of simple orientation selective receptive fields in the primary visual cortex

- A. simple receptive fields are thought to come about by the alignment of dLGN receptive fields along the preferred orientation axis
- B. are selective for complex features such as the shape of objects
- C. are strongly influenced by the animal's direction of gaze
- D. None of the above

Receptive fields of the primary visual cortex are characterized by

- A. An overall retinotopic arrangement of responsiveness to visual stimulation
- B. selectivity for features (e.g., orientation) that are not prominently featured in the retina
- C. having features that change gradually along the surface of the cortex, suggestive of a columnar organization of processing units
- D. All of the above

### Higher order visual areas

- A. Can be generally organized along areas that are designated for the processing of shape (ventral) versus colour (dorsal)
- B. Tend to exhibit receptive field properties that are selective for simple visual features
- C. Maintain exclusively retinotopic mapping throughout
- D. None of the above

### Cells in the inferotemporal cortex

- A. are selective for complex features such as face-like structures
- B. transform retinocentric coordinates to a more allocentric ("out there") reference frame
- C. is normally associated with the dorsal processing pathway
- D. all of the above

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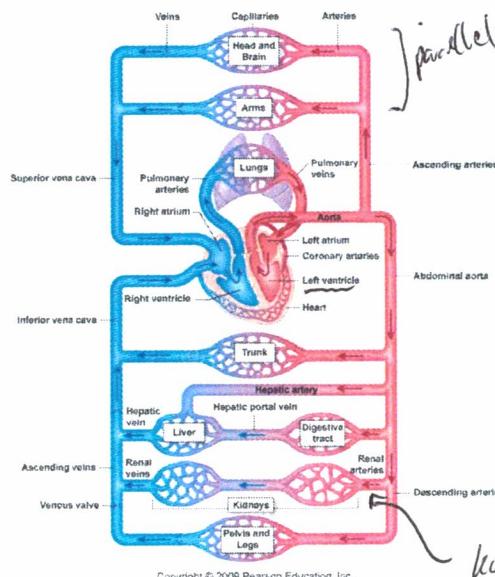
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## The Cardiovascular System 1

An introduction to the cardiovascular system and a review of hemodynamics

[sharon.hernes@sydney.edu.au](mailto:sharon.hernes@sydney.edu.au)

### General circuitry of the Cardiovascular System



- Arteries travel away from the heart
- Veins travel to the heart (regardless of degree of oxygenation).

Cardiac output is distributed throughout the organs

(*CAPILLARY*)  
Oxygenation occurs in the lungs

A red blood cell will run through vascular beds in series but not through beds running in parallel

Note capillary beds in series in the kidneys: filtration/reabsorption

*kidneys in series - series & parallel.  
filtration & reabsorption.*

## Learning Objectives

- To understand the general circuitry of the cardiovascular system
- To understand the relationships between flow, resistance and pressure as related to the cardiovascular system
- To understand the regulation of flow in the blood vessels

### Vessel structure matches function

	Diameter	Mean wall thickness	Endothelium	Elastic tissue	Smooth muscle	Fibrous tissue
Artery	4.0 mm	1.0 mm	thin	thick	thin	thin
Arteriole	30.0 μm	6.0 μm	thin	thin	thick	thin
Capillary	8.0 μm	0.5 μm	thin	thin	thin	thin
Venule	20.0 μm	1.0 μm	thin	thin	thin	thin
Vein	5.0 mm	0.5 mm	thin	thin	thin	thin

Artery – Conduit  
lot of *intervenous*, changes radius &  
Arteriole - Resistance

Capillary - Exchange  
Venule - Conduit

Veins – Conduit & Capacitance

*contractile fabric to pulsate flow.  
elastic peripherally.*

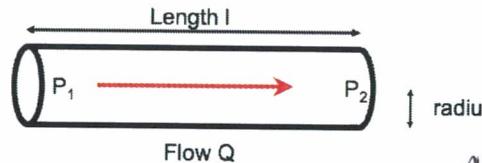
*carries construct/resistance*

*capacitive vessels, hold a lot of volume.*

## How blood moves: Flow, resistance and pressure gradients

Heart has high press.  
Rest has almost no press.

Single blood vessel



$$\text{Pressure gradient } (\Delta P) = P_1 - P_2 = QR$$

where R is the resistance to flow

Blood only flows if there is a positive pressure gradient

*positive gradient drives flow.*

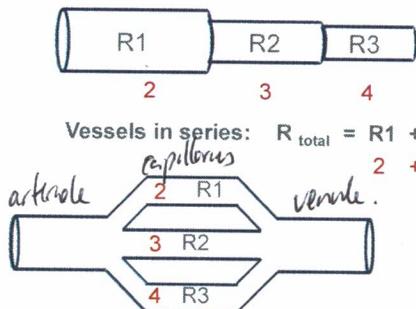
(Ohm's Law  $V=IR$ )

$Q = \text{flow}$ ,  $R = \text{resistance}$ .

*Factors of R*  
 - length of vessel  
 - radius of vessel  
 - viscosity (thick vs thin)

Coronary occlusion

## Resistance of a network of blood vessels



$$\text{Vessels in series: } R_{\text{total}} = R_1 + R_2 + R_3$$

*in series, total resist increases with more vessels.*



$$\text{Vessels in parallel: } \frac{1}{R_{\text{total}}} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3}$$

$$\frac{1}{R_{\text{total}}} = \frac{1}{2} + \frac{1}{3} + \frac{1}{4} = \frac{13}{12} \text{ so } R = \frac{12}{13} = 0.92$$

In the light of the above, explain why:

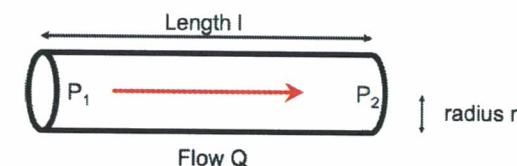
- 1) The arterial and venous systems offer relatively little resistance to flow
- 2) The arteriolar system as a whole has a relatively high resistance (60-70% of the total resistance of the entire circulation) responsible for 60-70% of total peripheral resistance.
- 3) The capillary system as a whole has a resistance which is less than that of the arteriolar system, even though capillaries have the narrowest internal diameter of all blood vessels. - all resistors in parallel.

*large diameters.*

*large diameters.*

## How blood moves: the determinants of resistance

Single blood vessel

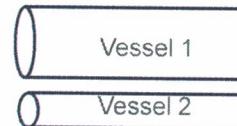


$$\text{Pressure gradient } (\Delta P) = P_1 - P_2 = QR \text{ where } R \text{ is the resistance to flow}$$

and

$$R = kl/r^4 \text{ (Poiseuille's Law)}$$

*$k = \text{viscosity}$ ,  $l = \text{length}$ ,  $r = \text{radius}$ .*



Radius of vessel 1 is twice that of vessel 2

Resistance of vessel 1 is ...?... that of vessel 2

Assuming pressure gradient ( $\Delta P$ ) is the same,  
Flow through vessel 1 is ...?... that of vessel 2

$$\text{width} = \frac{r}{16}$$

$$\text{flow } V_1 = 16V_2$$

## Cardiac output and total peripheral resistance

$$V=IR$$

For a system of vessels, Ohm's law also applies:

$$\text{Pressure gradient } (\Delta P) = Q R$$

- In the case of the entire systemic circulation, *pressure returning to heart.*  
 $\Delta P = \text{mean arterial pressure (MAP)} - \text{right atrial pressure (RAP)}$
- $Q = \text{total flow through the systemic circulation} = \text{cardiac output (CO)} \text{ (L/min)}$
- $R = \text{total resistance of the systemic circulation, referred to as the total peripheral resistance (TPR) of all resistors in circuit.}$
- Thus, for the entire systemic circulation,  $\text{MAP} - \text{RAP} = \text{CO} \times \text{TPR}$
- But  $\text{RAP} \sim 0 \text{ mmHg}$ , therefore (to a good approximation):

$$\text{MAP} = \text{CO} \times \text{TPR}$$

$$\text{MAP} - \text{RAP} = \text{CO} \times \text{TPR}$$

$$\text{RAP} \approx 0$$

$$\therefore \text{MAP} = \text{CO} \times \text{TPR}$$

Example: If  $\text{MAP} = 105$ ,  $\text{RAP} = 5 \text{ mmHg}$ , and  $\text{CO} = 5 \text{ L/min}$ ,  
 $\text{TPR} = (105-5)/5 = 20 \text{ mmHg/L/min}$

Note: Mean pulmonary arterial pressure is ~1/3 that of MAP, and therefore pulmonary vascular resistance is also ~1/3 that of TPR. Why must that be so?

*stroke volume = constant amount of colour per beat.*

$$\text{CO} = \text{HR} \times \text{SV}$$

$$\text{CO} = \text{cardiac output}$$

$$\text{HR} = \text{heart rate}$$

$$\text{SV} = \text{stroke volume}$$

## Slow blood flow velocity through capillaries

Changes in total cross-sectional area, and blood velocity, at different sites in the systemic circulation

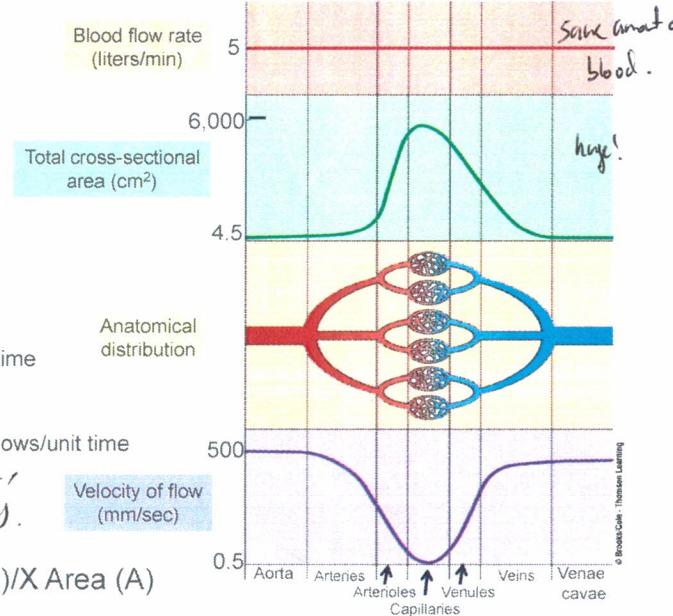
$$\text{Blood Flow} = \text{volume of blood/unit time}$$

$$\text{Flow Velocity} = \frac{dV}{dt}$$

speed, or distance blood flows/unit time

*(inflatus' distal colared, huge, : velocity decreases).*

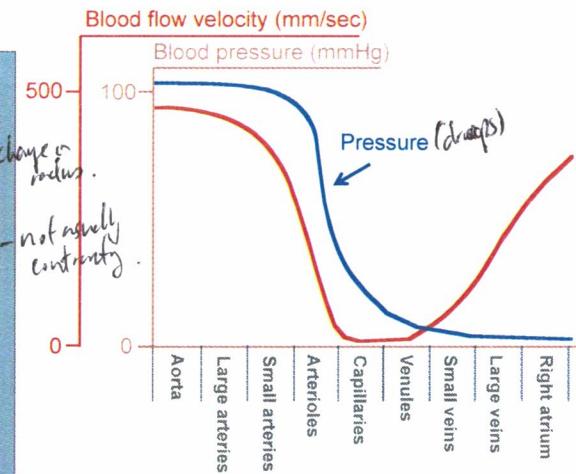
$$\text{Velocity (V)} = \text{Flow(Q)}/\text{X Area (A)}$$



## Blood pressure and blood flow velocity at different sites in the systemic circulation

Note that:

- the largest pressure drop is across the arterioles - large change in radius.
- pressure drop along arteries is minimal, therefore arterial pressure can be estimated at any site in the arterial tree
- right atrial and central venous pressure is close to zero
- the blood flow velocity in the capillaries is minimal, approximately 1/1000 that in the aorta



## Arterial and Venous Capacitance

The elastic properties of a blood vessel can be measured by determining the relationship between the static **pressure** and **volume** of a segment of that vessel.

This is called the **capacitance** (or sometimes **compliance**). Compliance ( $C$ ) =  $\Delta V/\Delta P$  where  $\Delta V$  is the change in volume, and  $\Delta P$  the corresponding change in pressure.

Venous capacitance is about 20 times arterial capacitance (walls of veins are more distensible).

that is why an increase or decrease in total blood volume is taken up into, or lost from, the venous system.

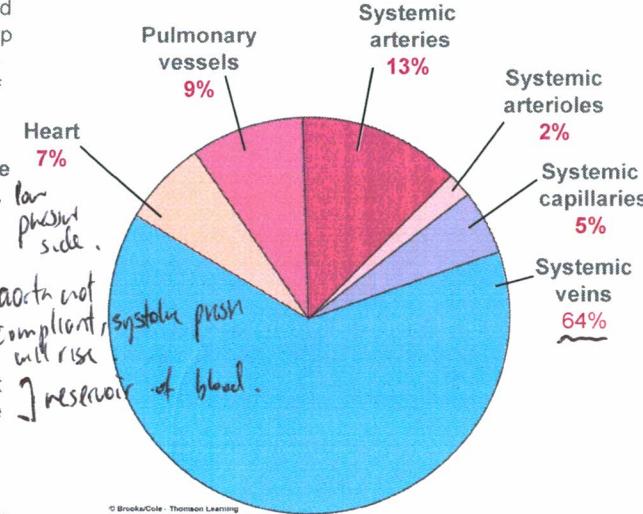


Figure 10-29 from Sherwood, L.A., Human Physiology, 4th ed., Brooks/Cole, Pacific Grove, CA, U.S.A.

## Test your knowledge...

- Which vessels produce the most resistance?  
*arterioles.*
- Which vessels hold the greatest volume of blood?  
*veins*
- In which vessels does the blood move most slowly?  
*capillaries.*
- In which vessels is pressure the lowest?  
*veins*

## Factors affecting arteriolar diameter (and therefore vascular resistance)

**Local factors:** myogenic activity, metabolites, histamine, heat/cold  
↑ allergic

**Autonomic nerves:** sympathetic vasoconstrictor nerves (nearly all beds), parasympathetic vasodilator nerves (some beds)

**Circulating hormones:** adrenaline (epinephrine), noradrenaline (norepinephrine), vasopressin, angiotensin II  
↓ vasoconstrictor

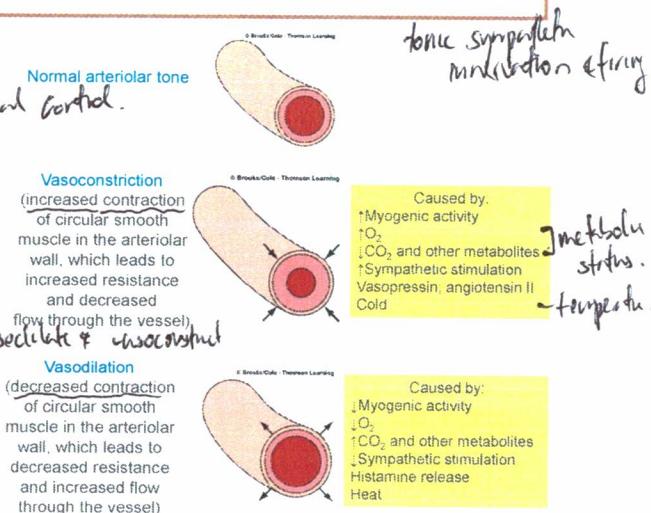


Figure 10-10 from Sherwood, L.A. 'Human Physiology' 4th ed., Brooks/Cole, Pacific Grove, CA, U.S.A.

## Test your knowledge...

Name the parameters given in Poiseuille's Law that determine Resistance in the blood vessels.

$$\text{resistance} = \frac{kL}{r^4} \Rightarrow k = \text{viscosity}$$

$$L = \text{length}$$

$$r = (\text{cross}) \text{ sectional area}$$

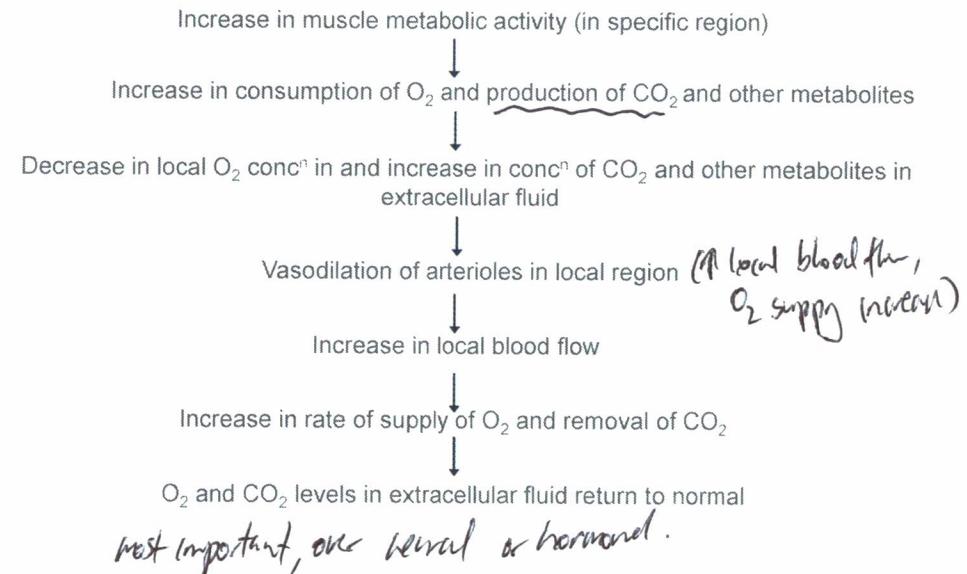
Contraction of the smooth muscle in the arterioles is called...?

Vasoconstriction

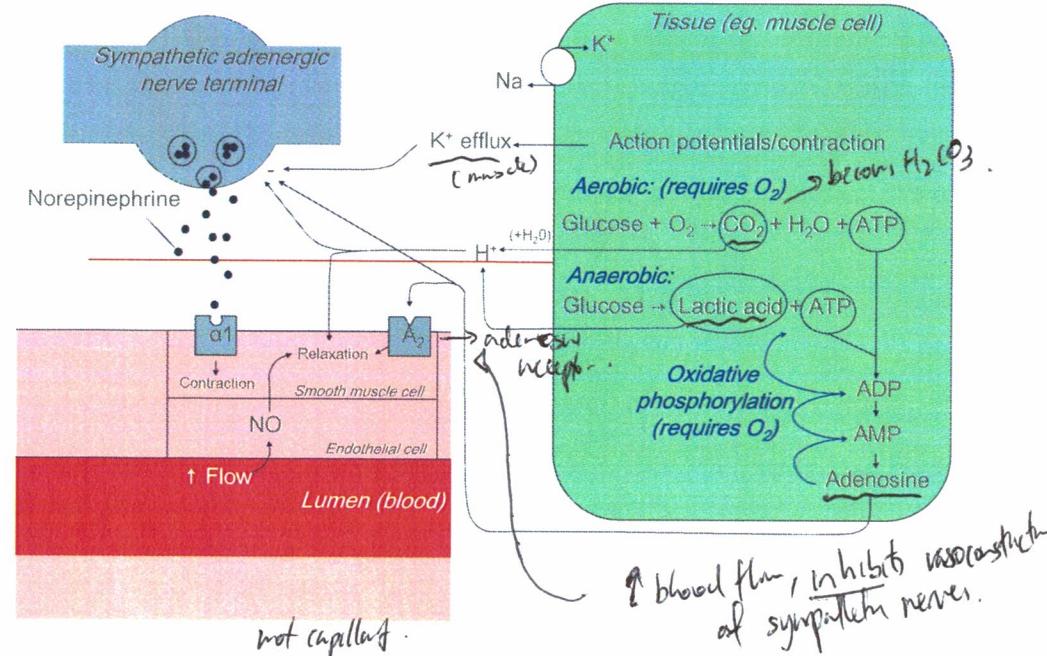
Production of local metabolites produces vasoconstriction or vasodilation of the vessels?

Vasodilation

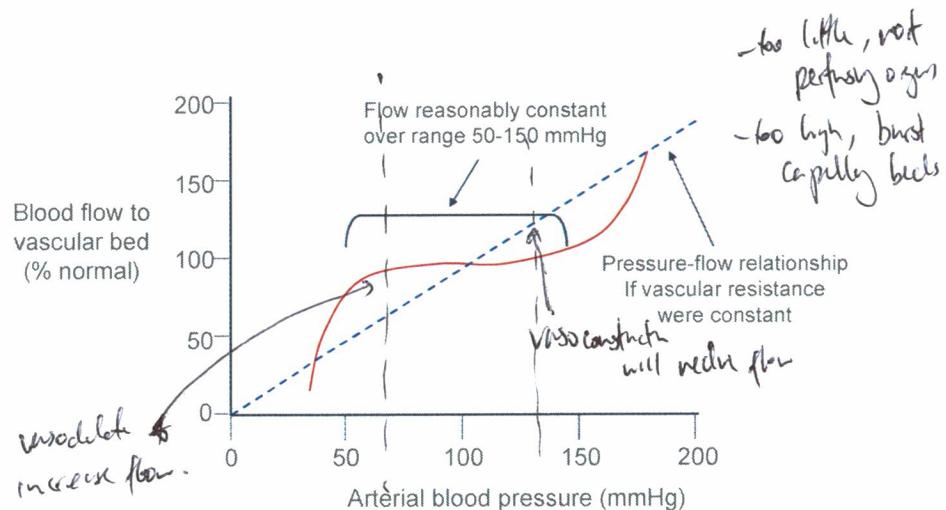
## Local factors: metabolites



## Local metabolic factors influencing vascular tone



## Autoregulation of blood flow to a vascular bed



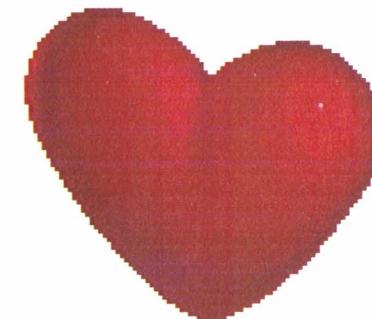
## Notes: Sympathetic control of blood vessels

- Sympathetic nerves innervate all types of blood vessels except capillaries.
- They are called **vasomotor** nerves.
- The density of innervation of sympathetic vasomotor nerves varies according to the **type** of vessel (greatest in arterioles, least in arteries) and ...
- the **region** (e.g. dense in arterioles in skin, skeletal muscle, kidney etc., but much less in brain and heart).
- Most sympathetic vasomotor nerves are **vasoconstrictor** - cause constriction of blood vessels that they innervate.
- The neurotransmitter is usually noradrenaline (norepinephrine). Therefore they are **adrenergic** nerves.
- Sympathetic vasoconstrictor nerves are **tonically active** - denervation causes dilatation of blood vessels (**vasodilation**).
- Pharmacological blockade of actions of sympathetic vasoconstrictor nerves causes blood pressure to decrease profoundly.
- High spinal section has the same effect, therefore source of the tonic activity is supraspinal (i.e. in the brain).
- The activity of sympathetic vasoconstrictor nerves is altered reflexly. They play a very important role in the reflex control of blood pressure.

## Notes: Circulating vasoactive hormones

- Adrenaline (epinephrine) and noradrenaline (norepinephrine) are circulating hormones.
- They are released from adrenal medulla in response to sympathetic stimulation.
- Adrenaline acts mainly on beta ( $\beta$ ) receptors to cause vasodilation, mainly in skeletal muscle vascular beds.
- Noradrenaline acts mainly on alpha ( $\alpha$ ) receptors to cause vasoconstriction, in nearly all vascular beds (except brain and heart).
- Vasopressin (also called antidiuretic hormone, ADH), is released from pituitary in response to haemorrhage and other stimuli.
- It has a potent vasoconstrictor action, but also an antidiuretic effect (i.e. reduces rate of urine production (or **diuresis**)).
- Angiotensin - the most potent vasoconstrictor agent known. (The pathway for its synthesis, and stimuli triggering activation of the renin-angiotensin system, will be described in a later lecture).

Remember your Socrative Quiz  
Room # 1800800



Name the parameters given in Poiseuille's Law that determine Resistance in the blood vessels.

Viscosity      Length      Radius

Contraction of the smooth muscle in the arterioles is called...?

vasoconstriction

Production of local metabolites produces vasoconstriction or vasodilation of the vessels?

vasodilation  
Test your knowledge answers... No peeking!

- Which vessels produce the most resistance?

arterioles

- Which vessels hold the greatest volume of blood?

veins

- In which vessels does the blood move most slowly?

capillaries

- In which vessels is pressure the lowest?

veins

Test your knowledge answers... No peeking!

- Veins are compliant - a reasonable change in volume only produces a small change in pressure (this is not the case in the arteries).
- Velocity is slowest in the capillaries as the area covered by the capillaries is largest.
- Velocity = flow/cross sectional area.
- Adrenline can induce vasodilation in beds with beta 2 receptors.
- The sympathetic nervous system can stimulate vasoconstriction through alpha 1 receptors.
- Acumulation induces local vasodilation.
- The production of local metabolites has powerful effects on arterial radius - Adenosine, H+, NO, K+, CO<sub>2</sub> causes constriction of blood vessels when smooth muscle in the vessel relaxes. Contraction of local muscles causes constriction of dilation occurs when smooth muscle contracts or relaxes.
- Resistance in series increases total resistance. Resistance in parallel reduces total resistance. The higher the resistance in series the greater the pressure drop across it.
- Resistance is dependent on length, viscosity and radius.  $R = k/L$  (Poiseuille's Law)
- Arteries are the resistance vessels. Veins are the capacitance vessels - they hold about 60% of the blood.
- Blood flows when there is a pressure gradient; delta P = Flow x R (resistance)
- Mean Arterial Pressure = Cardiac output x Total Peripheral Resistance
- Resistances in parallel circuits. Resistance in parallel reduces total resistance. The higher the resistance in parallel the greater the pressure drop across it.
- Blood leaves the right side of the heart under high pressure entering the systemic circulation (- 1/3 that of the pulmonary circulation).
- Become oxygenated in the lungs (pulmonary circulation).
- Blood leaves the left side of the heart under a lower pressure (- 1/3 that of the systemic circulation) to distribute throughout the body. Capillary beds may be in series or parallel.
- Venules ==> veins and returns to the right side of the heart. This is the systemic circulation. Cardiac output is distributed throughout the body. Capillary beds may be in series or parallel.
- Blood leaves the left side of the heart under high pressure entering the arteries ==> capillaries ==>

Summary:

## CV Worksheet 1 - Overview and Hemodynamics

### Activity 1:

How much flow?

100 mm Hg



100 mm Hg

0

$$\Delta P = QR,$$

$$\Delta P = 0,$$

$$\therefore Q = 0.$$

no pressure gradient

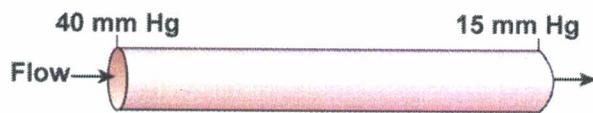
Which has the greater flow?

A



$$\Delta P = 25 \text{ mm Hg} = QR.$$

B



$$\Delta P = 25 \text{ mm Hg} = QR.$$

radius is same,  $\therefore R = k$ .

$\therefore \underline{Q \text{ is same}}$ .

Give an example of resistances in parallel in the circulation?

- arm beds (upper limbs) & legs (lower limbs).

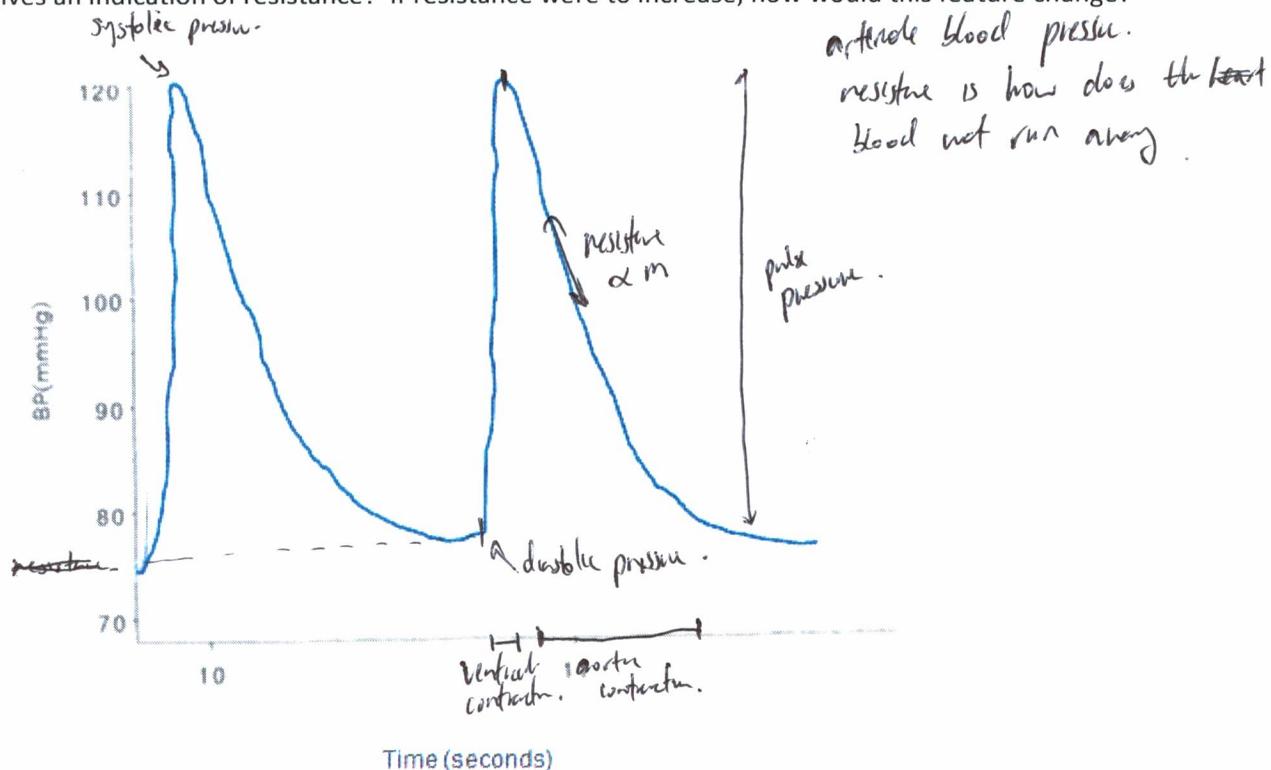
•

Give an example of resistances in series in the circulation?

- capillary bed in intestines & capillary bed in liver.
- kidney capillary beds
- lungs + anything

## Activity 2:

The following is a trace of continuous measurement of aortic blood pressure. Can you identify systolic pressure, diastolic pressure and the time points for ventricular contractions? Which feature in the trace gives an indication of resistance? If resistance were to increase, how would this feature change?



**Before you go.....** Fill in the correct terms for each definition. Terms to choose from are given below the table.

Definition	Term
Flow of blood returning to the heart from the veins	
The number of heart beats per minute (bpm)	
Total volume of blood ejected by the heart per unit time (L/min)	
Total resistance of the peripheral vasculature in the systemic circulation	
The lowest pressure reached in the arteries	
Volume ejected by the ventricle in a single heart beat	
The highest pressure in the arteries	

cardiac output (CO) / stroke volume (SV) / venous return (VR) / total peripheral resistance (TPR) / systolic pressure (SP) / diastolic pressure (DP) / heart rate (HR)

Don't forget to do your Socrative Quiz! – Room # 1800800

# THE CARDIOVASCULAR SYSTEM 2

## The mechanical events of the cardiac cycle



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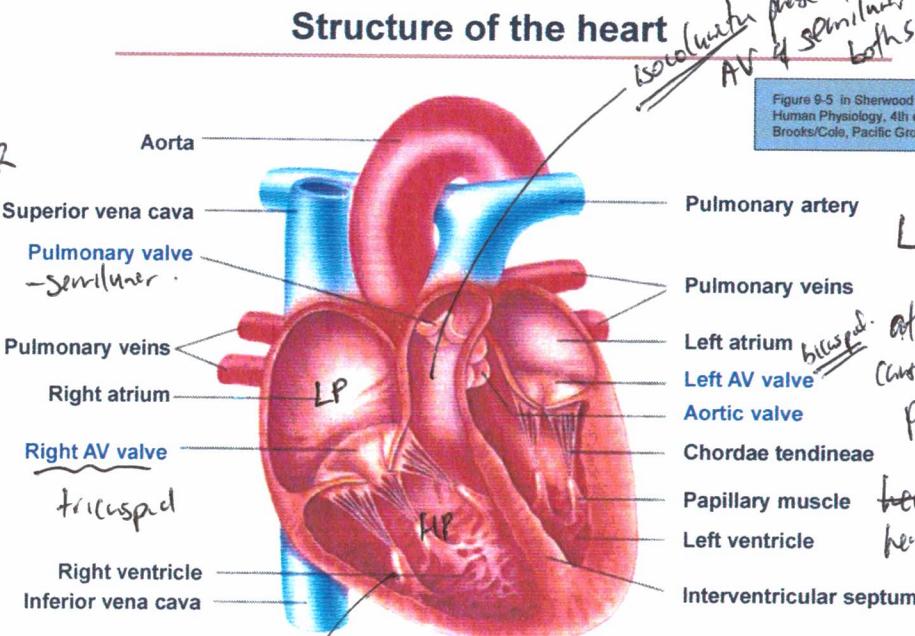
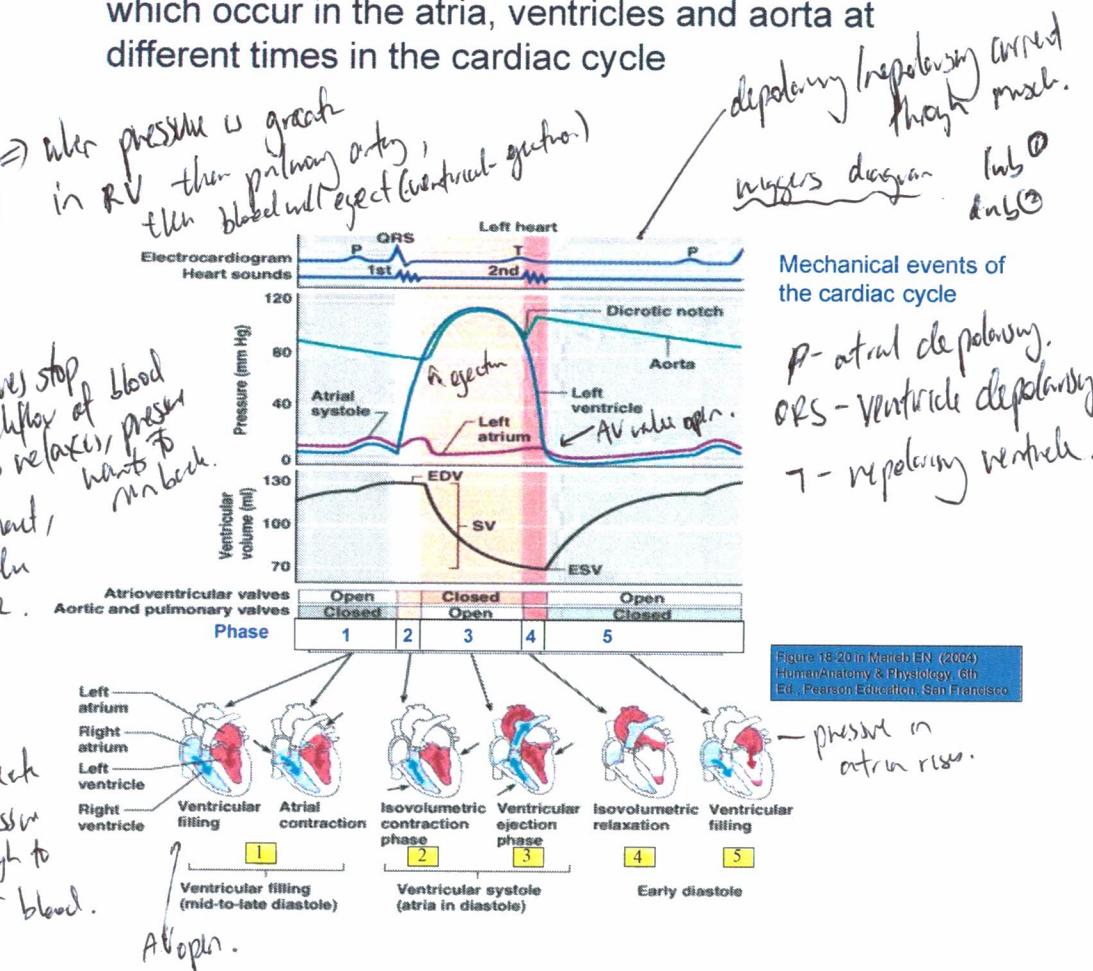


Figure 9-5 in Sherwood L. (2001)  
Human Physiology, 4th edition  
Brooks/Cole, Pacific Grove, Ca.



## Mechanical events of the cardiac cycle

- **Phase 1:** Late diastole
  - ventricular relaxation
  - passive flow of blood into left atrium (& left ventricle through mitral valve)
  - towards the end of this phase:
    - S-A node depolarizes
    - wave of depolarization sweeps over atria (which then contracts)
- **Phase 2:** Isovolumetric contraction
  - ventricular contraction
  - ventricular pressure rises
  - mitral valve closes
  - when this pressure exceeds aortic pressure: aortic valve opens
- **Phase 3:** Period of ejection
  - ejection most rapid during early part
  - terminated by the end of ventricular contraction
  - ventricular pressure falls rapidly and aortic valve closes
- **Phase 4:** Isovolumetric relaxation
  - all valves closed
  - aortic pressure falls much less rapidly than ventricular pressure (because aortic run-off is much less rapid, being dependent on peripheral resistance)
- **Phase 5:** Early diastole
  - ventricular filling
  - ventricles is >80% full prior to atrial systole occurs (which is during late diastole-Phase 1)

## Definitions

- Systole: contraction
- Diastole: relaxation
- Stroke volume (SV): volume of blood ejected by the left ventricle in one cardiac cycle
- End-diastolic ventricular volume (EDV): volume of blood in the ventricle at the end of ventricular diastole
- End-systolic ventricular volume (ESV): volume of blood in the ventricle at the end of ventricular systole
- Ejection fraction: ratio of stroke volume to end-diastolic ventricular volume (normally 50-70%)

## Note:

- \* Atrial pressure is normally low (close to zero); - draw blood to right heart.
- \* Ventricular pressure varies greatly during each cardiac cycle;
- \* Peak pressures in the right ventricle and pulmonary artery is much less (about 1/3) than peak pressures in the left ventricle and aorta

*systole  $\Rightarrow$  3x pulmonary.*

## Test your knowledge....

- During the period of isovolumetric contraction are:
  - A The AV valves shut but the semilunar open
  - B The Semilunar valves shut but the AV valves open
  - C Both AV and semilunar valves are shut
  - D Both AV and semilunar valves are open
- Stroke volume is
  - A The difference in volume between end-diastolic volume and end-systolic volume
  - B The volume left in the heart at the end of diastole
  - C The volume of blood left in the heart at the end of systole
  - D The amount of blood leaving the heart per minute

The three waveforms of the ECG are:

- A The P, ABC and Z waves
- B The P, QRS and T waves
- C The Q, RST and V waves
- D The T, PQR and S waves

## Work of the heart

*Volume work = many more volume flights thru heart*

The work done by the heart in pumping blood from the ventricle into the aorta during a cardiac cycle is dependent on 2 factors:

- (1) the stroke volume (**volume work**), and
- (2) the pressure against which the left ventricle pumps (**pressure work**). *→ push harder against the outside of the valve.  
eg. Heart pushing to open aortic valve to push blood out).*

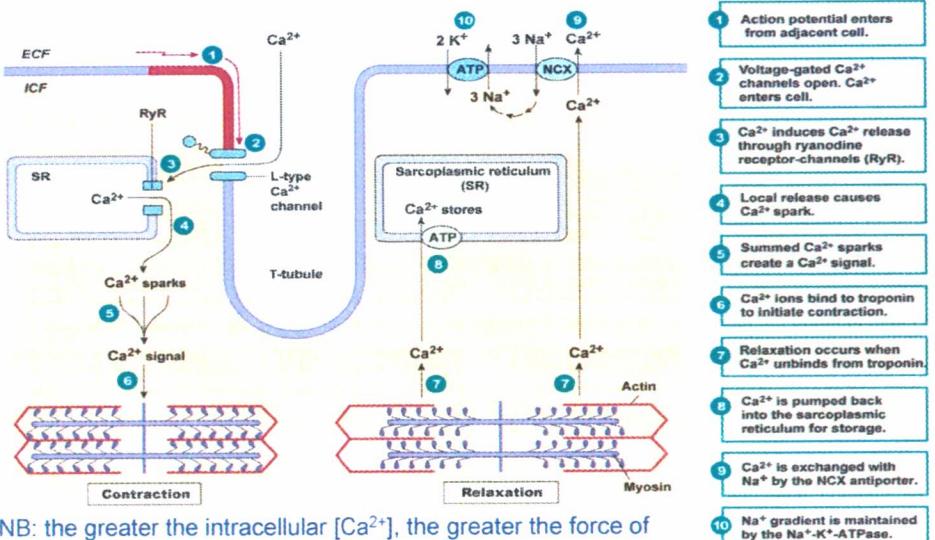
$$\text{Work} = \text{SV} \times \text{P}$$

Thus, the work of the heart is increased during exercise (when stroke volume increases) and also in people with high blood pressure (because of increased arterial pressure).

## Test your knowledge...

- During dynamic exercise (running around the Quad) will you increase the volume or pressure work of the heart?  
*reduce pressure work, increase volume*
  - Which pressure, systolic pressure or diastolic pressure, is usually of most concern in hypertension?  
*diastolic pressure & pressure work (defens pressure regn for ventriles open)*
  - What will happen if the left side of the heart starts to fail...that is the left ventricular muscle cannot contract with sufficient force? *not enough blood in circuit, hypotension*
  - The pulmonary artery carries oxygenated or deoxygenated blood?  
*deoxygenated*
- heart has auto rhythmicity.*

## Excitation Contraction coupling



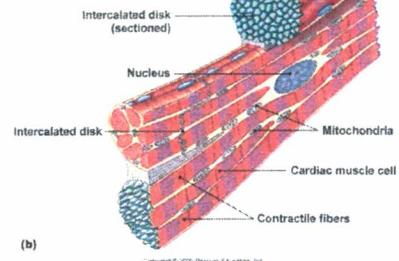
*calcium - induced - calcium overload.*

*not smooth, not skeletal.  
- branched  
- multi-nucleated  
- intercalated discs*

## Properties of cardiac muscle



(a)



(b)

### MYOCARDIUM (cardiac muscle):

- main constituent of the heart
- contraction triggered by depolarization of the membrane (an action potential, AP).

Coordinated so ventricular fibres contract virtually simultaneously (pumps effectively).

2 factors:

- 1) low-resistance junctions (intercalated discs) between muscle fibres (allow AP to pass)
- 2) specialized conducting muscle fibres (facilitate rapid & co-ordinated spread of excitation)

*cells: + pacemakers (gives initial current)  
+ gap junctions allow fast & potent very quickly, very fast AP for coordinated contraction*

## Summary:

- Blood returns to the heart through the vena cava into the right atrium through the AV valve and into the ventricle
- The right side of the heart pumps to the lungs (pulmonary circulation) and the left side to the body (systemic circulation).
- The AV (atrio-ventricular) valves prevent the backflow of blood into the atrium (when the ventricle contracts).
- The pulmonary and aortic valves prevent backflow of blood into the ventricles (from the lungs or the aorta) when the ventricles relax.
- The valves ensure blood travels through the heart in one direction.
- The valves open and close in response to the pressure differential across the valve.
- The cardiac cycle consists of phases of ventricular filling, atrial contraction, isovolumetric (same volume) ventricular contraction, ventricular ejection, and isovolumetric ventricular relaxation.
- Isovolumetric phases occur when both sets of valves are closed (therefore the volume in the ventricle cannot change).
- The volume of blood in the ventricle at the end of filling as the ventricle contracts and the AV valve closes is called the end-diastolic volume (EDV). The volume of blood left in the ventricle after the ejection phase is called the end-systolic volume (ESV). The difference between the EDV and the ESV is the stroke volume – the volume ejected with the ventricular contraction – and this is a fraction of the EDV (the ejection fraction).
- Aortic pressure traces have a maximum of systolic pressure and a minimum of diastolic pressure. Note that the aortic pressure remains high during ventricular relaxation (diastole) compared to the ventricular pressure trace.
- Large changes in pressure occur in the left ventricle. Atrial pressure changes are small by comparison.
- The ECG has three distinctive waveforms: P (atrial depolarization), QRS (ventricular depolarization & atrial repolarization) and T (ventricular repolarization). The ECG is seen when the current runs through the muscle mass (not when the current is being conducted through the conduction system).
- The two heart sounds S1 and S2: lub-dub are associated with the closing of the AV and aortic/pulmonary valves respectively. S1 occurs just after the QRS and S2 just after the T wave.
- Remember the electrical events precede the mechanical.

- During dynamic exercise (running around the Quad) will you increase the volume or pressure work of the heart? **Volume work of the heart - The cardiac output increases to supply more substrates to working muscles and to remove accumulated waste/metabolites. MAP may not increase much as DP may fall as SP rises.**
- Which pressure, systolic pressure or diastolic pressure, is usually of most concern in hypertension? **Diastolic pressure as this relates to the pressure work of the heart - also called the afterload. The diastolic pressure determines the pressure required by the ventricle to open the aortic valve. Long term increases in DP significantly increase the work of the heart.**
- What will happen if the left side of the heart starts to fail...that is the left ventricular muscle cannot contract with sufficient force? **The heart will not be able to eject the volume of blood that it receives - so blood will accumulate in the left ventricle - the end systolic volume will increase. This will build up the ventricular pressure affecting blood returning from the lungs and **oedema of the lungs** may develop.**
- The pulmonary artery carries oxygenated or deoxygenated blood?
- Deoxygenated**

Test your knowledge - answers... on peeling!

- During the period of isovolumetric contraction are:
    - A. The AV valves shut but the semilunar open
    - B. The Semilunar valves shut but the AV valves open
    - C. Both AV and semilunar valves are shut
    - D. Both AV and semilunar valves are open
  - Stroke volume is
    - A. The difference in volume between end-diastolic volume and end-systolic volume
    - B. The volume left in the heart at the end of diastole
    - C. The volume of blood left in the heart at the end of systole
    - D. The amount of blood leaving the heart per minute
- (Can you give the terms for the definitions given in options B, C and D?)

The three waveforms of the ECG are:

- A. The P, ABC and Z waves
- B. The P, QRS and T waves
- C. The Q, RST and V waves
- D. The T, PQR and S waves

(Can you describe the events that produce the waveforms?)

Test your knowledge - answers... on peeling!

**CV Worksheet 2 – Mechanical Events of the Heart****Did you know...**

Socrative quizzes in the Open All Hours Revision Room change over at the end of each lecture during the lecture series and then continue - changing Monday evenings each week during semester and daily during STUVAC and up until the day of your exam. The quizzes will get progressively more difficult. During STUVAC and the exam period the quizzes will include Short Answer Questions (SAQs) too. Be consistent. Don't miss a quiz. Conquer the Content!

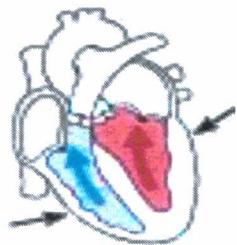
Don't forget to do  
your Socrative  
Revision Quiz before  
the next lecture!  
Room # 1800800

So....there are NO excuses for not knowing your cardiovascular content! I expect you to do well!

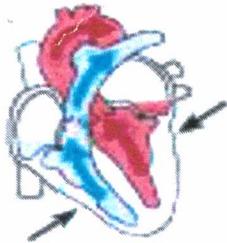
**Activity 1: Match the conditions on the left with the appropriate conditions on the right.**

1. Isovolumetric contraction (B)	A. AV valve closed and Aortic valve open
2. Ventricular ejection (A)	B. AV and Aortic valves shut
3. Atrial P > Ventricular P (E)	C. Ventricular filling
4. End diastolic volume (D)	D. Isovolumetric contraction
5. Stroke volume (F)	E. AV valve opens
6. Ventricular volume increases (C)	F. EDV - ESV

**Activity 2:** Study the pictures below and name the phase of the cardiac cycle they represent. A list of phases to choose from is given below.



isovolumetric contraction



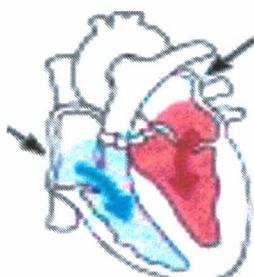
ventricle ejection



isovolumetric relaxation



ventricle fills



atrial contraction



Atrial contraction

Ventricular filling

Isovolumetric contraction

Ventricular ejection

Isovolumetric relaxation

# THE CARDIOVASCULAR SYSTEM 3

## The electrical events of the cardiac cycle



[sharon.herkes@sydney.edu.au](mailto:sharon.herkes@sydney.edu.au)

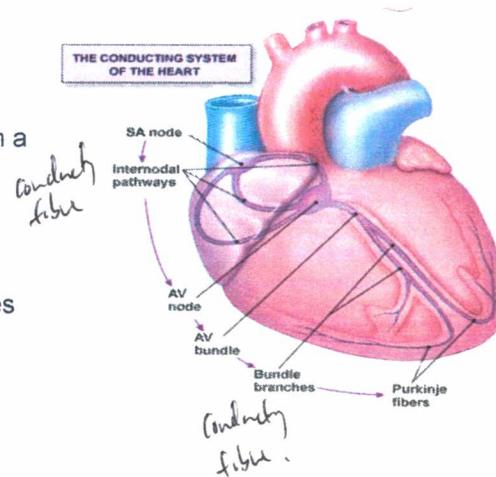
## Learning objectives:

- To understand how the pacemaker and contractile cells of the heart contribute to heart function
- To understand the mechanism for neural control of heart rate
- To understand the basic properties of cardiac muscle
- To understand the cardiac conduction system
- To understand the normal waveforms of the ECG and what they represent (next lecture)

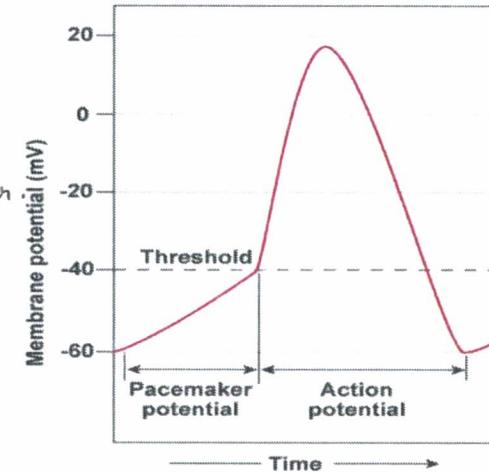
## Cell types in the heart

### 3 types of cardiac cells:

- 1 pacemaker cells (generating APs in a rhythmic fashion)
- 2 specialized conducting fibres
- 3 normal contracting myocardial fibres (Atrial and Ventricular)

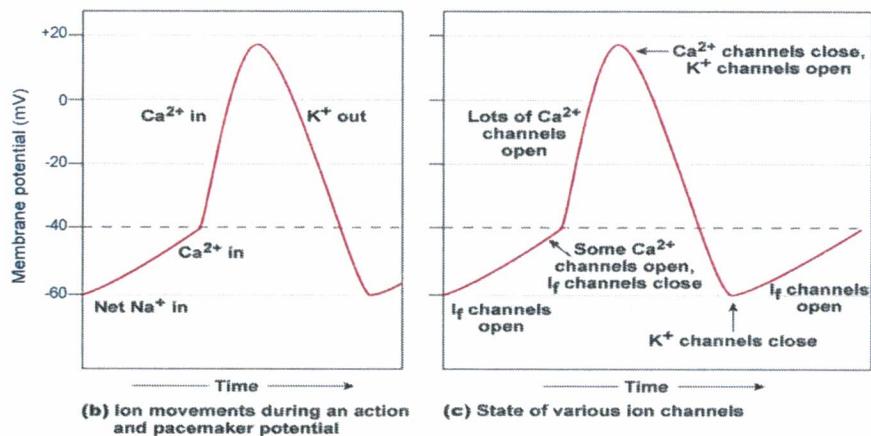


## Action potential in sino-atrial nodal cell



(a) The pacemaker potential gradually becomes less negative until it reaches threshold, triggering an action potential.

## How is the Pacemaker Potential Generated?



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If channels (funny channels) allow  $\text{Na}^+$  &  $\text{K}^+$  to move together in opp direction  $\rightarrow$  opening hyperpolarization.

## Test your knowledge...

What type of membrane potential is found in the SA node?

Pacemaker membrane potential.

Which channels are involved in the pacemaker potential of the SA node reaching threshold?

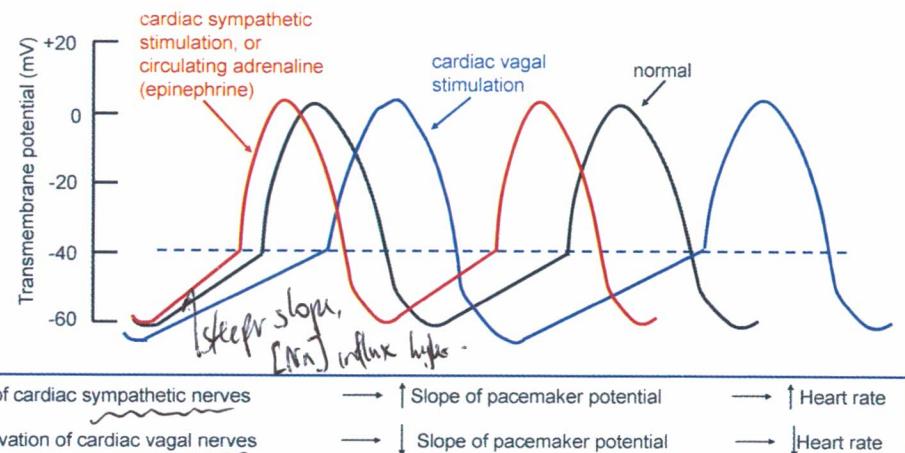
$\text{Ca}^{2+}$  channels.  $\text{Na}^+$  channels.

If funny channels &  $\text{Ca}^{2+}$  channels

Parasympathetic stimulation increases or decreases the slope of the pacemaker potential?

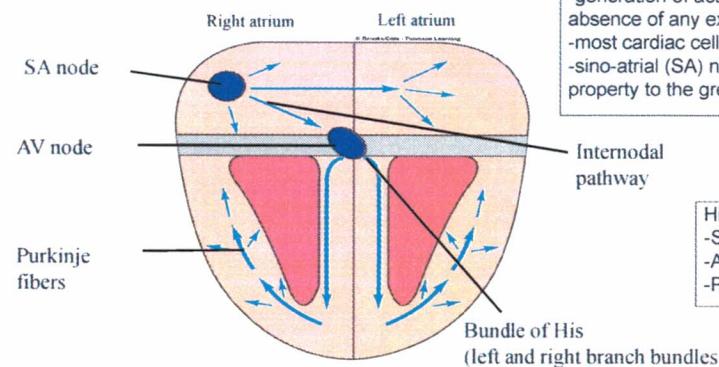
decreases.

## SA node is affected by autonomic nerves and circulating catecholamines



↓ heart rate  $\downarrow$  ↓ heart rate

## Pacemaker activity



"Autorhythmicity":  

- generation of action potentials in the absence of any external stimulus
- most cardiac cells have capability
- sino-atrial (SA) node possess this property to the greatest degree

Hierarchy of pacemakers:  

- SA node (60-100)
- AV node (40-60)
- Purkinje system (15-40)

Figure 9-14: In Silverthorn L. (2001)  
Human Physiology, 4th edition  
Brooks/Cole, Pacific Grove, Ca

SA, AV, purkinje can all set HR's.  
fully block atria, destroy SA node, HR will be lower due to A.V.

## Spread of excitation throughout the heart

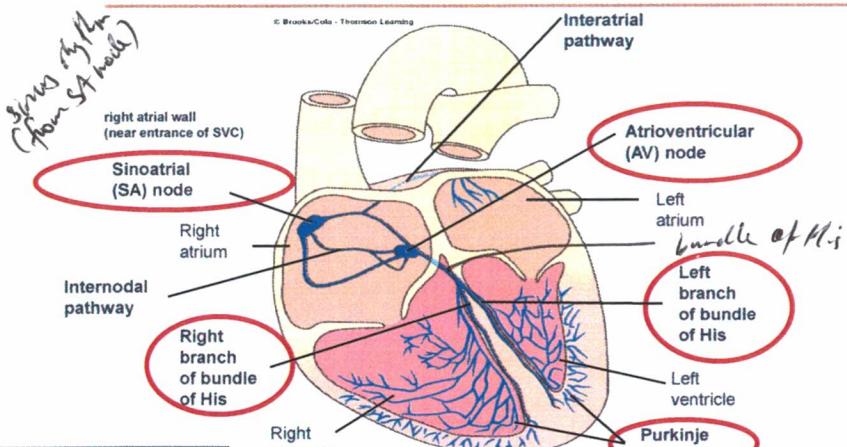
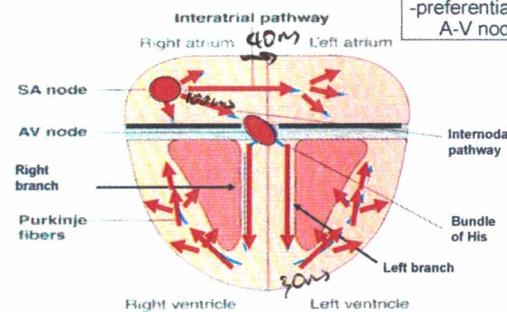


Figure 9-11 In Sherwood L. (2001). Human Physiology, 4th edition. Brooks/Cole, Pacific Grove, Ca.

## Spread of excitation throughout the heart



### Rapid propagation of APs through atria:

- from the S-A node
- wave of depolarization, almost simultaneous (~40msec)
- preferential routes by which APs travel between the S-A node and the A-V node

### A-V node:

- only means by which excitation (wave of depolarization) can reach ventricles (rest is separated by non-conductive connective tissue)

### Propagation of APs through A-V node:

- delayed ~100 msec
- (fibres of A-V node are narrow & branching = v. slow conduction velocity/long delay)

Figure 9-14 In Sherwood L. (2001). Human Physiology, 4th edition. Brooks/Cole, Pacific Grove, Ca.

### Bundle of His, right & left branches & the Purkinje network:

- all consist of fast-conducting (2-4 m/s) "Purkinje fibres"
- Purkinje system: conduction ~30 msec  
(+ 30 msec for ventricular myocardium depolarization)

## Action potential in myocardial contracting fibre

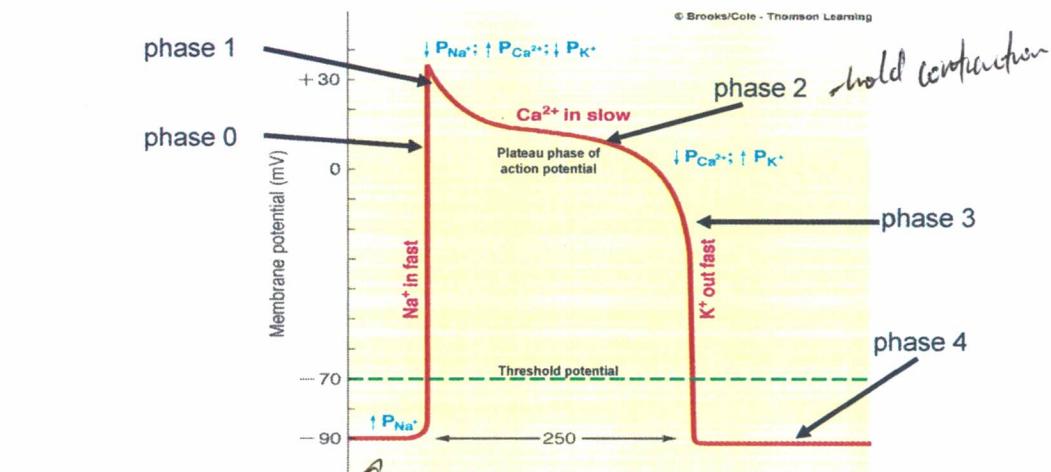
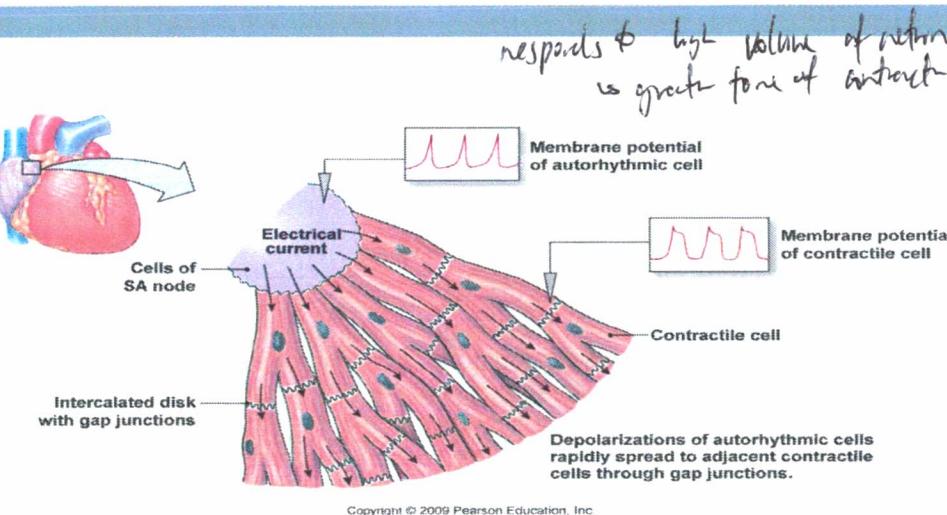


Figure 9-15 In Sherwood L. (2001). Human Physiology, 4th edition. Brooks/Cole, Pacific Grove, Ca.



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not prevent potential.

## Test your knowledge...

- Put a cardiac muscle cell into a calcium free solution and what will happen?

*will no longer contract*

- And a skeletal muscle cell.....?

*no longer contract  
can still contract*

## Action potential in myocardial contracting fibre

Ion concentrations (as with other cells):

- $[K^+]$  inside > outside
- opposite for  $[Na^+]$

### Phase 0: (rapid depolarization)

- almost entirely due to  $\uparrow P_{Na}$
- caused by the opening of fast, voltage-dependent  $Na^+$  Chs
- inward flow of  $Na^+$  ions is regenerative (+ve feedback)
- When the membrane potential reverses,  $Na^+$  channels close, preventing further influx of  $Na^+$

### Phase 1:

- $\downarrow P_{Na}$

### Phase 2: (plateau of AP -near 0mV)

- weak inward flow of  $Ca^{2+}$  (slow Chs),
- balanced by slow outward flow of  $K^+$  (driven by concentration gradient)

### Membrane depolarization

- (by an arriving AP)
- critical value (threshold)
- propagation of an AP

### Resting membrane potential dependent on:

- 1) relative internal and external  $[Na^+]$  &  $[K^+]$
- 2) their relative permeabilities ( $P_{Na}$  &  $P_K$ )

### Phase 3: (final repolarization)

- depends on:

  - 1)  $\uparrow P_K$  (voltage dependent)
  - 2) inactivation of slow inward  $Ca^{2+}$  Chs (efflux of  $K^+$  no longer balanced)
  - regenerative (+ve feedback) process

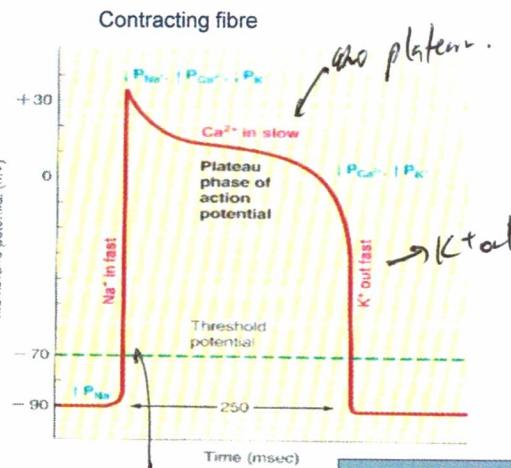
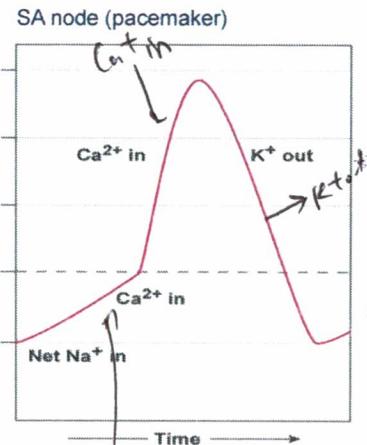
### Phase 4: (rest period)

- $Na^+$ - $K^+$  pump eliminates excess  $Na^+$  that entered during phases 0 and 1 in exchange for  $K^+$  that exited during phases 2 and 3.

Figure 9-15 in Sherwood L. (2001)  
Human Physiology, 4th edition  
Brooks/Cole, Pacific Grove, Ca.

*until next normal card arrt A.P.*

## Different action potentials in the heart



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*finng channels,*

## Test your knowledge...

- The plateau phase of the ventricular AP is caused by the balanced movement of two different ions....which ions?

*Ca2+ in, K+ out.*

- What is the duration of a typical ventricular AP?

*250ms.*

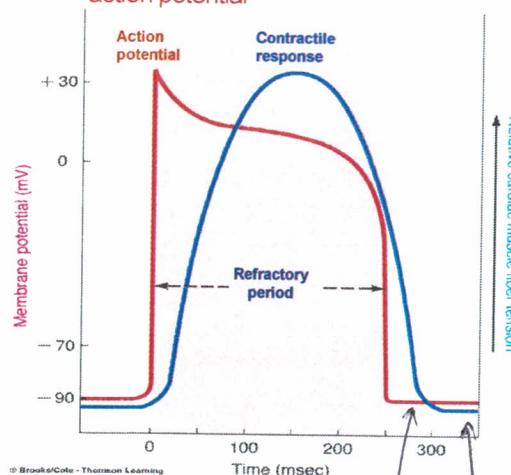
- Which kind of action potential (SA node) or Ventricular muscle depolarizes the fastest?

*SA node*

*Ventricular muscle*

*(steep up-slope)*

Duration of the cardiac contractile response is very similar to that of the cardiac action potential

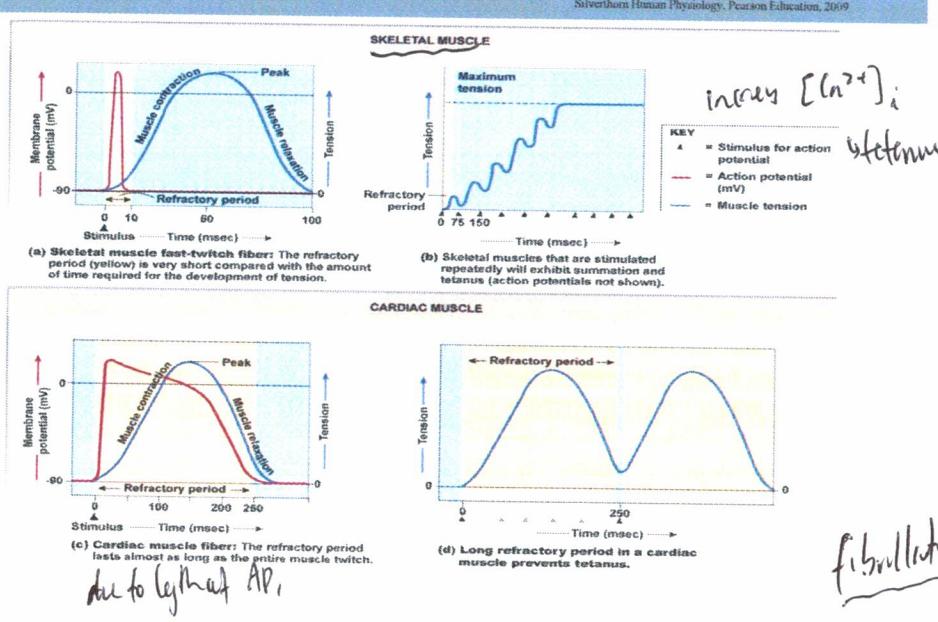


cannot stimulate another contraction.  
muscle relaxed before next contraction.

Figure 9-17 in Sherwood L. (2001)  
Human Physiology, 4th edition  
Brooks/Cole, Pacific Grove, Ca.

## Absolute refractory period

- period following an action potential when a new action potential cannot be generated (~250 msec in cardiac muscle)
- continuous re-excitation of the atria or ventricles not allowed (no tetanic contractions)



## Summary:

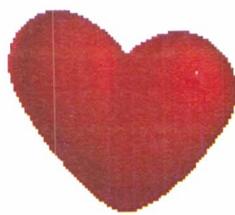
- Cells in the heart (i) generate APs automatically (ii) conduct the current quickly through the heart or (iii) contract.
- Pacemaker cells spontaneously depolarize to threshold generating an action potential and a cardiac contraction.
- Sympathetic stimulation increases the slope of the pacemaker potential and makes the starting point of the potential more positive by changing ion permeability. This increases the heart rate.
- Parasympathetic control of the heart rate is dominant and decreases heart rate by decreasing the slope of the pacemaker potential and by shifting the starting point of the potential to a more negative value.
- Movement of ions (both Na and K) through the "funny" channels brings the pacemaker potential towards threshold. Calcium channels open when funny channels close and bring the potential to threshold.
- Depolarization is due to the influx of calcium ions. Repolarization due to the efflux of potassium.
- The cardiac pacemaker cells (SA node, AV node and purkinje) demonstrate autorhythmicity and can generate a heart rate without an external stimulus. The inherent rates are SA node > AV node > purkinje.
- Usually conduction is initiated in the SA node, travels through the intermodal fibres to the AV node through the bundle of His, left and right branch bundles and the purkinje fibres. The atria and ventricles are electrically isolated from each other – conduction through the AV node only with a ~100 msec delay.
- Cardiac muscle cells are dependent on extracellular calcium for contraction – Calcium-induced calcium release. Extracellular calcium is required for release of calcium from the sarcoplasmic reticulum. Force of contraction is dependent on intracellular calcium concentration.
- Ventricular muscle action potentials display a long plateau phase 2 (balance of calcium influx and potassium efflux). Depolarization is due to Na influx (not calcium like pacemaker cells). The long duration of the action potentials ~250 msec prevents tetanic contractions occurring in cardiac muscle cells.

fibrillation of ventricle.

- What type of membrane potential is found in the SA node?  
**Pacemaker**  
Which channels are involved in the pacemaker potential of the SA node reaching threshold?  
**I<sub>f</sub> – the funny channels (Hheto) Calcium channels**
- Parasympathetic stimulation increases or decreases the slope of the pacemaker potential?  
**Decreases (slows down the time to threshold and decreases the HR)**
- Put a cardiac muscle cell into a calcium free solution and what will happen?  
**No contraction**
- And a skeletal muscle cell.....?      **Can contract**
- The plateau phase of the ventricular AP is caused by the balanced movement of two different ions....which ions?
  - Calcium ions (moving in)
  - Potassium ions (moving out)
- What is the duration of a typical ventricular AP?  
**250 msec (Skeletal Muscle 2-4 msec)**
- Which kind of action potential (SA node) or Ventricular muscle depolarizes the fastest?
  - **Ventricular (steep upstroke)**

*Test your knowledge...answers...no peeking!!*

## CV Lecture Worksheet 3 – Electrical Events of the Heart



Don't forget to do your  
Socrative Revision Quiz  
before the next lecture!  
Room # 1800800

### Activity 1:

Find your pulse. Count for 15 seconds and x by 4 so you have your heart rate in beats per minute.

$$\begin{array}{r} 19 \times 4 = 40 + 36 \\ \hline = 76 \text{ bpm} \end{array}$$

> 100 tachycardia  
< 60 bradycardia

Then..... stand up,

- HR increases  $\rightarrow$  sympathetic N.S.
- $\hookrightarrow$  anticipation of exertion
- $\hookrightarrow$  exercise n sympathetic N.S.
- $\hookrightarrow$  grants) reflex MAP (blood goes don't brain).
- $\Rightarrow$  baroreceptors / stretch receptors will stimulate
- Sympathetic N.S., cause vasoconstriction to PMAP & cause TMR.

athletes have higher stroke volumes due to ventricular hypertrophy.

### Activity 2:

A. Order the following to indicate the sequence in which conduction moves through the heart:

6. Purkinje fibres
- 3 AV node
- 1 SA node
- 5 Left & right branch bundles
- 2 Internodal pathways
- 4 Bundle of His

Through which of the above is there a significant delay in conduction? What would happen if there was no delay at this point?

signif. delay  
in AV node

interventricular pathway  
 $\hookrightarrow$  would result in atrial contraction & no blood return.  
 $\hookrightarrow$  no cardiac contraction

B. Ben has a cardiac myopathy. His heart is failing and he needs a heart transplant. He wonders what he will be able to do when he has a transplanted heart. Will he be able to run a marathon? How will his resting heart rate (after his transplant) compare to a normal non-transplanted heart rate?

no, he has no sympathetic innervation, HR will not change to account for exercise → RHR will be ~~lower~~ <sup>higher</sup> than normal non-transplanted heart rate.

Consider: normal will have ~~more~~ vagal innervation which lowers HR.

What is a normal heart rate?

↳ can exercise, talk easily.

Innervation of the heart.....

Regulation of normal heart rate.....

Control of heart rate when exercising....

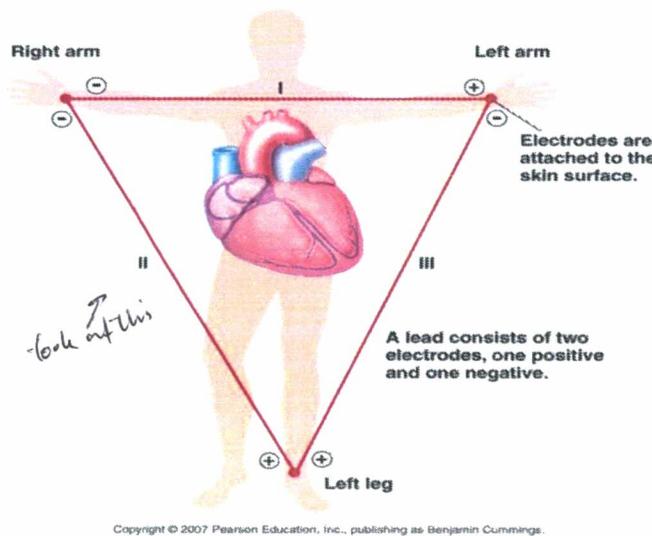
# THE CARDIOVASCULAR SYSTEM 4

## The Venous Return & Cardiac Output



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## ECG...



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## Learning objectives:

At the end of this lecture you should understand:

- the concepts of cardiac preload and afterload
- the factors which regulate venous return
- the action of the skeletal muscle pump
- the factors which regulate cardiac output and the mechanisms by which it can be redistributed

coordinated activity allows to see a recognising pattern.

## The electrocardiogram (ECG)

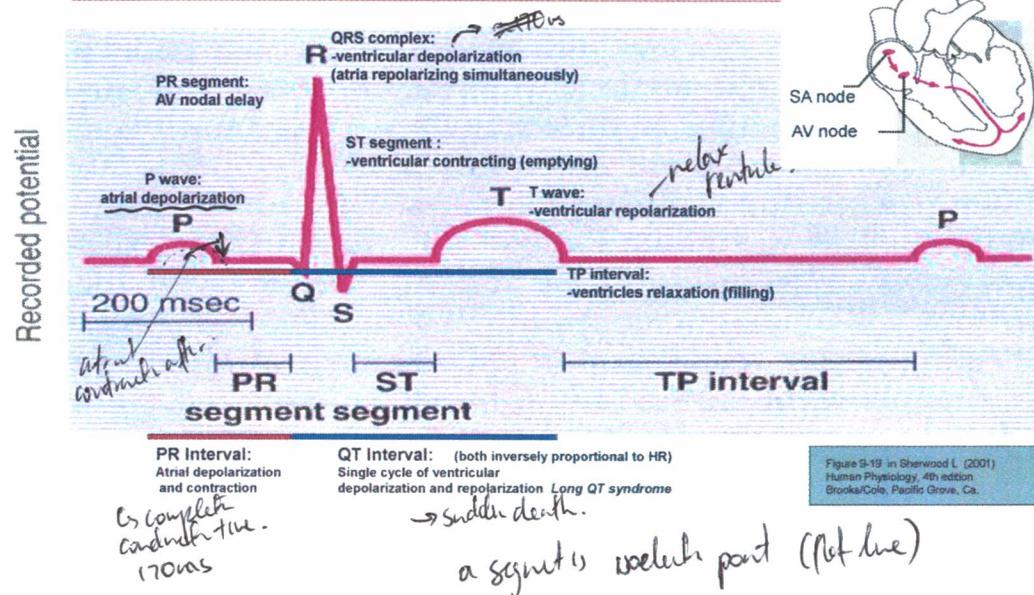


Figure 9-19 in Sherwood L (2001)  
Human Physiology, 4th edition  
Brooks/Cole, Pacific Grove, Ca.

## Pre-load and after-load

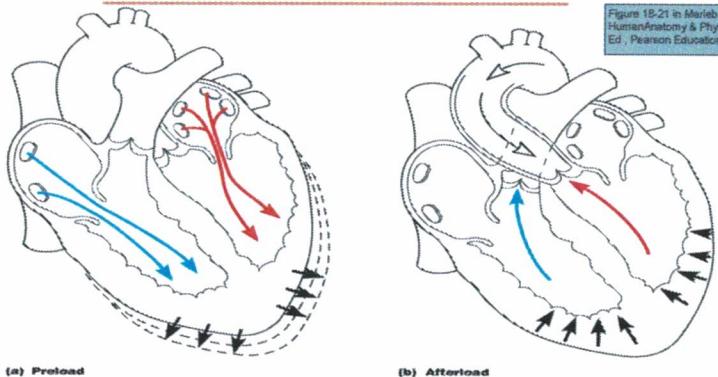


Figure 18.21 in Marieb EN (2004). Human Anatomy & Physiology, 6th Ed., Pearson Education, San Francisco.

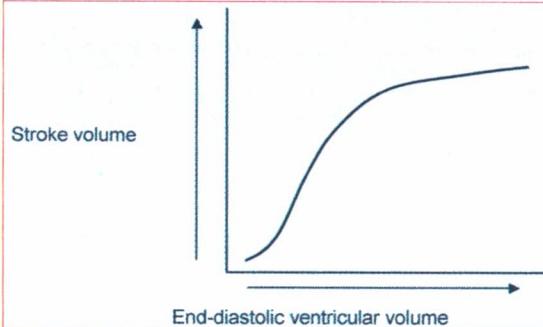
**•Pre-load:** defined as the tension in the ventricular wall at the end of diastole. For practical purposes this is measured as the ventricular end-diastolic pressure.

highest vol.  $\in$  EDV  $\rightarrow$  wall by very long.

equivalent to optimal length.  
stretch muscle, causing large force at contraction

$\Delta$ EDV  $\Rightarrow$  more optimal stretch  
for harder contraction.

## Frank-Starling Law of the Heart



**• Frank-Starling Law:** The greater the filling of the ventricle (i.e. end-diastolic ventricular volume), the greater will be the force of contraction (and hence stroke-volume)

heart responds to input,  
correspondingly output.

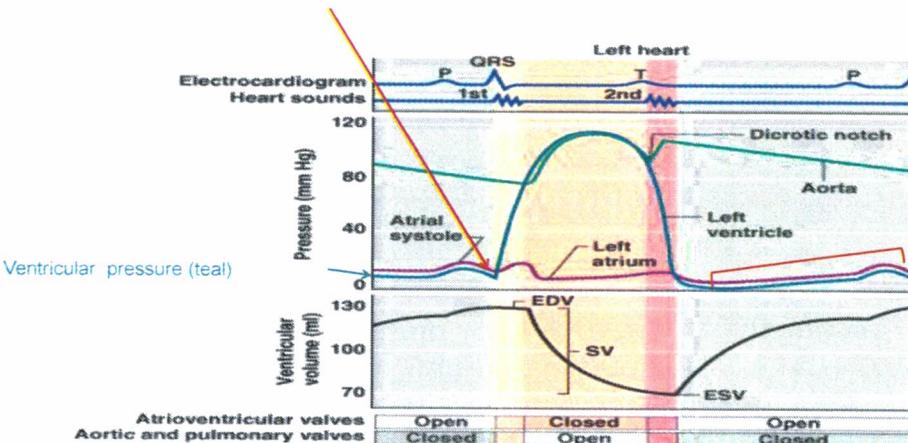
### Consequences of Frank-Starling Law

- A change in return of blood to right or left ventricle is immediately followed by a change in output (e.g. on changing posture when venous return suddenly decreases or increases).
- The cardiac output tends to be maintained in the face of changing aortic pressure (afterload). Explain why.

↑  
responds to pre-load + pressure body against.

**•Pre-load:** defined as the tension in the ventricular wall at the end of diastole. For practical purposes this is measured as the ventricular end-diastolic pressure.

**Preload...**  
according to The Wigger's Diagram



## Frank-Starling law: effects of change in venous return

Increase in venous return

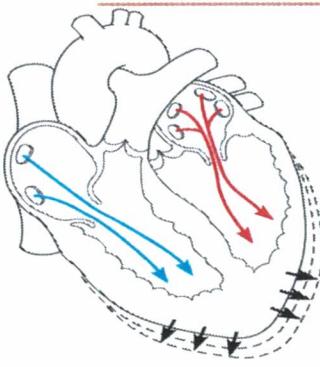
↓  
Increased end-diastolic ventricular volume

↓  
Increased force of ventricular contraction

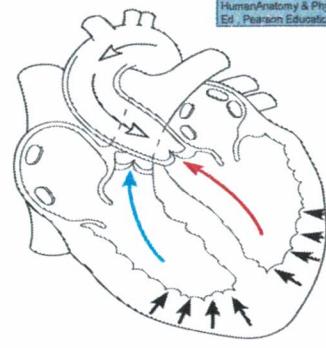
↓  
Increased stroke volume

↓  
Increased cardiac output

## Pre-load and after-load



•Pre-load:



•After-load: defined as the pressure that the ventricles must overcome to eject blood. This is the aortic pressure at the time the aortic valve opens.

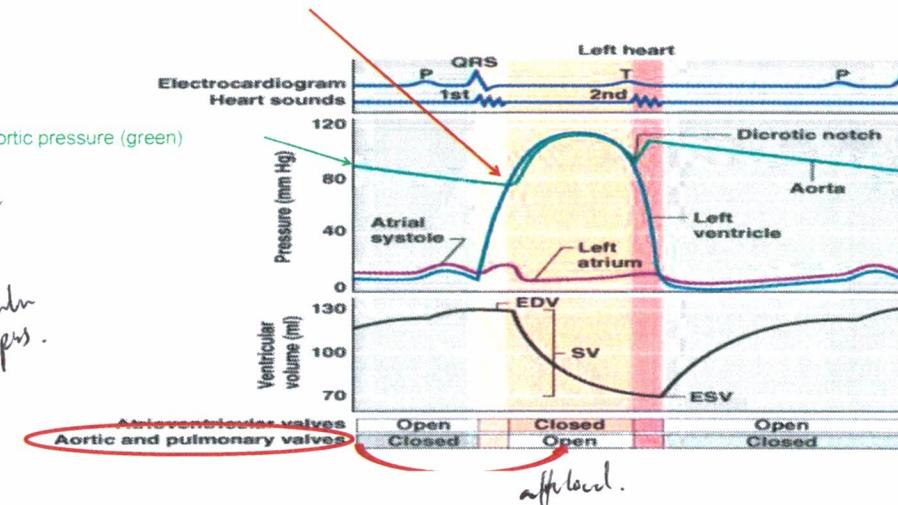
diastolic pressure when ventricle contract.

hypertension - high diastolic pres  
↳ more often no volume increase  
before transition to ejection phase  
⇒ pressure both of heart large in hypertension

Figure 18-21 in Marieb EN (2004)  
Human Anatomy & Physiology, 6th Ed., Pearson Education, San Francisco

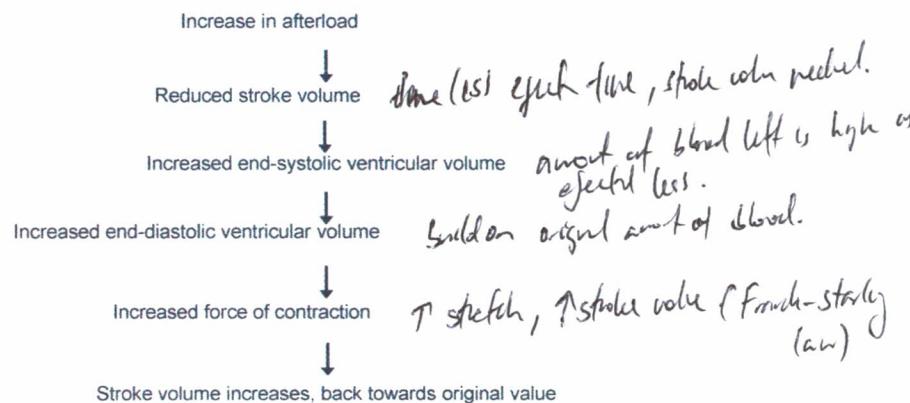
•After-load: defined as the pressure that the ventricles must overcome to eject blood. This is the aortic pressure at the time the aortic valve opens.

The Wiggers Diagram



## Frank-Starling law: effects of change after-load

The cardiac output tends to be maintained in the face of changing aortic pressure (afterload). Explain why.



## Test your knowledge...

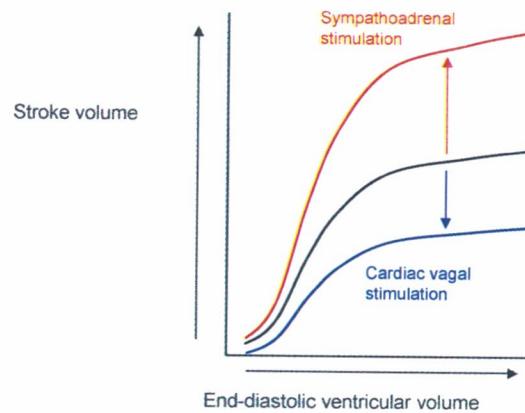
The Frank-Starling Law of the heart relates which two variables:

- A. force of contraction/cardiac output
- B. stroke volume/force of contraction
- C. end diastolic volume/stroke volume

Diastolic pressure determines preload or afterload?

preload.

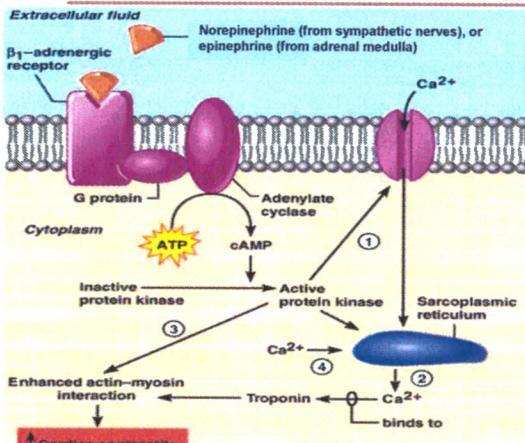
## Neural and hormonal control of cardiac contractility



- Cardiac contractility is defined as the ability of the heart to contract, at any given end-diastolic ventricular volume
- Activation of cardiac sympathetic nerves, or an increase in circulating adrenaline, increases cardiac contractility (indicated by red arrow). This effect is due to an increase in intracellular  $[Ca^{2+}]$  in myocardial fibres.
- Activation of cardiac vagal nerves leads to a decrease in myocardial intracellular  $[Ca^{2+}]$ , resulting in a reduced cardiac contractility (indicated by blue arrow).
- NOTE: The force of contraction of the heart therefore depends upon both the end-diastolic ventricular volume and extrinsic factors that affect contractility.

para  $\rightarrow \downarrow [Ca^{2+}]$ ; don't forget  
load, nervous, hormones

## Neural and hormonal control of cardiac contractility



- Cyclic AMP activates protein kinases, which then phosphorylate:
  - (1) slow  $Ca^{2+}$  channels, promoting entry of more  $Ca^{2+}$  from the extracellular space; **CaRulin**.
  - (2) an SR protein that causes the SR to release more  $Ca^{2+}$ , and
  - (3) myosin, which increases the rate of myosin cross bridge cycling. (**faster contract**)
  - (4) In addition, phosphorylation of the SR calcium uptake pump removes  $Ca^{2+}$  more rapidly from the sarcoplasm, thus promoting relaxation.

## Test your knowledge...

Stimulation of sympathetic nervous activity has a positive or negative inotropic effect on the heart?

*positive.*

Stimulation of sympathetic nervous activity has a positive or negative chronotropic effect on the heart?

*plus.*

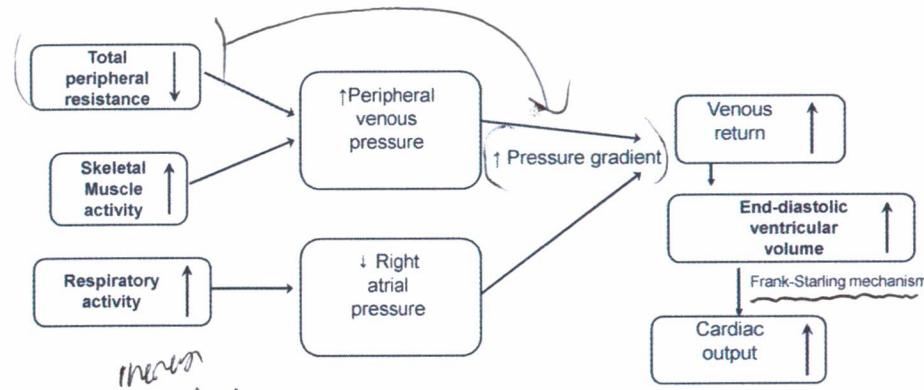
Stimulation of beta 1 or alpha 1 receptors increases cardiac contractility?

$\beta^1$

$\beta_1$  receptor  $\uparrow$  force of contract.

## Factors which affect venous return (VR)

The most important factor that determines venous return is the pressure gradient for venous return, i.e. difference in pressure between peripheral veins and right atrium. During exercise, the following changes all occur, and all increase VR by increasing this pressure gradient. Explain why.

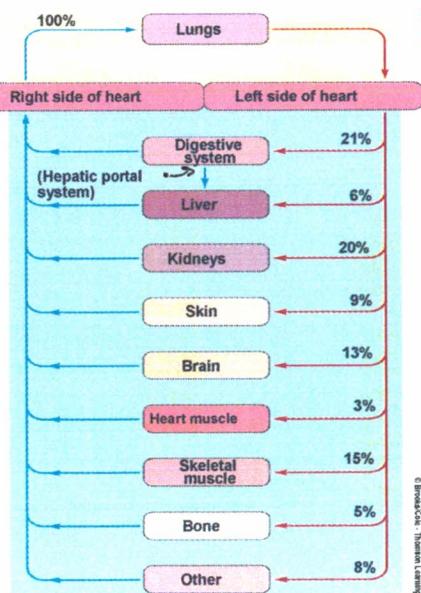


*more pressure gradient in —*

$$\text{MAP} = \text{CO} \times \text{TPR}$$

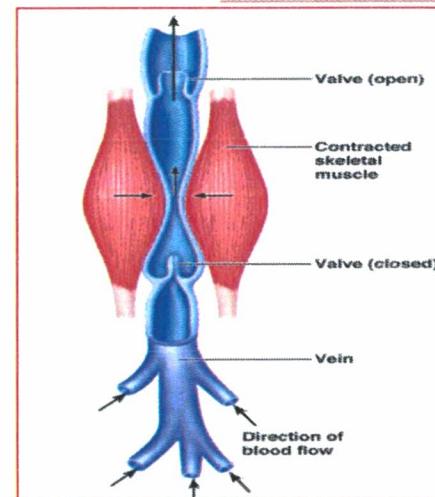
$\uparrow \text{MAP} = \text{venous pressure}$ .  $\Delta P = \text{MAP} - \text{RAP}$ .

## Distribution of Cardiac Output



Sherwood  
Figure 10.1  
Page 344

## Skeletal muscle pump



Two factors promote venous return:

- Alternate contraction and relaxation of skeletal muscles
- One-way valves prevent backflow
- This is a significant factor increasing venous return during dynamic exercise (e.g. running, cycling)

Figure 19-6 in Marieb EN (2004)  
Human Anatomy & Physiology, 6th Ed., Pearson Education, San Francisco

## Redistribution of cardiac output during exercise

### Reasons for blood flow changes:

- Heart and skeletal muscle: mainly local metabolic factors causing vasodilation
- In the **heart**, blood flow occurs mainly during ventricular diastole (coronary vessels are compressed during ventricular systole)
- **Skin**: mainly decrease in sympathetic vasoconstrictor effects, plus effects of bradykinin in sweat, both causing vasodilation, as part of thermoregulatory reflexes
- **Kidney and abdominal viscera**: mainly increase in sympathetic vasoconstrictor activity
- **Brain**: no change, because cerebral blood flow mainly affected by local metabolic activity (i.e. neural activity), which does not change as a result of exercise

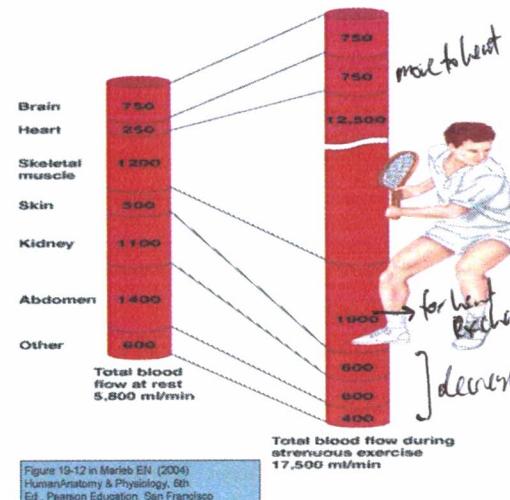


Figure 19-12 in Marieb EN (2004)  
Human Anatomy & Physiology, 6th Ed., Pearson Education, San Francisco

## Test your knowledge...

During exercise cardiac output is redistributed so that more or less blood flow goes to the gut?

(less).

The most important factor determining blood flow through working muscle is

A: the generalized vasoconstrictor effect of alpha 1 stimulation

OR

B: the accumulation of local metabolites

Which of the following aids venous return:

skeletal muscle pump      respiratory pump      ↓ arteriolar resistance

## DEFINITIONS

- **Inotropic** : affects the contractility of the myocardium
- Thus, positive and negative inotropic effects refer to increases or decreases, respectively, in cardiac contractility  
(eg adrenaline +ve, barbiturates -ve)
- **Chronotropic**: affects the heart rate
- Thus, positive and negative chronotropic effect refers to increases or decreases, respectively, in heart rate  
(eg adrenaline +ve, acetylcholine -ve)

## Summary....

- Cardiac preload = the amount of stretch/tension on the ventricular walls just prior to contraction (or at the end of diastole). This is equivalent to the EDV or end-diastolic ventricular volume.
- Cardiac afterload = the amount of force the ventricular muscle has to overcome to eject the blood. This is equivalent to the diastolic pressure which is the pressure the ventricles must exceed to open the aortic valve and eject the blood.
- The Frank-Starling Law of the heart describes the relationship between EDV and SV (Stroke Volume).
- As more blood returns to the heart and increases the EDV this stretches the ventricular muscle resulting in more optimally aligned actin and myosin filaments => increasing the force of the subsequent contraction and the stroke volume ejected from the heart.
- Contractility relates to the increase or decrease in stroke volume for a given EDV.
- Increased contractility = increased force of contraction for a given EDV = positive inotropic effect
- Decreased contractility = decreased force of contraction for a given EDV = negative inotropic effect
- SNS and adrenaline: positive inotropic effect PNS: negative inotropic effect
- Chronotropic effects relate to an increase or decrease in heart rate.
- Increases in contractility and HR occur with Beta 1 receptor stimulation (by noradrenaline/adrenaline) which allows (i) increased calcium influx (ii) increased release of sarcoplasmic calcium (iii) enhanced rate of cross bridge cycling and (iv) increased uptake of calcium => speeding up of muscle relaxation. All this provides a faster and more forceful contraction.
- Venous return aided by respiratory pump, skeletal muscle pump and decreased resistance. VR determined by pressure gradient between peripheral veins and right atrium.
- Cardiac output is distributed amongst the organs/tissue beds and can be redistributed by changes in resistance and accumulation of metabolites. Alpha 1 receptor activation causes generalized vasoconstriction. Local factors have greatest influence on flow.

Test your knowledge answers..... No peeking!

Afterload

Diastolic pressure determines preload or afterload?

C. end diastolic volume/stroke volume

B. stroke volume/force of contraction

A. force of contraction/cardiac output

The Frank-Starling Law of the heart relates which two variables:

During exercise cardiac output is redistributed so that more or less blood flow goes to the gut?

less blood flow

The most important factor determining blood flow through working muscle is

A: the generalized vasoconstrictor effect of alpha 1 stimulation

OR

B: the accumulation of local metabolites

Which of the following aids venous return:

skeletal muscle pump      respiratory pump      ↓ arteriolar resistance

All of the above can aid increases in venous return.

Test your knowledge answers...no peeking!

Stimulation of sympathetic nervous activity has a positive or negative inotropic effect on the heart?

positive inotropic effect

Stimulation of sympathetic nervous activity has a positive or negative chronotropic effect on the heart?

positive chronotropic effect

Stimulation of beta 1 or alpha 1 receptors increases cardiac contractility?

Beta 1

Test your knowledge answers...No peeking!

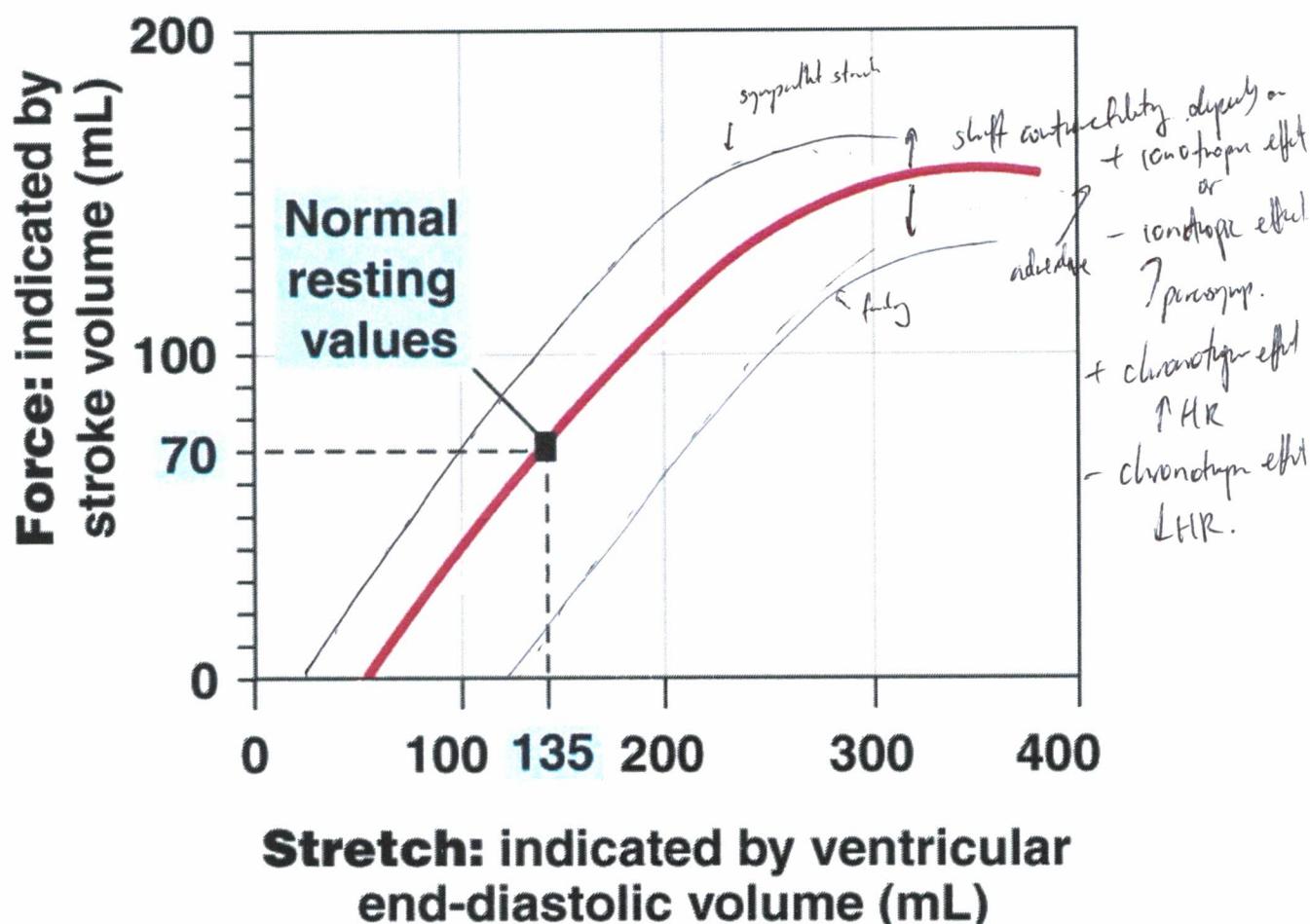
## CV Lecture Worksheet 4 – Cardiac Output &amp; Venous Return

Don't forget to do your  
Socrative Revision Quiz  
before the next lecture!  
Room # 1800800

## Activity 1:

Draw lines on the graph to indicate the relationship between SV and EDV

- (i) in a failing heart and
- (ii) with increased sympathetic stimulation



**Activity 2:** Draw a flow diagram showing how the following are related.

Stroke Volume

Parasympathetic Nervous System

Heart Rate

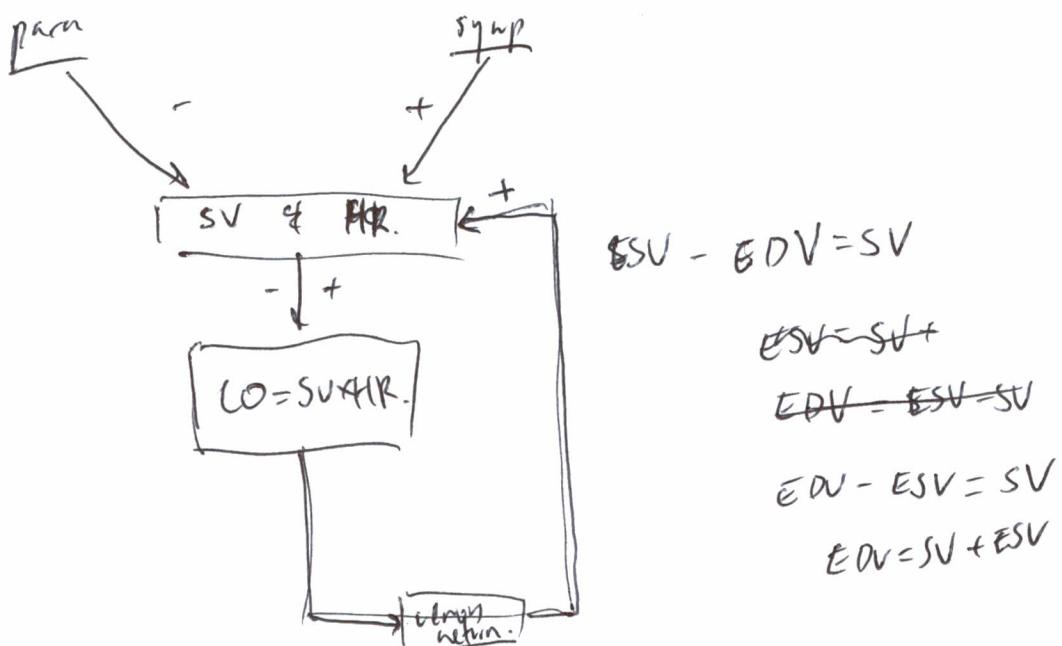
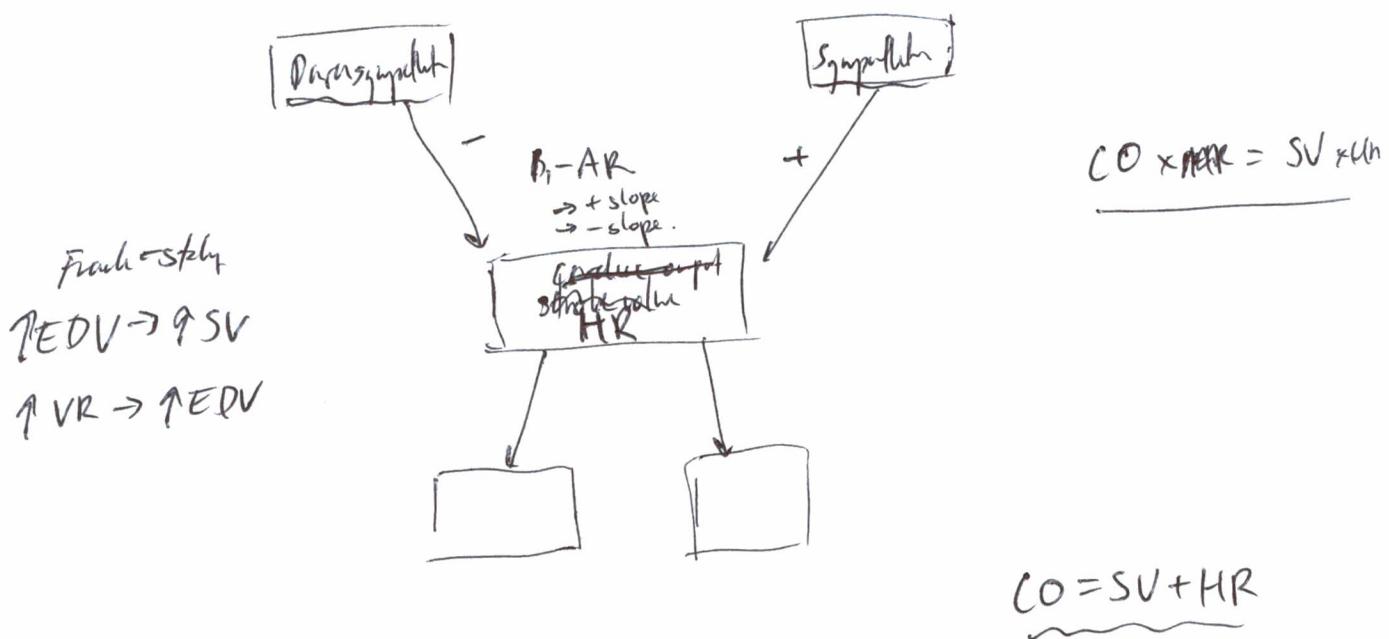
Venous Return

End-Diastolic Volume

Sympathetic Nervous System

Cardiac Output

sympathetic



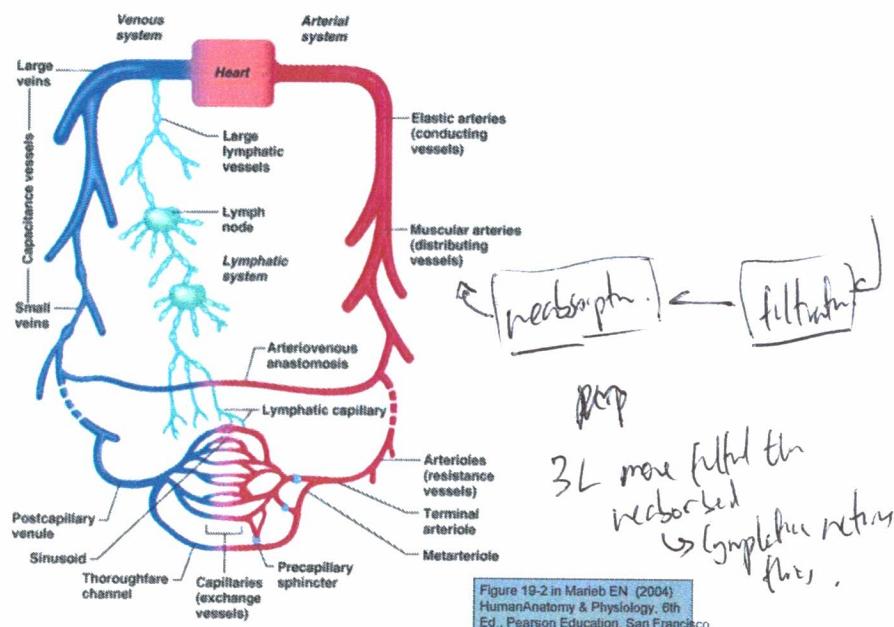
$\alpha_1$ - Vasodilatation  
 $\beta_2$ - Vasoconstriction

# THE CARDIOVASCULAR SYSTEM 5

The micro- and specialized circulations – distribution of cardiac output



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## Learning objectives:

At the end of this lecture you should understand:

- The forces involved in the movement of substances across the capillary membrane
- The function of the lymphatic system as it relates to the circulation
- The mechanisms involved in redistribution of blood flow
- Features of specialized circulations

## The microcirculation

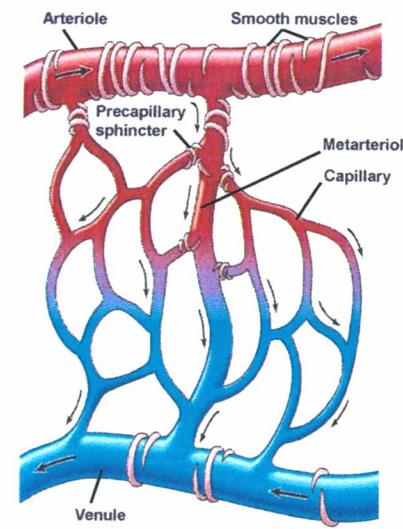
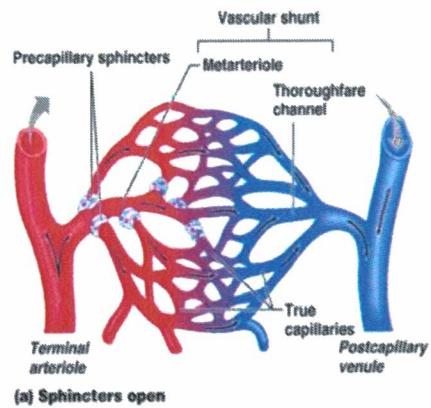


Figure 10-17 from Sherwood, L.A. "Human Physiology" 4th ed., Brooks/Cole, Pacific Grove, Ca., U.S.A.

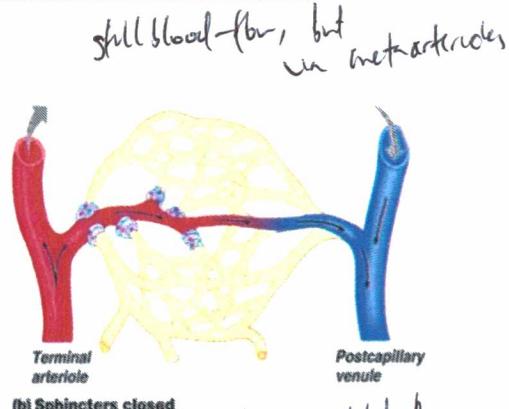
- Arterioles contain relatively high proportion of smooth muscle; thick walls, i.d. 30-500 µm; resistance vessels. They are innervated by sympathetic nerves. ( $\alpha_1$  -  $\beta_2$ )
- Capillaries consist only of a single layer of endothelial cells. i.d. ~8 µm; exchange vessels. They form a complex network.
- There are pre-capillary sphincters (band of smooth muscle) at their origin. These open in response to increase in metabolite concn.  $\rightarrow$  contract decomp. and shut down less blood needs tissue.
- E.g. during exercise, the number of open capillaries in skeletal muscle may increase 20-fold.
- The density of capillaries varies in different tissues, according to the normal metabolic activity of that tissue (e.g. high in skeletal muscle, brain, glands, much less in bone or cartilage).
- Venules have an i.d. of ~20µm; mainly consist of connective tissue.
- The metarterioles contain some smooth muscle, and serve either as arterio - venous shunts (esp. in skin), or else give rise to capillaries.

## The microcirculation

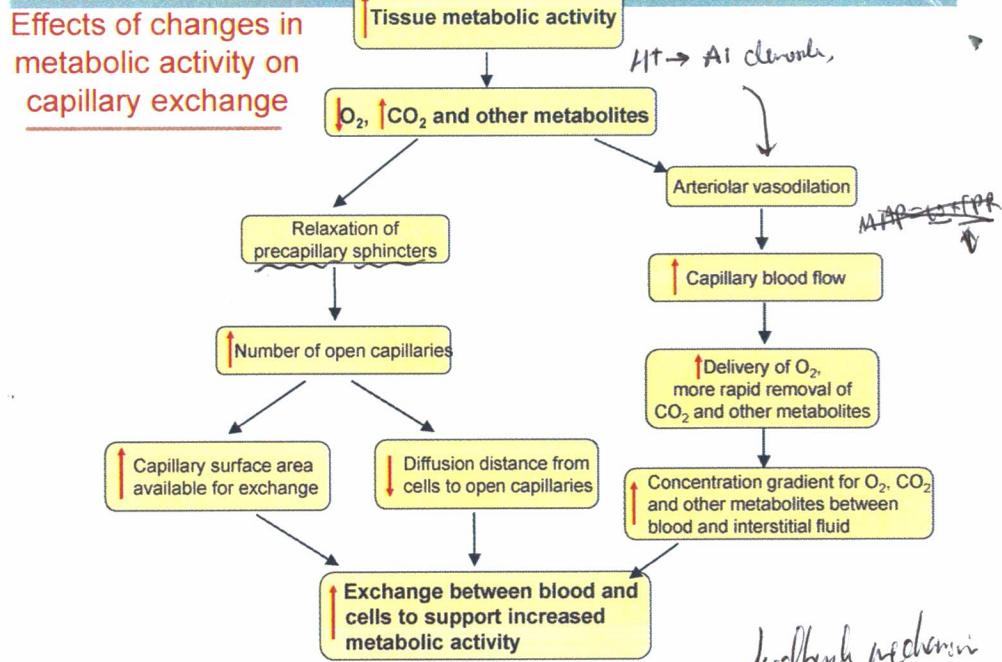


This shows the effects of opening or closing precapillary sphincters on the number of open capillaries. If the number of open capillaries is increased, then the average time for exchange within the capillaries is also increased

Figure 19-4 in Marieb EN (2004)  
Human Anatomy & Physiology, 6th  
Ed., Pearson Education, San Francisco



**hindters closed**  
less diffusion, slower, matched with reduced withdrawal activity.



# Control of Special Circulations

Circulation	Local Metabolic Control	Vasoactive Metabolites	Sympathetic Control
Coronary	Most important	Hypoxia Adenosine	Least important
Cerebral	Most important	CO <sub>2</sub> H <sup>+</sup> <i>and blood glucose.</i>	Least important
Skeletal Muscle	Most important during exercise	Lactate K <sup>+</sup> Adenosine	Most important at rest (α <sub>1</sub> - vasoconstricts β <sub>2</sub> – vasodilates)
Skin	Least important		Most important for Temperature reg.
Pulmonary	Most important	Hypoxia vasoconstricts *	Least important

Myocardial and Skeletal Muscle contractions disrupt blood flow

## Test your knowledge...

Precapillary sphincters open or close in response to decreased concentrations of metabolites?

Is the following statement TRUE or FALSE?

Increasing flow through capillary beds decreases the distance for diffusion of substances between the blood and the cells.

$\beta_1$  - heart rate  
↑  
cardiac output

deoxyg to lymph  
pickup O<sub>2</sub>.

## Mechanisms for control of regional blood flow

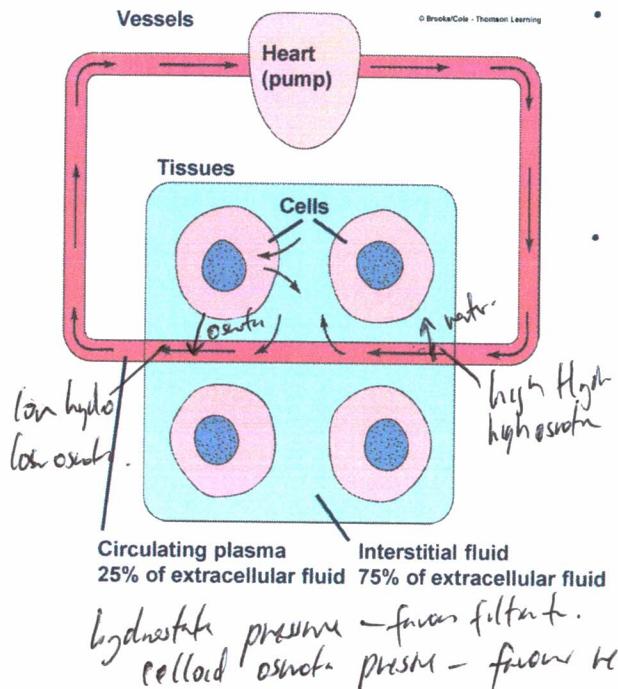
### LOCAL CONTROL

- Autoregulation: constant blood flow with changing pressures (e.g. kidneys, brain, heart)
 

*keep value relatively const.*
- Active hyperemia: blood flow is proportional to metabolic activity (e.g. skeletal muscle)
- Reactive hyperemia: increased blood flow in response to a period of decreased blood flow (e.g. Skeletal muscle, cardiac muscle)
 

*blood activity to get through.*
- Myogenic hypothesis: when vascular smooth muscle is stretched it contracts
- Metabolic hypothesis: as a result of metabolic activity the tissues produce vasodilator metabolites ( $H^+$ ,  $K^+$ , lactate, adenosine,  $CO_2$ )
 

*accountants.*



## Mechanisms for control of regional blood flow

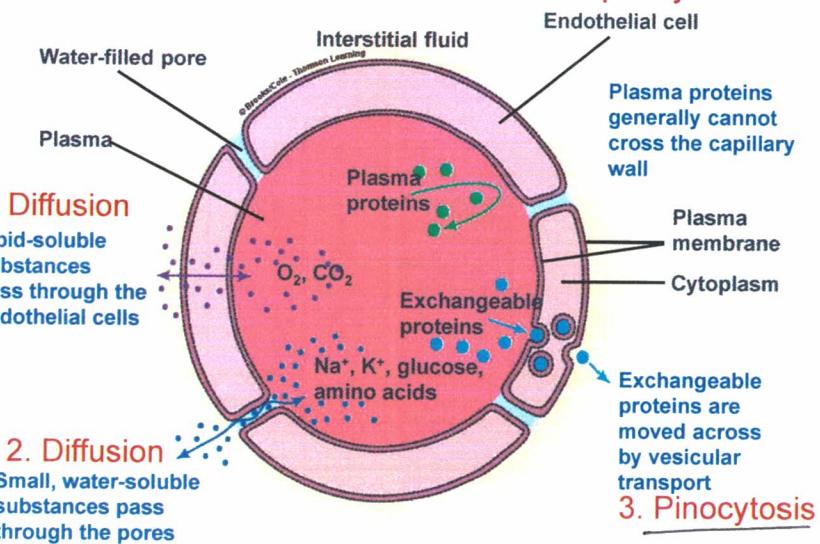
### NEURAL AND HORMONAL CONTROL

- Sympathetic innervation:
 

*greater vasoconstrict..*

  - High in skin and skeletal muscle
  - Low in coronary, pulmonary and cerebral
- Vasoactive substances:
  - Histamine and Bradykinin – dilate arterioles yet constrict venules => local edema *allergic reaction.*
  - Serotonin – in response to vessel damage – vasoconstricts => vascular spasm & migraine
  - Prostaglandins – various effects
- Vasopressin and Angiotensin II – vasoconstrictors (increase Total Peripheral Resistance – TPR)

## Movement of substances across the capillary wall



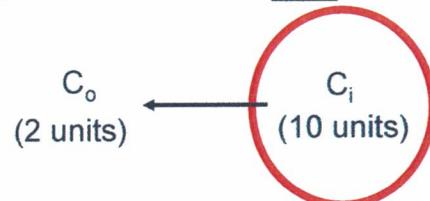
## Diffusion

- The rate of transfer of water and solutes across the capillary wall is primarily by diffusion.

- Process of diffusion is described by Fick's law:

$$J = -PS(C_o - C_i)$$

$J$  = rate of diffusion OUT of the capillary



*concentration gradient*

Example:

Concentration outside (interstitial fluid) < inside (capillary).

$$C_o - C_i = 2 - 10 = -8$$

Thus:  $J = -PS(-8) = +8 \text{ PS}$  as the final value is positive the direction of the diffusion is OUT of the capillary.

## Diffusion

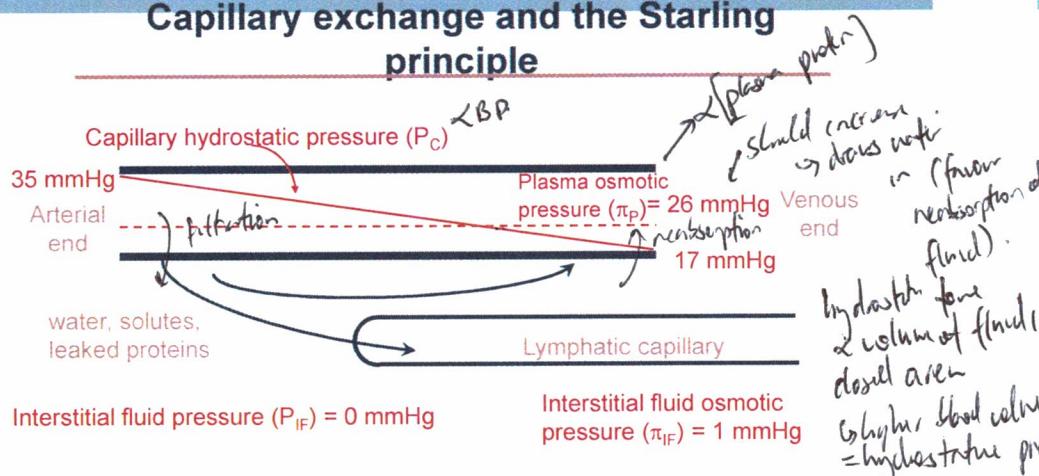
- The rate of transfer of water and solutes across the capillary wall is primarily by diffusion.

- Process of diffusion is described by Fick's law:

$$J = -PS(C_o - C_i)$$

- where  $J$  = quantity of substance moved per unit time
- $P$  = capillary permeability for a particular molecule (inversely related to molecular weight)
- $S$  = surface area available for exchange
- $C_o$  = concentration of the substance outside the capillary, and
- $C_i$  = concentration of the substance inside the capillary
- Lipid-soluble substances** such as  $O_2$  and  $CO_2$  pass directly through membrane of endothelial cell (not limited to slit pores).
- Lipid-insoluble small molecules** such as  $H_2O$ ,  $Na^+$ ,  $Cl^-$ , urea and glucose pass readily through slit pores.
- With lipid-insoluble molecules of increasing size, the rate of diffusion becomes progressively less, until at a molecular weight of 60,000 the diffusion is minimal.
- permeability of the capillary endothelial wall is not the same in all tissues, e.g. very high in liver capillaries, low in brain capillaries

## Capillary exchange and the Starling principle



Starling's hypothesis states that :

Fluid flow outwards =  $k \{ \text{sum (outward forces)} - \text{sum (inward forces)} \}$

Therefore, fluid flow outwards =  $k \{ (P_c + \pi_{if}) - (P_{if} + \pi_p) \}$ .

## Capillary exchange and the Starling principle

### FILTRATION

Capillary hydrostatic pressure ( $P_c$ )

35 mmHg

Arterial end

water, solutes,  
leaked proteins

Interstitial fluid pressure ( $P_{if}$ ) = 0 mmHg

### REABSORPTION

Plasma osmotic pressure ( $\pi_p$ )

= 26 mmHg

Venous end

17 mmHg  
Lymphatic capillary

Interstitial fluid osmotic pressure ( $\pi_{if}$ ) = 1 mmHg

- Fluid flow outwards =  $k \{ (P_c + \pi_{if}) - (P_{if} + \pi_p) \}$
- At arterial end, fluid flow outwards =  $k \{ (35 + 1) - (0 + 26) \} = 10k$
  - This value is **positive**, therefore FILTRATION occurs
  - At venous end, fluid flow outwards =  $k \{ (17 + 1) - (0 + 26) \} = -8k$
  - This value is **negative**, therefore REABSORPTION occurs

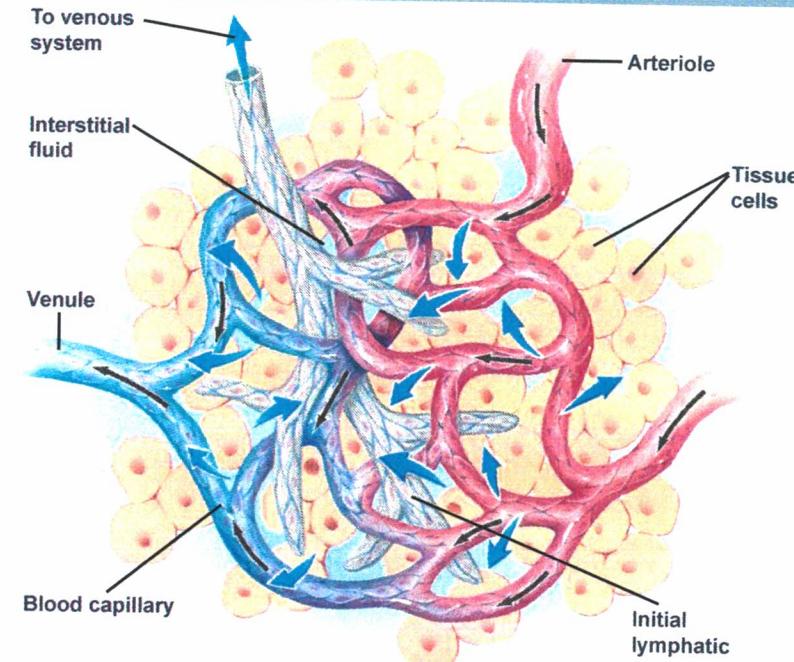
## Test your knowledge...

Diffusion of substances across the capillary membrane is related to which of the following?

- Concentration gradient between inside and outside the cell
- Permeability of the capillary membrane
- The surface area for diffusion
- All of these

Is the following statement true or false?

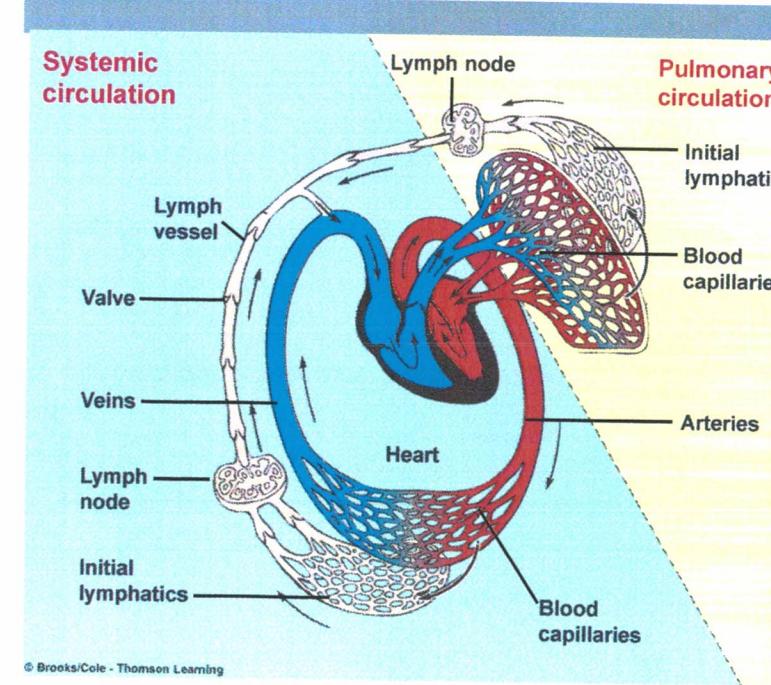
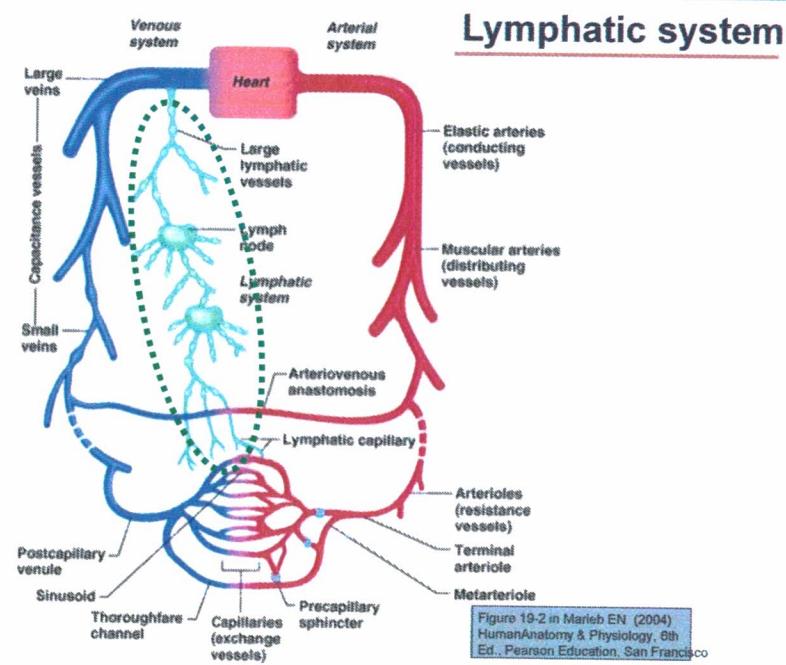
The concentration of proteins is greater in the interstitial fluid than in the blood.



heavy blood on peripheral bed, results in edema because blood is not moving.

Fig. 10.25(1)  
Page 368

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## Lymphatic system

- On average, slightly more fluid is filtered out of the capillaries than is reabsorbed (~3 litres/day).
- This, plus protein that leaks out of capillaries, is returned to the circulation via the lymphatic system
- Transport of lymph occurs by means of compression of lymphatic vessels by skeletal muscle contraction, aided by one-way valves in vessels
- The lymph percolates through **lymph nodes** which contain phagocytes that destroy bacteria - part of body's defence system
- Oedema (edema) is buildup of fluid in interstitial space. *The volume of interstitial fluid that due to filtration out of the capillaries exceeds the ability of the lymphatics to return it to the circulation.* *outward force > inward force*
- This occurs as a result of (1) reduced concentration of plasma protein; (2) increased capillary permeability, e.g. via histamine in allergic reactions or tissue injury; (3) increased venous pressure, causing increased capillary hydrostatic pressure; (4) blockage of lymphatic vessels.

Test your knowledge answers... No peeking!

TRUE

Increasing flow through capillary beds decreases the distance for diffusion of substances between the blood and the cells.

Is the following statement TRUE or FALSE?

CLOSE

Precapillary sphincters open or close in response to decreased concentrations of metabolites?

## Summary

- Arterioles are innervated by the SNS and can be stimulated via alpha 1 receptors to vasoconstrict.
- Capillaries have only a single cell layer – allows for exchange.
- Pre-capillary sphincters regulate flow to a capillary bed in response to changes in metabolite concentration.
- Capillary beds open when tissues are metabolically active due to precapillary sphincter action. Opening of capillary beds increases flow to the cells, providing more energy substrates and removing metabolites and also decreases the distance for diffusion of substances between cells and blood.
- Vasodilation occurs with hypoxia (low oxygen levels in the tissues) except in the pulmonary vessels where hypoxia produces vasoconstriction.
- Vasoactive substances include Angiotensin II (most potent endogenous vasoconstrictor) and Vasopressin (also called ADH).
- Sympathetic innervation is high in skeletal muscle and skin but low in heart, lungs and brain which are regulated mainly by local factors.
- Filtration occurs at the arterial end of the capillaries and reabsorption at the venous end due to a balance of hydrostatic and oncotic forces within the capillary and the interstitial fluid.
- Fick's Law describes the process of diffusion.  $J = PS(C_o - C_i)$
- Capillary hydrostatic pressure equates to blood pressure at this point and is affected by volume.
- Plasma oncotic (colloid osmotic) pressure relates to the concentration of plasma proteins within the blood.
- Oncotic pressure in the interstitial fluid is usually close to zero unless proteins leak from the capillaries.
- Filtration and reabsorption from capillaries does not match and the fluid remaining in the interstitium is returned to the blood volume via the lymphatic vessels.

Test your knowledge answers....no peeking!

FALSE

The concentration of proteins is greater in the interstitial fluid than in the blood.

Is the following statement true or false?

- All of these
- The surface area for diffusion
- Permeability of the capillary membrane
- Concentration gradient inside and outside the cell

Diffusion of substances across the capillary membrane is related to which of the following?

## CV Lecture 5 Worksheet

### Activity 1: What are the effects of Dynamic Exercise on CV parameters?

Indicate below if there would be an:      Increase      Decrease      or      No change

Provide reasons for your answers.

(Remember: MAP = CO x TPR and CO = HR x SV)

Cardiac Output:

Total Peripheral Resistance:

Mean Arterial Pressure: ~~With~~

No change (probably mild elevation).

Heart Rate:

Stroke Volume:

Don't forget to do your  
Socrative Revision  
Quizzes before the next  
lecture!

Mechanisms for redistribution of blood flow during dynamic exercise:

Region	Blood Flow Increased/Decreased ?	Mechanisms?
Working skeletal muscles	increase	sympathetic N.s. local metabolism ( $\text{CO}_2$ ) dilate of arterioles & precipitally sphincters.
Gastrointestinal Tract	decreased	sympathetic N.s. ( $\alpha_1$ - vasoconstrict) shut blood flow,

**Activity 2: Will capillary filtration increase or decrease under the following conditions?**

Condition	Increased or Decreased Filtration ?
Increase in blood pressure	increase. ↑ hydrostatic capillary. ✓
Increase in [plasma protein]	decrease      ↓ osmotic in capillary      ✓
Increased interstitial pressure	decrease.      ↓ hydrostatic in interstitial cells. ✓
Increased interstitial fluid osmotic pressure	increase.      ↑ osmotic interstitial      ✓
Starvation	decrease.      very little protein, reduced
Venous blockage	decrease. x filtration increase.      ↑ hydrostatic pressure -
Decreased blood volume	decrease      less hydrostatic force.

# THE CARDIOVASCULAR SYSTEM 6

## The regulation of blood pressure

COMMONWEALTH OF AUSTRALIA

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[sharon.herkes@sydney.edu.au](mailto:sharon.herkes@sydney.edu.au)

## Why is the regulation of arterial blood pressure important in homeostasis?

- The arterial blood pressure is essentially the same as the perfusion pressure for all organs (difference between arterial pressure and venous pressure).
- Homeostasis depends upon the blood flow to all regions in the body being sufficient for the metabolic requirements of each region.
- Regional blood flow can vary according to local demand, via metabolic autoregulation.
- However this in turn depends upon the perfusion pressure (i.e. arterial blood pressure) being maintained within reasonable narrow limits.
- The main mechanism regulating blood pressure in the short term (i.e. seconds or minutes) is the **baroreceptor reflex**.

BP too high,  
→ blood still  
flows.

## Learning objectives:

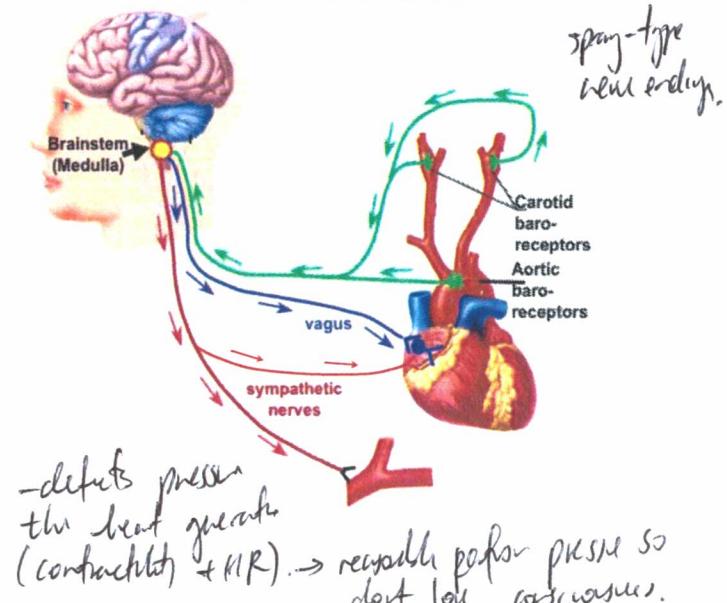
At the end of this lecture you should understand:

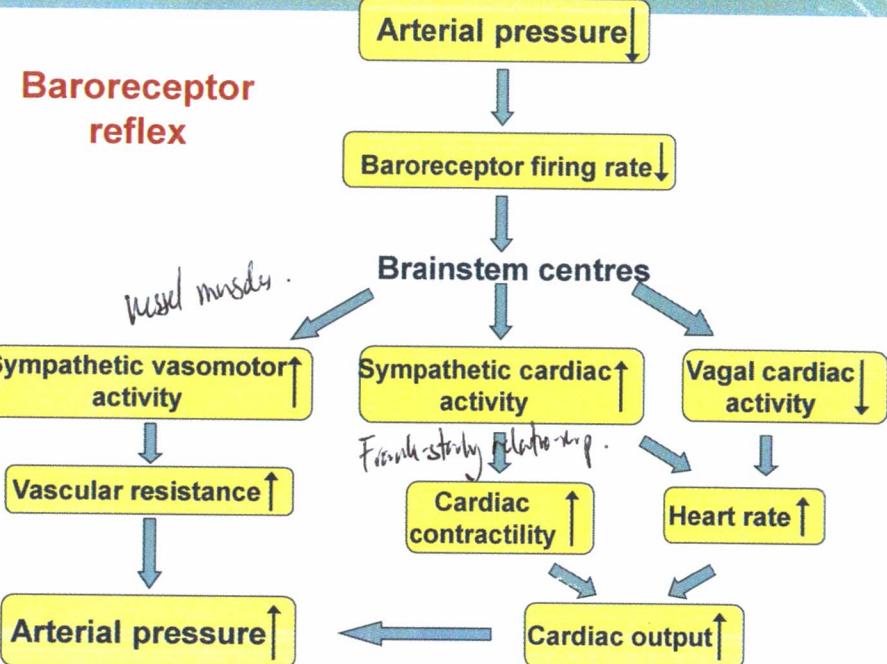
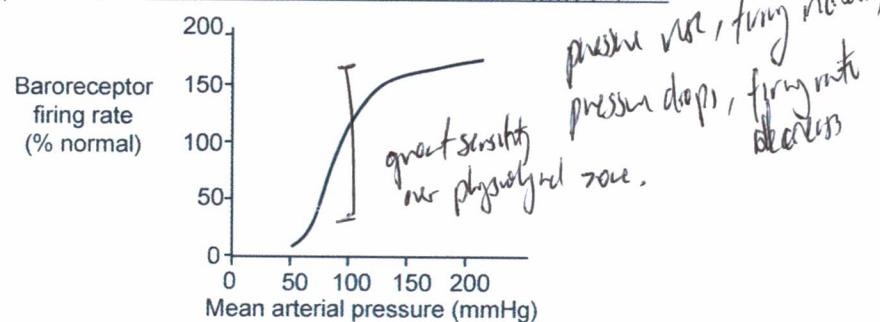
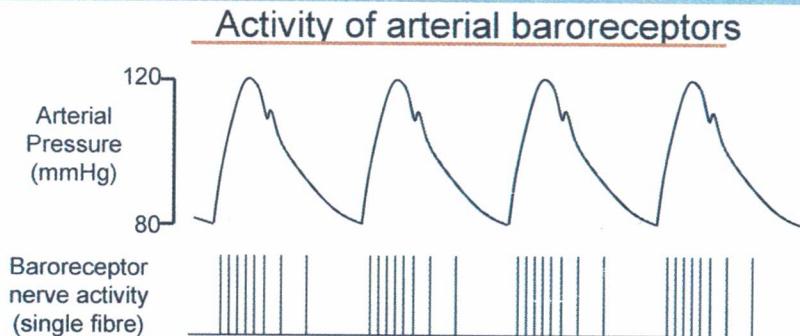
- How mean arterial pressure is controlled
- The baroreceptor reflex
- Sympathetic influences on the heart and circulation
- Hormonal influences on the heart and circulation

## Short-term control of blood pressure

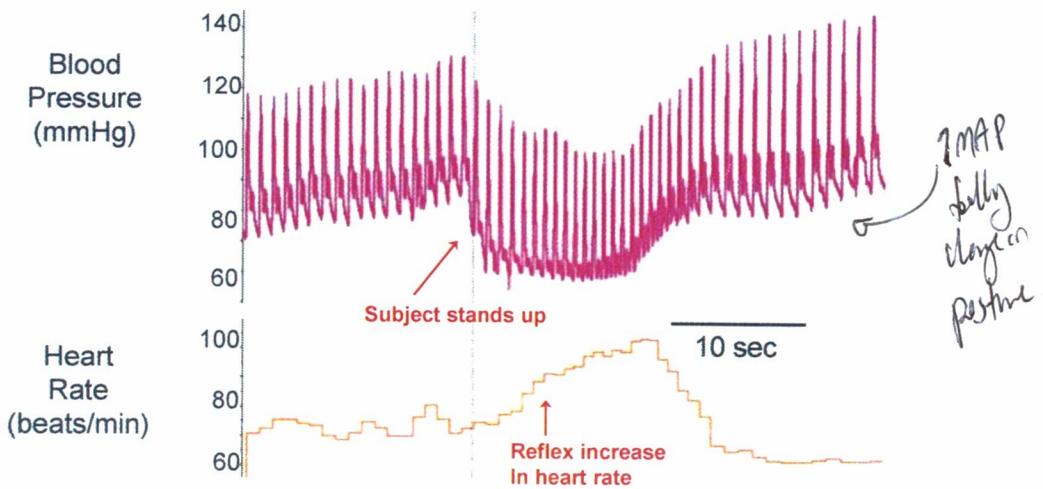
### The baroreceptor reflex

- Baroreceptors are spray-type nerve endings lying in the walls of arteries that are stretched when the pressure increases.
- They are tonically active at normal levels of arterial pressure, and are able to detect changes in mean pressure over the range 50 mmHg (threshold) to 160 mmHg (saturation level)

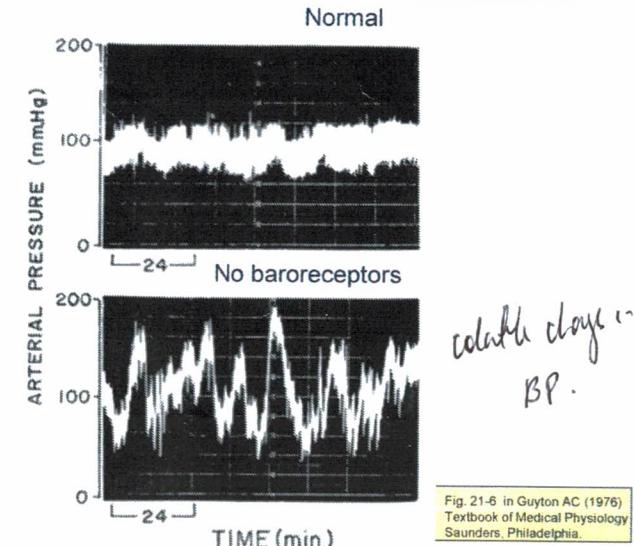




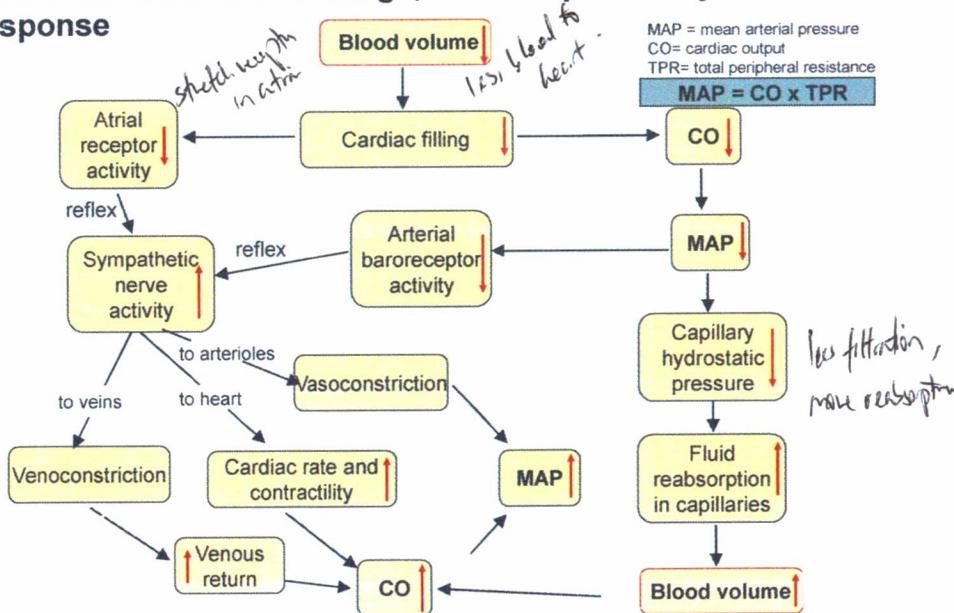
### Baroreceptor reflex control of blood pressure - the effect of posture



### Baroreceptor reflex minimizes fluctuations in blood pressure (buffering system)



## Effects of acute haemorrhage, and compensatory response



- Apart from these short term effects of severe blood loss, hormonal mechanisms are also activated, which reinforce the neural reflexes and other short term compensatory responses
  - Vasopressin (antidiuretic hormone) is released (antidiuretic hormone)
  - The renin-angiotensin-aldosterone system is also activated
- conserve water*  
*conserves salt & fluid in body*  
*RAS*

## Test your knowledge...

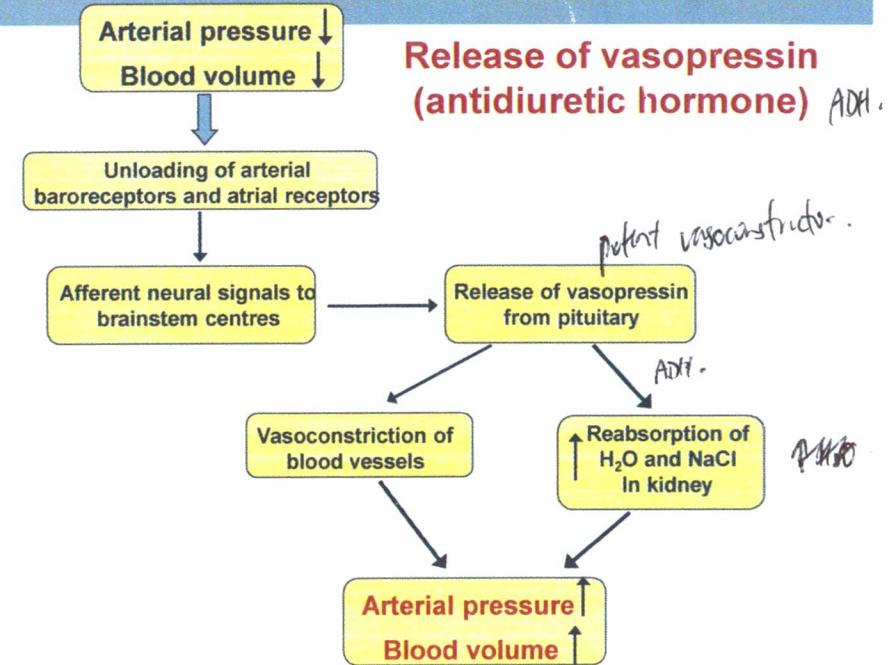
When you stand up the firing rate of your baroreceptors increases or decrease?

stand up, MAP drops, baroreceptor firing drops.

Does venous return increase or decrease immediately upon standing up?

increase  $\times$  decrease

## Release of vasopressin (antidiuretic hormone) ADH



## Test your knowledge...

What happens to total peripheral resistance in the 10-30 seconds after you go from sitting to standing?

increases to twice MAP is constant.

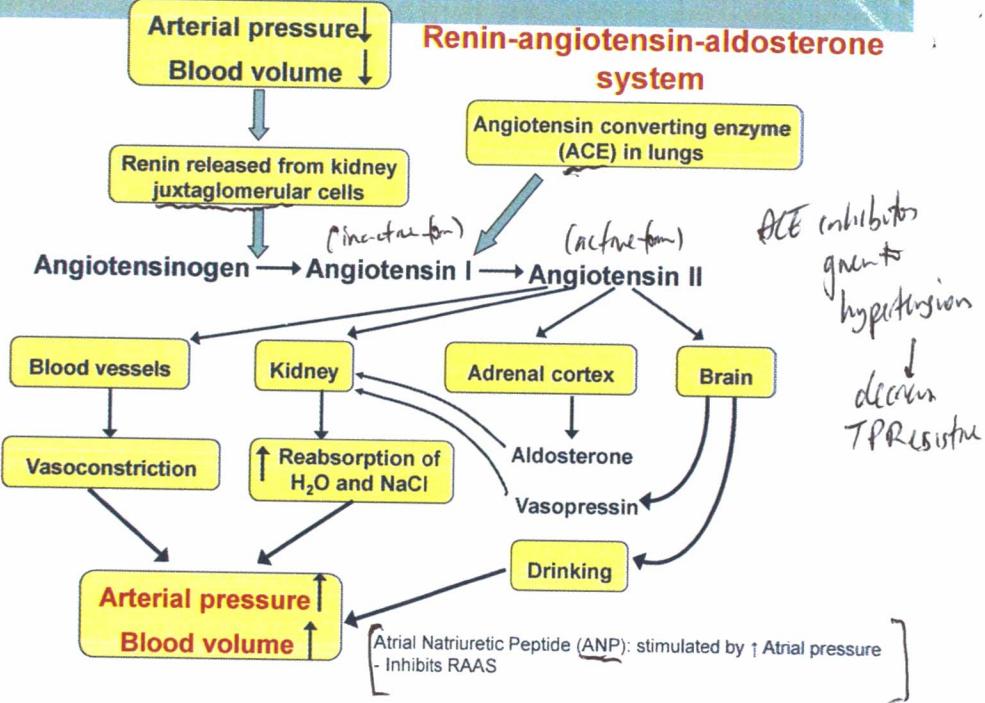
When MAP falls which nervous system increases its activation?

### Sympathetic or Parasympathetic

## Sympathetic-

## Summary

- Baroreceptors (stretch receptors in the aortic arch and carotid vessels) regulate blood pressure.
  - When MAP falls the firing rate of the baroreceptors falls.
  - The baroreceptor reflex is tonically active and helps to buffer changes in blood pressure.
  - A fall in MAP detected by the baroreceptors causes stimulation of the SNS -> vasoconstriction of arterioles and increased HR and contractility. Vasoconstriction increases TPR and raises DP which aids to increase MAP. An increase in cardiac contractility aids increases in SP also affecting MAP.
  - Falls in blood pressure may relate to changes in blood volume or posture etc.
  - The Renin-Angiotensin-Aldosterone System is involved in the long-term regulation of blood pressure and acts to increase the reabsorption of salt and water from the kidney tubules thereby increasing blood volume and blood pressure.
  - Renin is released in response to falls in MAP. Angiotensin II is a potent vasoconstrictor and stimulates conservation of salt and water. Aldosterone stimulates reabsorption of salt from the kidney tubules and is associated with homeostasis of salt levels in the body.
  - Vasopressin stimulates the conservation (reabsorption) of water from the kidney tubules.
  - The factors which determine HR are neural (SNS and PNS) and hormonal (Adrenaline etc.) and local (atrial stretch).
  - Factors determining systolic pressure (SP) include force of ventricular contraction, SV, neural and hormonal factors affecting contractility and previous DP.
  - DP is determined largely by HR, TPR and previous SP.  
  - Don't Forget Your Socrative Quizzes....
  - Visit the Open All Hours Revision Room #1800800



Test your knowledge answers...No peeking!

DECREASE

Does venous return increase or decrease when you stand up?

DECREASES

When you stand up the firing rate of your baroreceptors increases or decreases?

What happens to total peripheral resistance in the 10-30 seconds after you go from sitting to standing?

It increases

When MAP falls which nervous system increases its activation?

Sympathetic or Parasympathetic

peeling!  
Test your knowledge answers...no

**CV Lecture Worksheet 6**

Don't forget to do your  
Socrative Revision  
Quizzes in  
Room # 1800800

**Activity 1:**

This table shows MAP and CO during control conditions and 2 levels of blood loss.

Condition	MAP (mmHg)	CO (L/min)
Control	93	5.7
10% blood loss	91	5.1
20% blood loss	90	4.3

$$\text{MAP} = \text{CO} \times \text{SVR}$$

$$\text{CO} = \frac{\text{SV}}{\text{HR}}$$

What would you predict happens to the following as blood loss increases?

blood loss increas,

MAP decreas, CO decreas, SVR increas.

Heart Rate:

decreas increas. ✓

hemorrhage,  
↳ baroreceptor reflex  
↳ maintain MAP.  
→ blood calm not engorged  
→ reversible shock.

Stroke Volume:

decreas variable value low,  
decreas in SV.

Total Peripheral Resistance:

increas. ✓

high sympathetic,  
arterial vasoconstrict,  
no filtration of blood.

Angiotensin II levels:

increas. ✓

Vasopressin levels:

increas. ✓

Atrial Natriuretic Peptide levels:

decreas. ✓

Thirst:

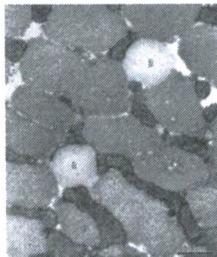
increas. ✓

## Lecture 1 – Energetic Pathways in Muscle During Exercise

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## Learning Objectives



- The main pathways for regenerating ATP inside skeletal and cardiac muscle fibres and what processes consume ATP during muscle activity.
- The different energy pathways utilized in anaerobic vs aerobic exercise.
- The metabolic differences between skeletal and cardiac muscle as well as the different fibre types of skeletal muscle.

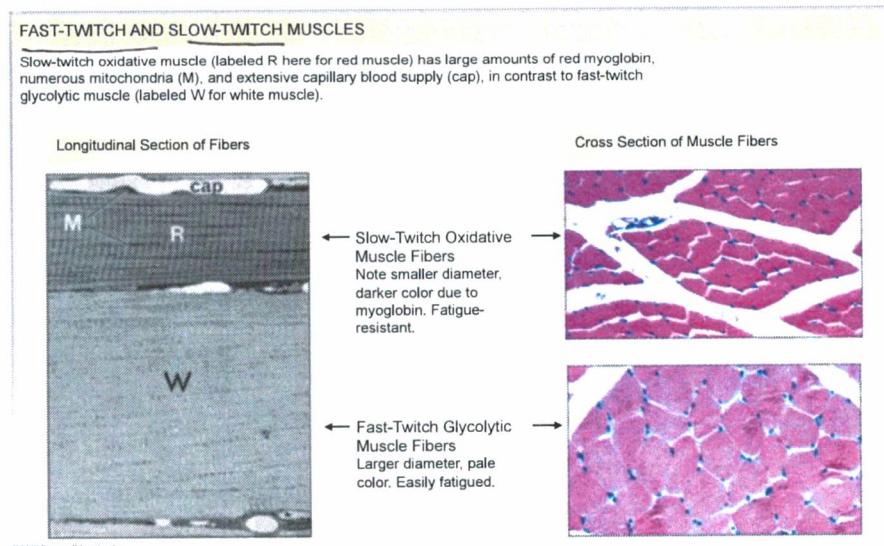
# Metabolic Characteristics

Table 12.3 Comparison of the Three Muscle Types

Comparison of the Three Muscle Types				Table 12.3
	Skeletal	Smooth	Cardiac	
<b>Appearance under light microscope</b>	Striated	Smooth	Striated	
<b>Fiber arrangement</b>	Sarcomeres	No sarcomeres	Sarcomeres	
<b>Location</b>	Attached to bones; a few sphincters close off hollow organs	Forms the walls of hollow organs and tubes; some sphincters	Heart muscle	
<b>Tissue morphology</b>	Multinucleate; large, cylindrical fibers	Uninucleate; small spindle-shaped fibers	Uninucleate; shorter branching fibers	
<b>Internal structure</b>	T-tubule and sarcoplasmic reticulum	No t-tubules; sarcoplasmic reticulum	T-tubule and sarcoplasmic reticulum	
<b>Fiber proteins</b>	Actin, myosin; troponin and tropomyosin	Actin, myosin; tropomyosin	Actin, myosin; troponin and tropomyosin	
<b>Control</b>	<ul style="list-style-type: none"> <li>• <math>\text{Ca}^{2+}</math> and troponin</li> <li>• Fibers independent of one another</li> </ul>	<ul style="list-style-type: none"> <li>• <math>\text{Ca}^{2+}</math> and calmodulin</li> <li>• Some fibers electrically linked via gap junctions; others independent</li> </ul>	<ul style="list-style-type: none"> <li>• <math>\text{Ca}^{2+}</math> and troponin</li> <li>• Fibers electrically linked via gap junctions</li> </ul>	
<b>Contraction speed</b>	Fastest	Slowest	Intermediate	
<b>Contraction force of single fiber twitch</b>	Not graded	Graded	Graded	
<b>Initiation of contraction</b>	Requires ACh from motor neuron	Stretch, chemical signals. Can be autorhythmic	Autorhythmic	
<b>Neural control of contraction</b>	Somatic motor neuron	Autonomic neurons	Autonomic neurons	
<b>Hormonal influence on contraction</b>	None	Multiple hormones	Epinephrine	

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Figure 12.14

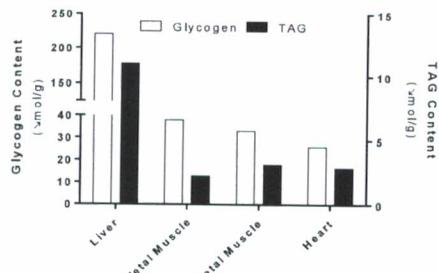


density, number  
ATP generation is  
different b/w the  
cycles.

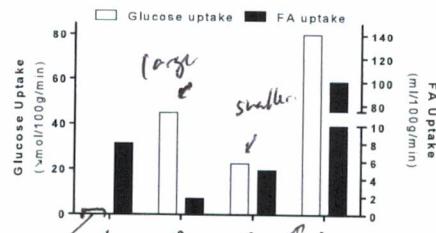
	Type I	Type IIa	Type IIb
	Slow-Twitch Oxidative; Red Muscle	Fast-Twitch Oxidative-Glycolytic; Red Muscle	Fast-Twitch Glycolytic; White Muscle
<b>Speed of development of maximum tension</b>	Slowest	Intermediate	Fastest
<b>Myosin ATPase activity</b>	Slow	Fast	Fast
<b>Diameter</b>	Small	Medium	Large
<b>Contraction duration</b>	Longest	Short	Short
<b>Ca<sup>2+</sup>-ATPase activity in SR</b>	Moderate	High	High
<b>Endurance</b>	Fatigue resistant	Fatigue resistant	Easily fatigued
<b>Use</b>	Most used: posture	Standing, walking	Least used: jumping; quick, fine movements
<b>Metabolism</b>	Oxidative; aerobic	Glycolytic but becomes more oxidative with endurance training	Glycolytic; more anaerobic than fast-twitch oxidative-glycolytic type
<b>Capillary density</b>	High	Medium	Low
<b>Mitochondria</b>	Numerous	Moderate	Few
<b>Color</b>	Dark red (myoglobin)	Red	Pale
<b>Major Storage Fuel</b>	Triglyceride	Glycogen	ATP/PCr

## Basal Characteristics

*low stored very glycogen.*



*will glucose  
will dephosphorylate,  
will not accumulate  
in tissue -*



*large  
smaller  
and fast in heart.*

Gerski and Kryluk, Eur J Appl Physiol 1980

Glucose Uptake data – Hemigadchi et al. Diabetes 1996  
FA Uptake data – Hegany et al. Diabetes 2000

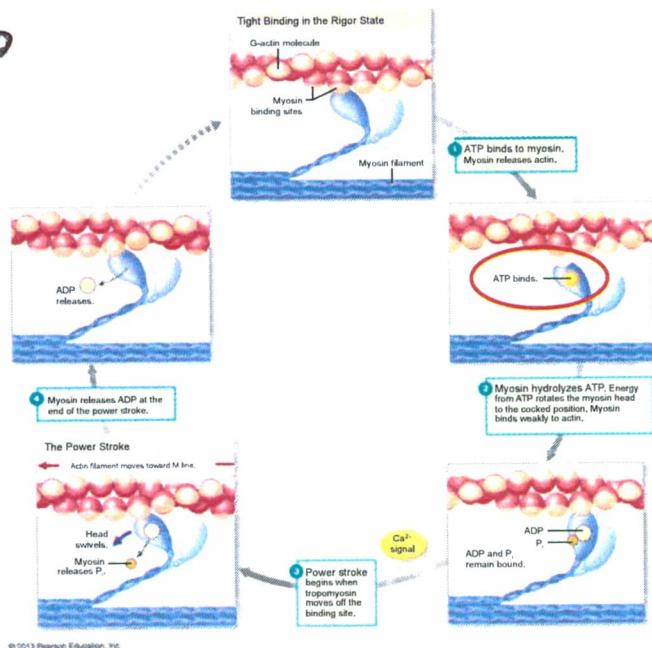
## Metabolic Pathways

## Consumption of ATP

### Muscle Contraction

- Power Stroke
  - 1 per myosin head per contraction

THE CONTRACTION CYCLE    Figure 12.9



## Consumption of ATP

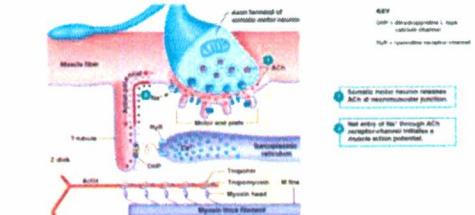
### Muscle Contraction

- Power Stroke
- Calcium Clearance
  - $Ca^{2+}$  enters SR via ATP using  $Ca^{2+}-ATPase$ .

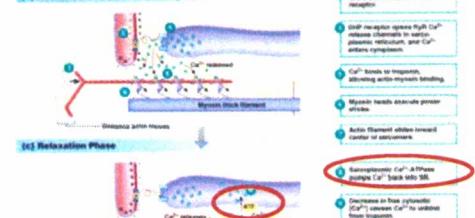
Fig. 12.10 ESSENTIALS

#### Excitation-Contraction Coupling and Relaxation

##### (a) Initiation of Muscle Action Potential



##### (b) Excitation-Contraction Coupling



##### (c) Relaxation Phase



KEY

 $Ca^{2+}$  = divalent cation;  $i$ ,  $o$ ,  $c$ ,  $r$  $Ca^{2+}$  = calcium ion;  $Ca^{2+}$  = calcium channel $Ca^{2+}$  = calcium ion channel

- 1 Acetylcholine (ACh) triggers a depolarization of the membrane.
- 2 Acetylcholine receptor (AChR) binds to ACh.
- 3 Calcium ( $Ca^{2+}$ ) enters the cell through voltage-gated calcium channels.
- 4 Calcium ( $Ca^{2+}$ ) triggers a depolarization of the membrane.

- 1 Action potential in T-tubule triggers conformation of DHP receptors.
- 2 DHP receptor opens. Calcium ( $Ca^{2+}$ ) release channels in sarcoplasmic reticulum and T-tubule open.
- 3 Calcium ( $Ca^{2+}$ ) ions are released, activating actin-myosin binding.
- 4 Myosin heads execute power stroke.
- 5 Actin filament slides inward or outward.

- 1 Sarcoplasmic ( $Ca^{2+}$ -ATPase) pump ( $Ca^{2+}$ ) back into SR.
- 2 Decrease in free  $Ca^{2+}$  triggers  $Ca^{2+}$  to bind to tropomyosin.
- 3 Tropomyosin no longer blocking adenosine triphosphate (ATP) binds to actin-myosin binding site.

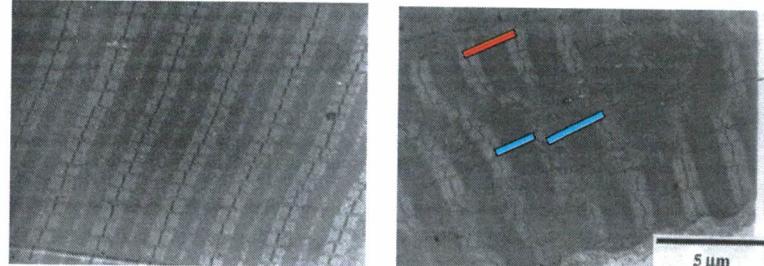
- 4 Actin filament slides outward or inward.
- 5 Myosin heads release ADP and  $P_i$ .

- 6 Tropomyosin no longer blocking adenosine triphosphate (ATP) binds to actin-myosin binding site.

## Consumption of ATP

### Muscle Contraction

- Power Stroke
- Calcium Clearance
- Post-Exercise Repair  
↳ structural muscle damage,



Note regions of overstretched and understretched sarcomeres

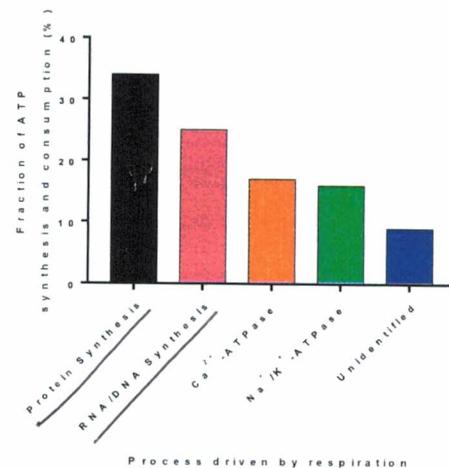
These regions of damaged sarcomeres cause membrane damage, loss of intracellular proteins and cause inflammation which is why muscles become sore & tender.

## Consumption of ATP

### Muscle Contraction

- Power Stroke
- Calcium Clearance
- Post-Exercise Repair

↳ growth new protein &  
new nucleotides.  
→ 2 largest source of energy use.



Adapted from Buttigereit F1, Brand MD. Biochem J. 1995 Nov 15;312 ( Pt 1):163-7.

## Consumption of ATP

### Muscle Contraction

- Power Stroke
- Calcium Clearance
- Post-Exercise Repair

### Substrate Metabolism

- Blood glucose:
  - Glucose + **2 ATP** → lactate + H<sup>+</sup> + **4 ATP**
  - Glucose + **2 ATP** + O<sub>2</sub> → 6CO<sub>2</sub> + 6H<sub>2</sub>O + **36 ATP**
- Fatty acids: *no structural modification*
  - fatty acid (C16) + **ATP** + 26O<sub>2</sub> → 18CO<sub>2</sub> + 17H<sub>2</sub>O + **129 ATP** *phosphat.*
  - Blood FAs or from intramyocellular triglycerides *gives a lot of ATP.*

## Regeneration of ATP

### Immediate And Anaerobic Pathways

- ATP pool
  - ATP → ADP + Pi *carries out ADP.*
  - ~5 mmol/kg wet muscle
- Immediate:
  - Phosphocreatine – PCr
    - PCr + ADP → Cr + ATP
    - Net reaction: PCr → Cr + Pi *gives new ATP.*
  - ~15 mmol/kg wet muscle
- Anaerobic:
  - Glycolysis
    - Glucose → lactate + H<sup>+</sup> *carries on without O<sub>2</sub>.*

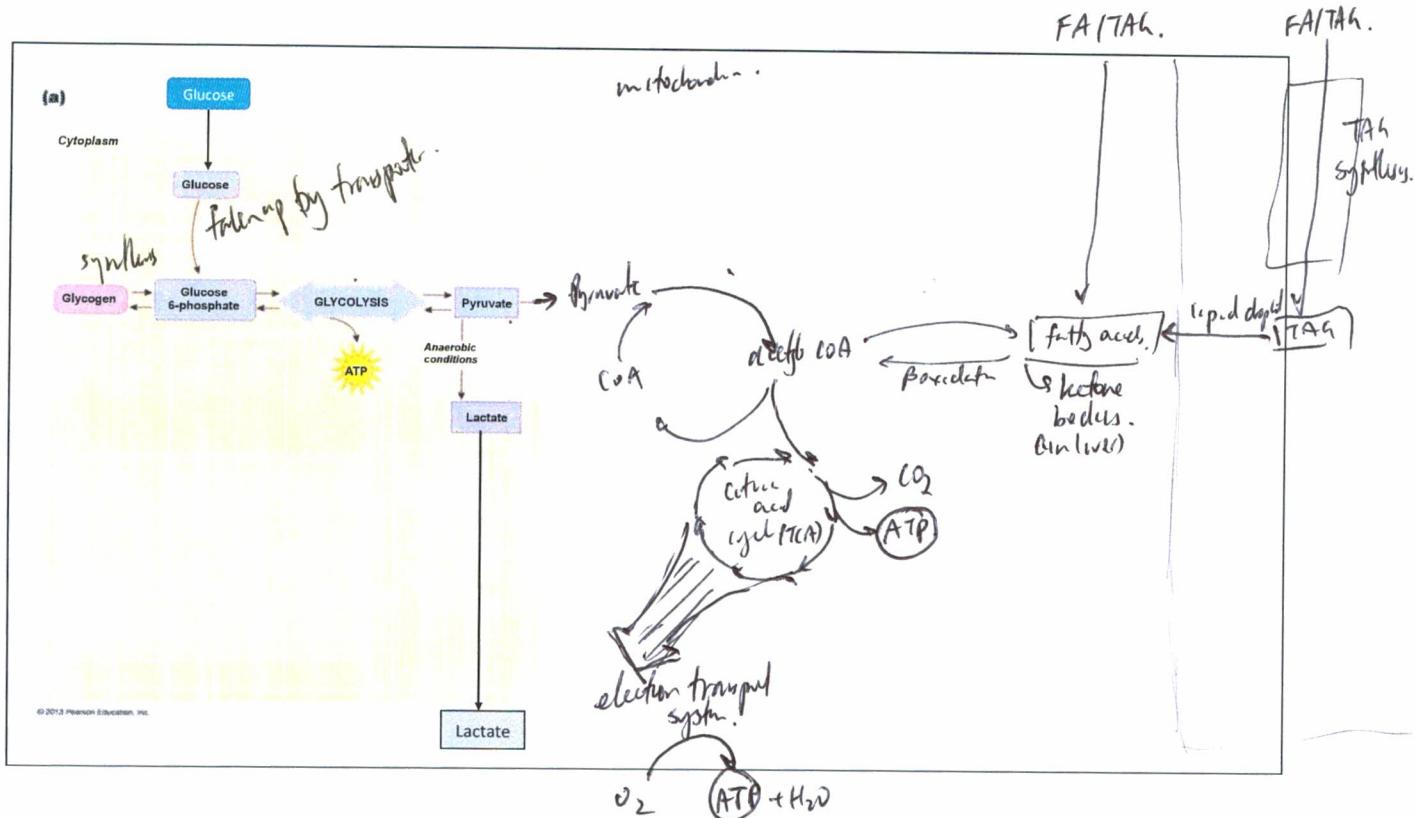
### Aerobic Pathways

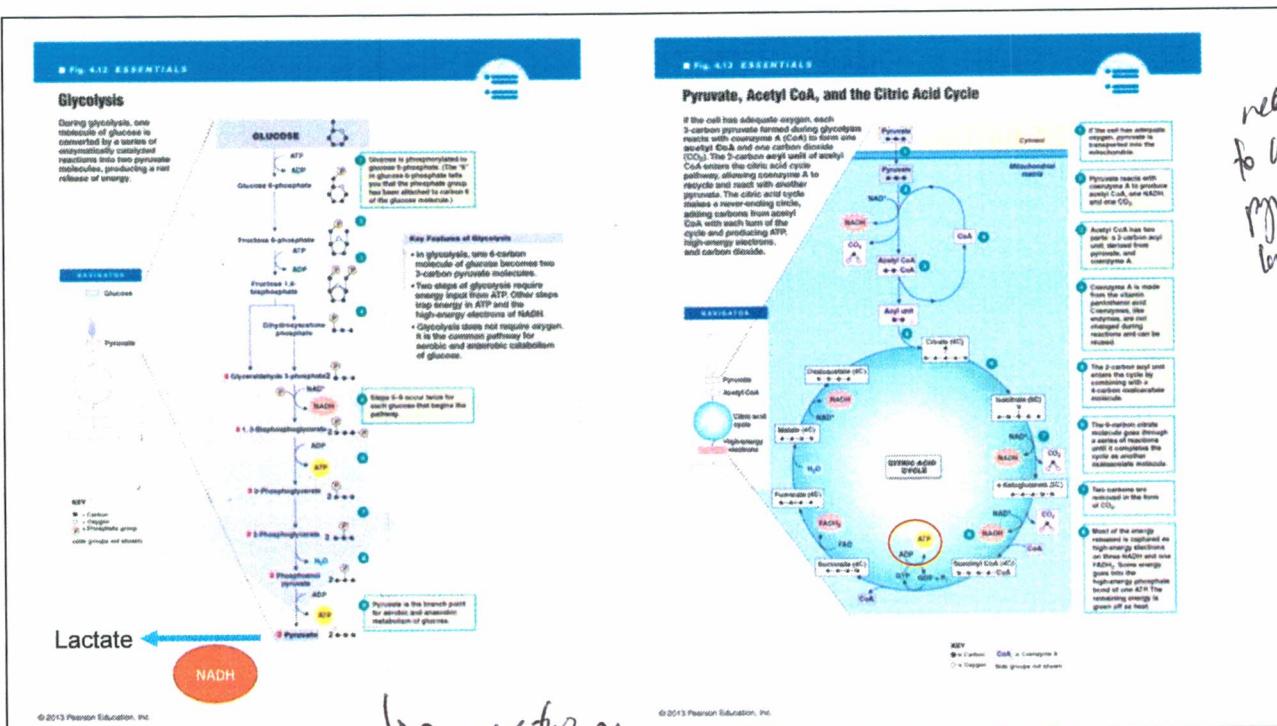
- Glucose Oxidation
  - Includes glycolysis + TCA cycle + ETC
  - Glucose + 6O<sub>2</sub> → 6CO<sub>2</sub> + 6H<sub>2</sub>O
- FA Oxidation
  - Fatty acid (C16) + 26O<sub>2</sub> → 18CO<sub>2</sub> + 17H<sub>2</sub>O

*pyruvate enters cycle*

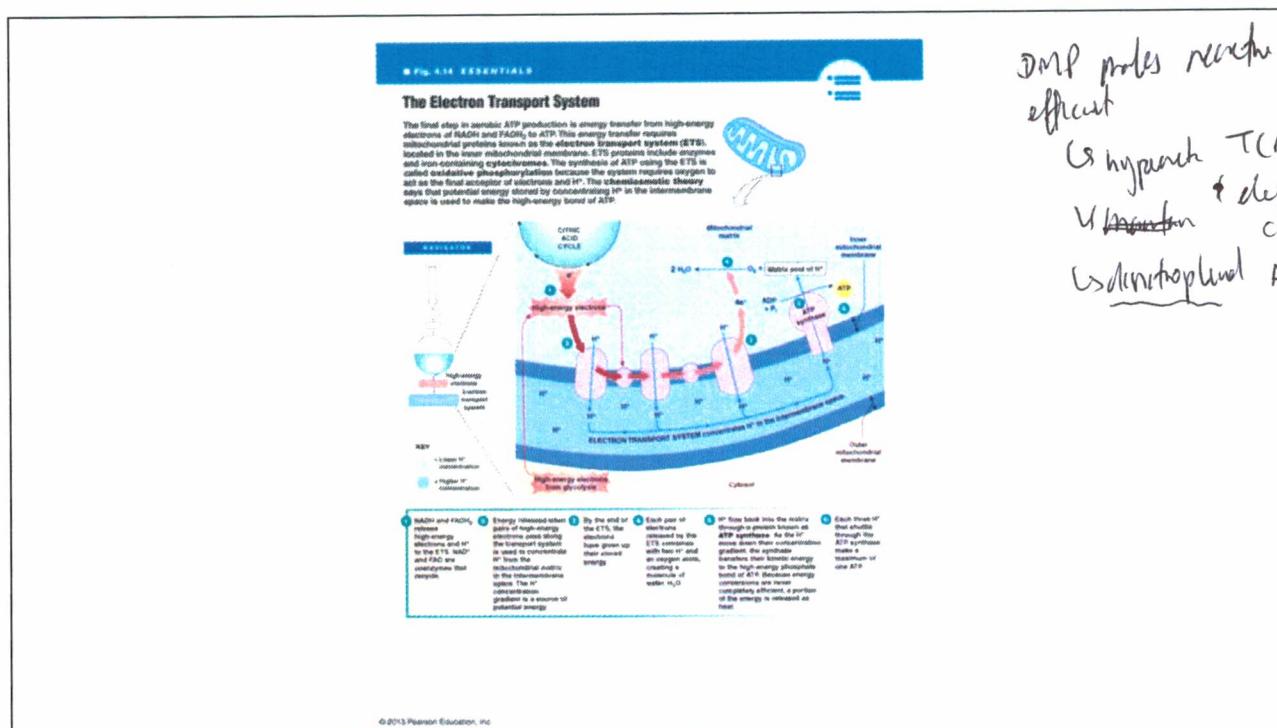
## Net ATP Production

Reaction	ATP change per glucose
Anaerobic glycolysis	2
Aerobic glycolysis + oxidation	36
Reaction	ATP change per palmitate (C16:0)
Fatty acid/ $\beta$ -oxidation	17 per cycle
8 cycle – 2 ATP (C16:0 to C16:0-CoA)	129





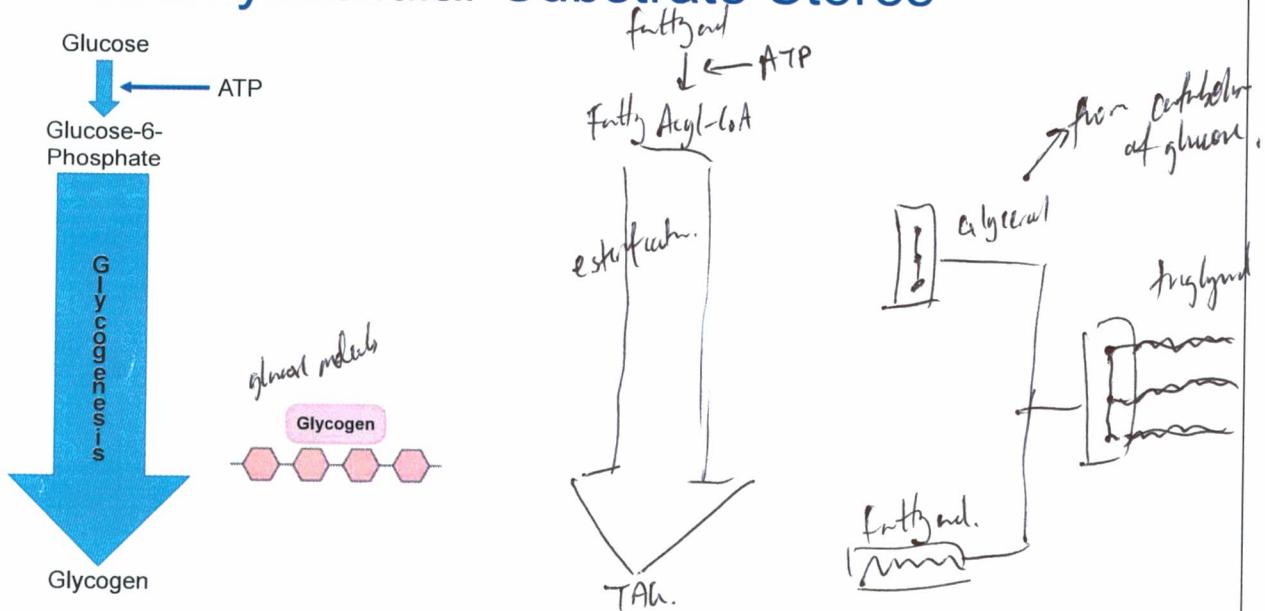
↳ 2 x reductors as  
glucon → 2 Pyruvate



DMP probes reaction  
effluent

- (S) hyperach TCA cycle
- ~~U~~ ~~transport~~ & electron transport chain
- (S) denitrification ATPase high

## Intramyocellular Substrate Stores



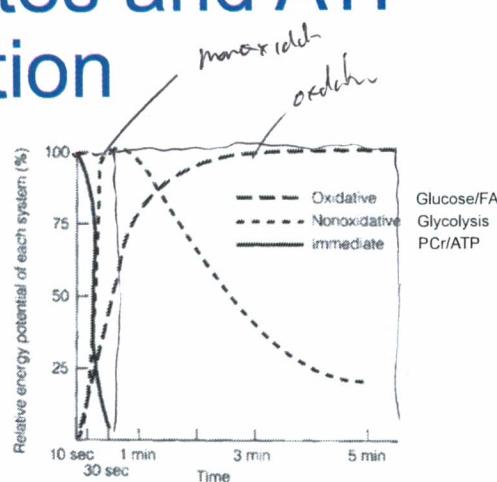
## Aerobic vs Anaerobic Metabolism

# Definitions

- **Aerobic:** is physical exercise of low to high intensity that depends primarily on the aerobic energy-generating process. Aerobic literally means "relating to, involving, or requiring free oxygen", and refers to the use of oxygen to adequately meet energy demands during exercise via aerobic metabolism. *Oxidative metabolism uses oxygen.*
- **Anaerobic:** A form of exercise involving highly intense activities that triggers anaerobic metabolism, especially when the aerobic pathways become insufficient in supplying energy at the required rate.  
*in which so great,*

# Substrates and ATP Generation

Changes over

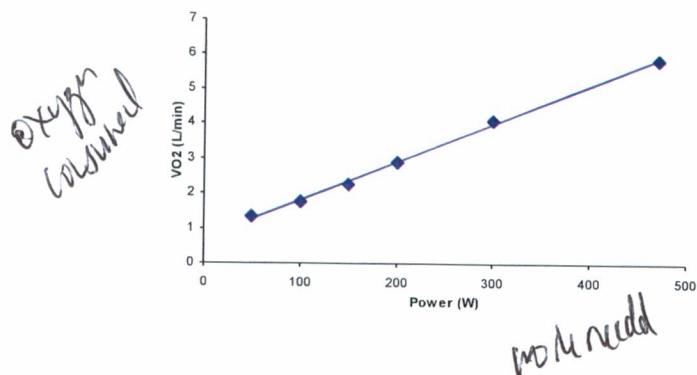


**Figure 3-1** Energy sources for muscle as a function of activity duration. Schematic presentation showing how long each of the major energy systems can endure in supporting all-out work. SOURCE: Edington and Edgerton, 1976. Used with permission.

[http://www.ncbi.nlm.nih.gov/courses/ans304/public\\_html/section1/Metabolism.htm#box](http://www.ncbi.nlm.nih.gov/courses/ans304/public_html/section1/Metabolism.htm#box)

# Substrates and ATP Generation

Changes with intensity - Aerobic



## Exercise Studies

They aren't all the same....frustratingly



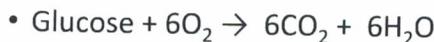
No types of exercise are similar due to different intensities.

- Work Rate (%  $\dot{V}O_2$  Max/Peak)
- Duration
- Type of exercise

# Substrates and ATP Generation

## Changes over time

- Glucose Oxidation



- FA Oxidation

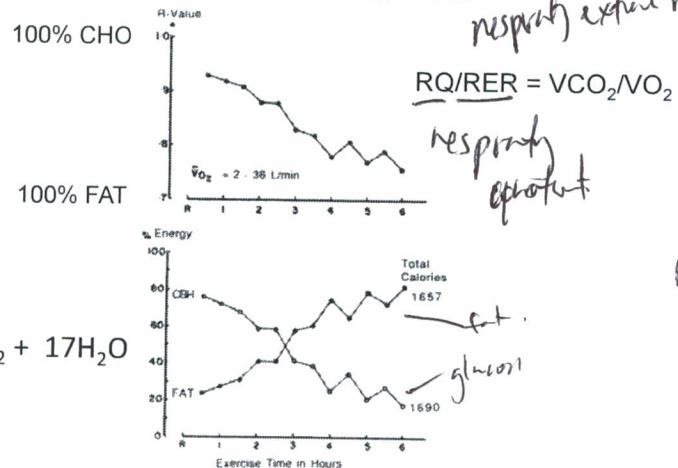


FIG 1. The reduction in respiratory-exchange ratio (R-value) is illustrated in an experiment where the subject exercised at an oxygen uptake of 2.4 l/min for 6 h. The contribution of carbohydrate (CHO) and fat was also calculated (from ref 5; 1 kcal = 4.2 kJ).

© 1984 by the American Physiological Society [Volume 143, Number 4]

# Substrates and ATP Generation

## Changes over time

TABLE III  
Arterial Concentrations of Glucose, Lactate, Pyruvate, Glycerol, Insulin, and Glucagon at Rest and During Prolonged Exercise\*

	Rest‡	Exercise			
		40 min	90 min	180 min	240 min
Glucose, mmol/liter	4.51 ± 0.13	4.57 ± 0.15	4.30 ± 0.15	3.53 ± 0.19	3.12 ± 0.29
Lactate, mmol/liter	1.06 ± 0.13	1.31 ± 0.11	1.32 ± 0.09	1.38 ± 0.13	1.80 ± 0.28
Pyruvate, mmol/liter	0.068 ± 0.006	0.087 ± 0.008	0.091 ± 0.009	0.092 ± 0.010	0.109 ± 0.012
Glycerol, mmol/liter	0.04 ± 0.01	0.19 ± 0.03	0.25 ± 0.03	0.39 ± 0.04	0.48 ± 0.05
FFA, mmol/liter	0.66 ± 0.06	0.78 ± 0.07	0.93 ± 0.12	1.57 ± 0.15	1.83 ± 0.18
Glucagon, pg/ml	75 ± 15	76 ± 16	99 ± 17	201 ± 67	408 ± 103
Insulin, µU/ml	13.9 ± 1.9	12.3 ± 1.6	10.0 ± 1.4	7.2 ± 1.9	6.2 ± 1.4

\* Data presented as mean ± SEM.

† Data for the resting state represent the mean of two to three observations at 5- to 10-min intervals in each subject.

resting steady state  
increases, not concurrent, increases to fat fuel.  
significant increase.  
significant change due to changes in glucose levels.

# Substrates and ATP Generation

## Changes over time

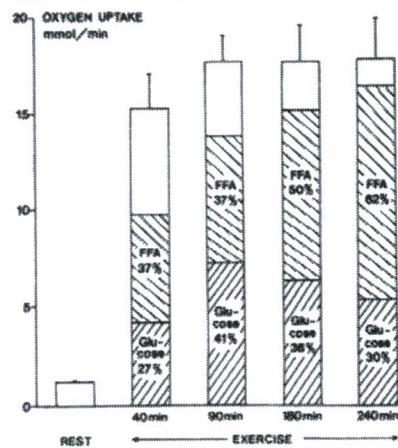


FIGURE 3 Leg uptake of oxygen and substrates in the basal state and during exercise. The height of the bars represents the mean ( $\pm$ SEM) oxygen uptake. The cross-hatched areas indicate FFA and glucose uptake expressed in oxygen equivalents. The percent values represent the proportion of total oxygen uptake contributed by oxidation of these substrates.

Audiberg et al. J Clin Invest 1994

# Substrates and ATP Generation

## Changes over intensity – skeletal muscle substrate pool contribution

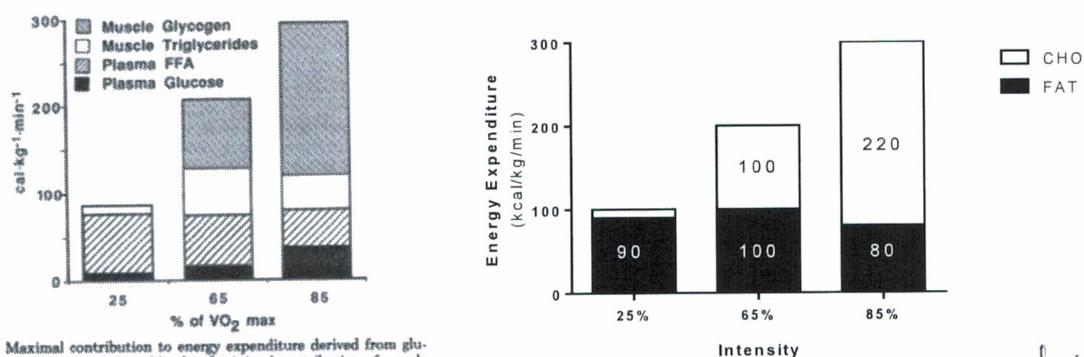


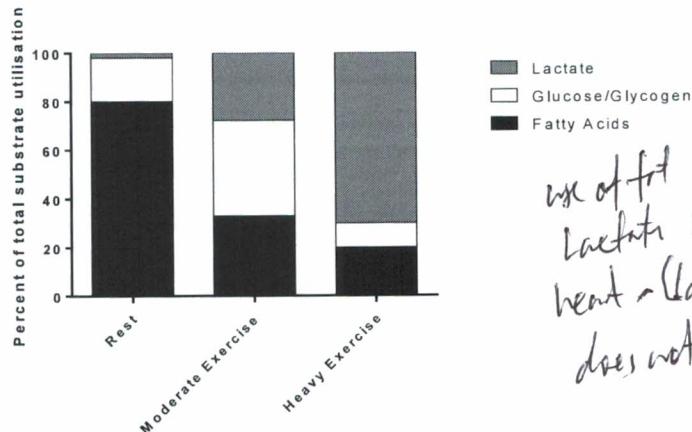
Fig. 8. Maximal contribution to energy expenditure derived from glucose and FFA taken up from blood and minimal contribution of muscle triglyceride and glycogen stores after 30 min of exercise, expressed as function of exercise intensity. Total amount of calories (cal) available from plasma does not change in relation to exercise intensity.

Romijn et al. AJP-Endo 1990

- low energy rate, most fat contribute to energy -

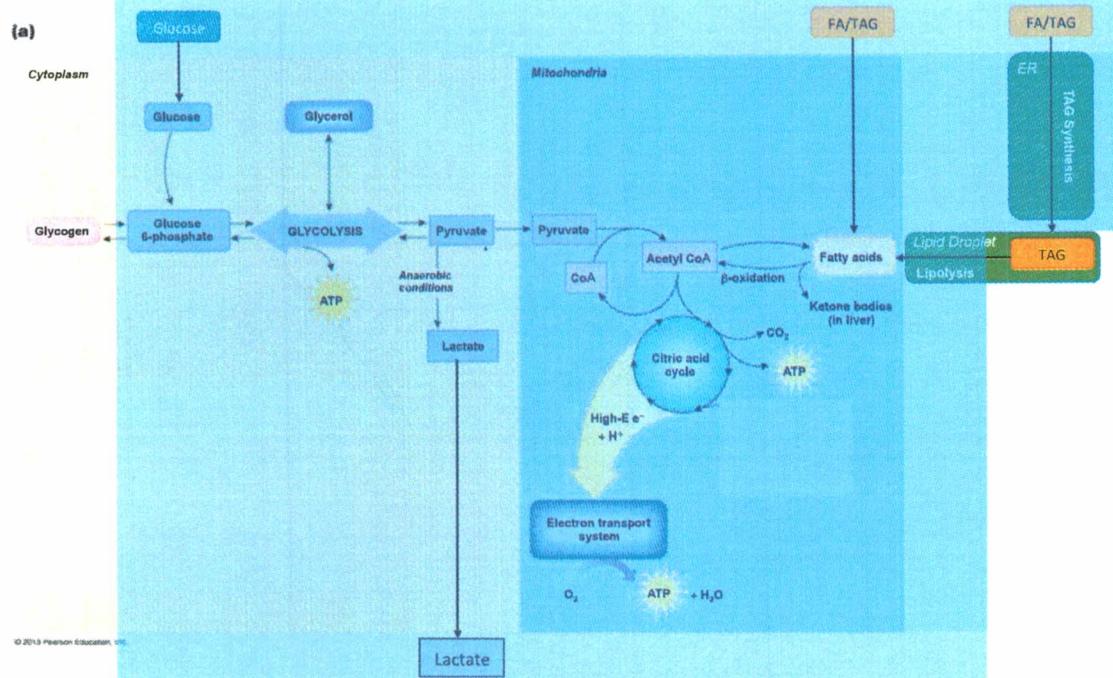
# Substrates and ATP Generation

Changes over intensity – heart substrate pool selection



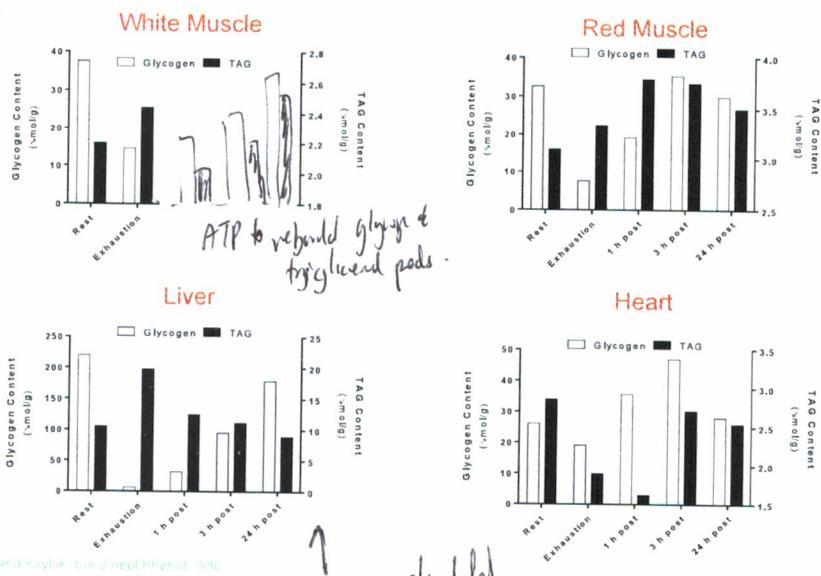
use of fat decreases  
Lactate raised by the  
heart + (lactate) in blood  
does not increase.

McArdle, Katch and Katch, Exercise Physiology: Energy, Nutrition and Human Performance, 4. Ed



## Effect of Treadmill Running on Substrate Levels in Rats

post run  
half used to oxidise  
carbohydrates to ATP pool  
so glycogen pool can be reduced.



Corsko and Kaylie, Eur J Appl Physiol, 1990

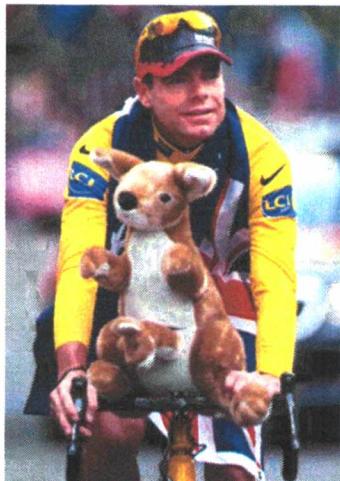
post recovery  
downward

lipid pool (TAG)  
reduced post exhaustion -  
vs frank glycogen recovery.

## Next Time

- The delivery of oxygen to working muscle
- The role that the nervous system plays in:
  - the control of the cardiovascular system
  - mobilising stored substrates during aerobic exercise
- The role of oxygen delivery in the development of fatigue

## Lecture 2 - Aerobic Exercise



Dr Andrew Hoy

Lipid Metabolism Laboratory  
Discipline of Physiology  
Charles Perkins Centre

Ph: 9351 2514  
[andrew.hoy@sydney.edu.au](mailto:andrew.hoy@sydney.edu.au)

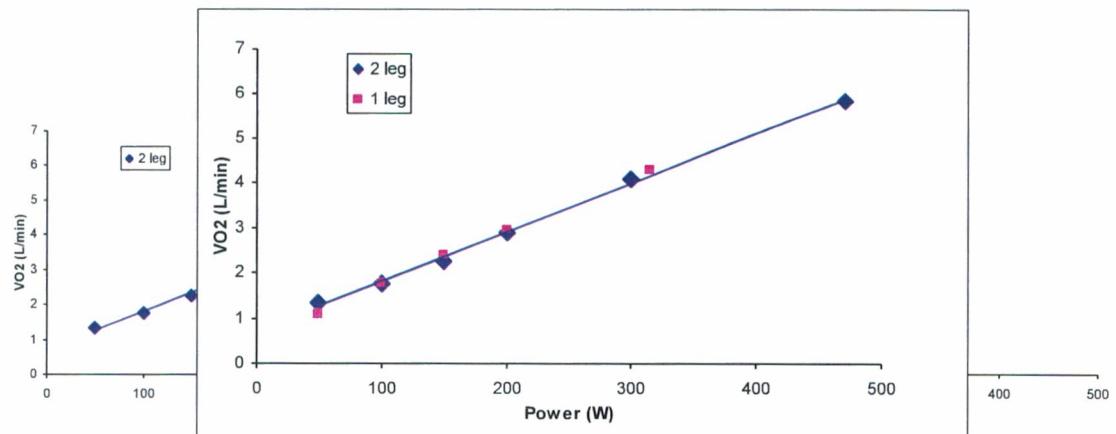


## Learning Objectives



- The delivery of oxygen to working muscle involves 5 steps.
- The role that the nervous system plays in mobilising stored substrates during aerobic exercise.
- That oxygen delivery is thought to be a cause of fatigue and why this might be, or not be, the case.

## Muscle Mass- $\text{VO}_2$



2 leg even & 1 leg even is same.

## Homeostasis



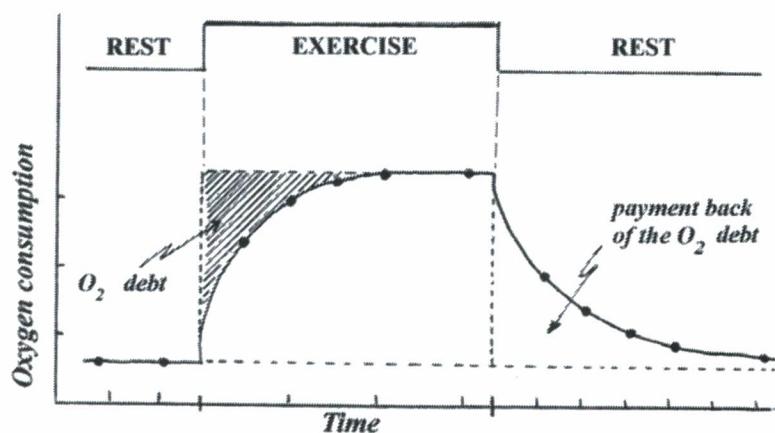
Claude Bernard

- Linear relationship between work-rate and oxygen consumption
- Requires coordination of various systems to support exercise performance.
  - Systems to monitor the internal environment
  - Systems to prevent disruption to normal cellular function – i.e. pathophysiological state

*Homeostasis*

# Getting Oxygen to Working Muscle

## Disruption of Oxygen Balance



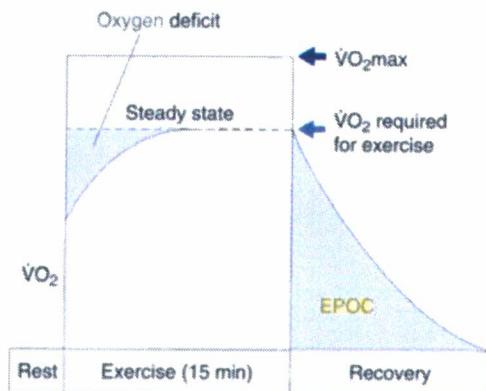
Time to steady state is dependent upon:

- Type of activity
- Intensity

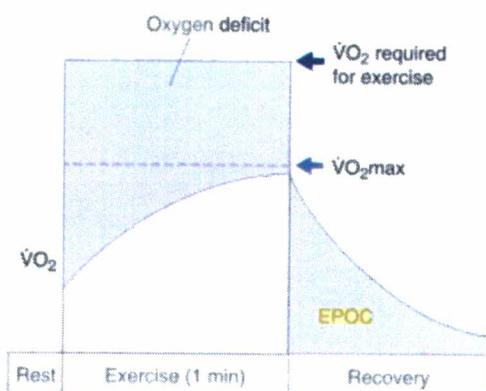
[http://www.medicine.mcgill.ca/physio/resp-web/Fig\\_jpm/FIG1-1.jpg](http://www.medicine.mcgill.ca/physio/resp-web/Fig_jpm/FIG1-1.jpg)

## EPOC - Excess post-exercise oxygen consumption

Low-intensity, steady-state exercise



High-intensity, non-steady-state

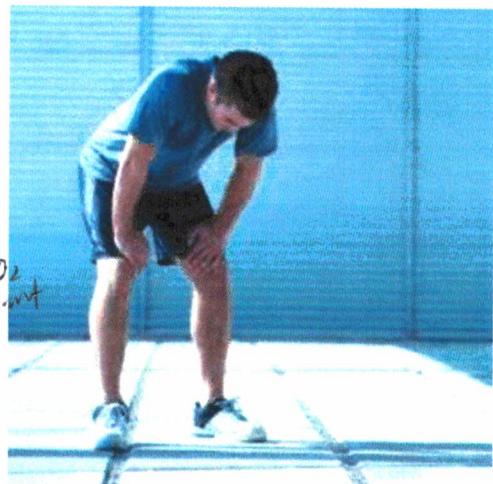


EPOC – PCr replenishment, lactate metabolism, HR recovery, plus other processes

<http://archive.yeahmanh.com.s97240.gridserver.com/wp-content/uploads/2009/05/nsca-epoc.jpg>

## The 5 Steps

1. Ventilation, *into lungs*
2. Diffusion, *across lung*
3. Transport of  $O_2$  to the tissues,
4. Increased blood flow, *↑ rate of delivery* *↑  $O_2$  content*
5. Uptake of  $O_2$  by muscle cells

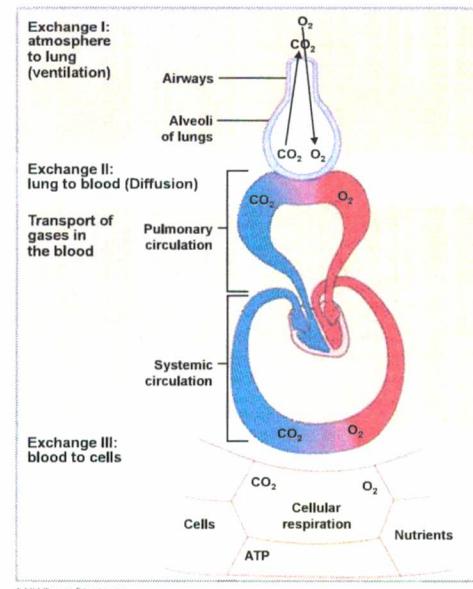


<http://www.adamwakefieldpt.com/wp-content/uploads/2013/01/Post-exercise-exhaustion.jpg>

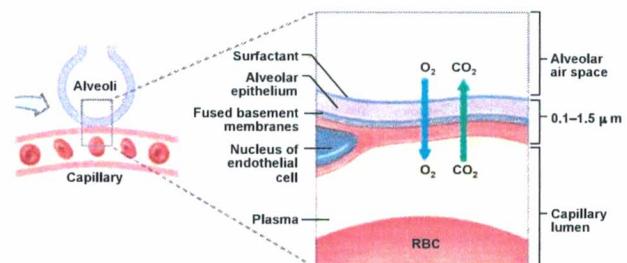
- 1. Ventilation,**
2. Diffusion,
3. Transport of O<sub>2</sub> to the tissues,
4. Increased blood flow,
5. Uptake of O<sub>2</sub> by muscle cells

#### EXTERNAL RESPIRATION

The respiratory and circulatory systems coordinate to move oxygen and CO<sub>2</sub> between the atmosphere and the cells.



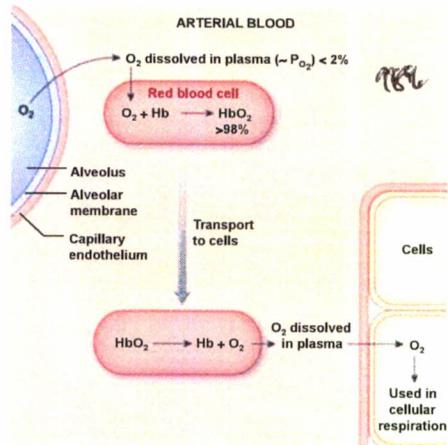
1. Ventilation,
- 2. Diffusion,**
3. Transport of O<sub>2</sub> to the tissues,
4. Increased blood flow,
5. Uptake of O<sub>2</sub> by muscle cells



1. Ventilation,
2. Diffusion,
- 3. Transport of O<sub>2</sub> to the tissues,**
4. Increased blood flow,
5. Uptake of O<sub>2</sub> by muscle cells

#### OXYGEN TRANSPORT

More than 98% of the oxygen in blood is bound to hemoglobin in red blood cells, and less than 2% is dissolved in plasma.



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1. Ventilation,
2. Diffusion,
3. Transport of O<sub>2</sub> to the tissues,
- 4. Increased blood flow,**
5. Uptake of O<sub>2</sub> by muscle cells

*Martin adapt, delte or*

#### CARDIAC OUTPUT DURING VIGOROUS EXERCISE 25.6 L/MIN

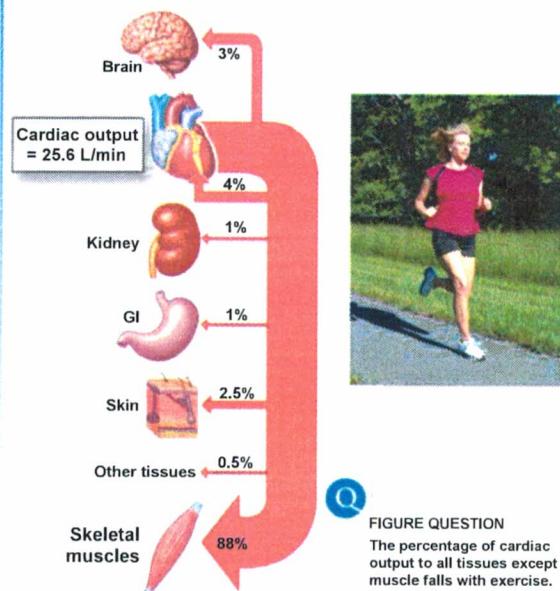
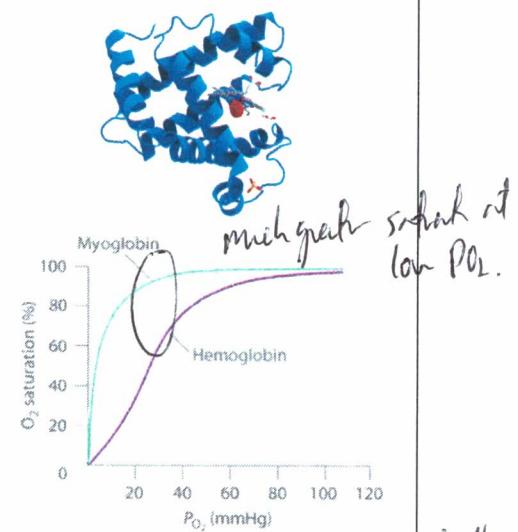
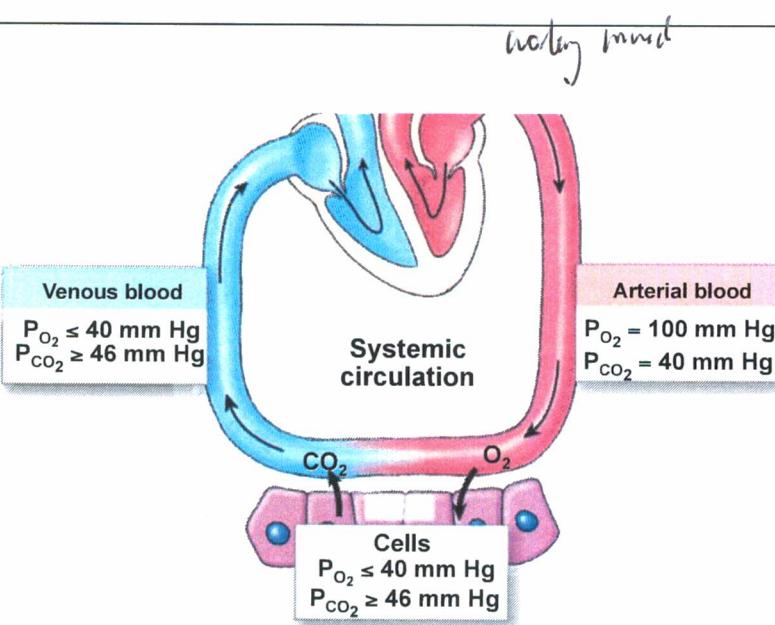
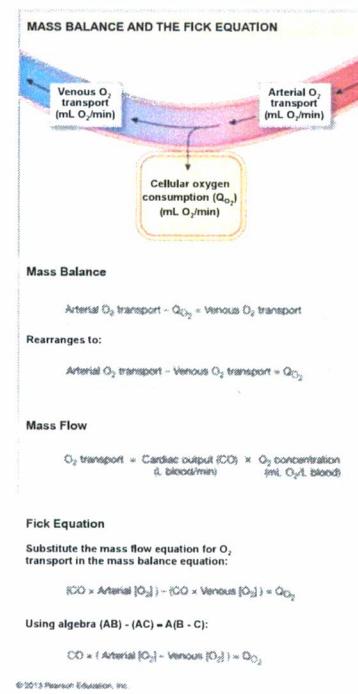


FIGURE QUESTION  
The percentage of cardiac output to all tissues except muscle falls with exercise. In which tissues does actual blood flow decrease?

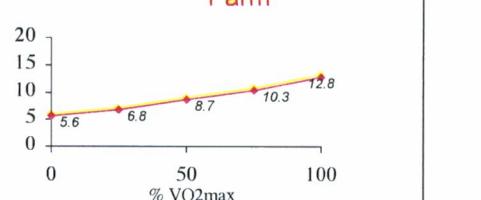
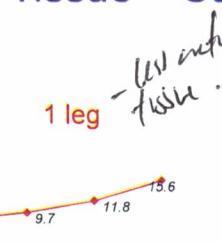
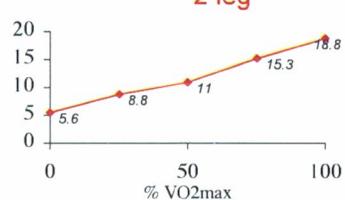
1. Ventilation,
2. Diffusion,
3. Transport of  $O_2$  to the tissues,
4. Increased blood flow,
- 5. Uptake of  $O_2$  by muscle cells**



myoglobin attracts  $O_2$   
at lower pressures than hemoglobin  
(@)

# Central Control of Cardiovascular System to Support Exercise Performance

## Cardiovascular Response: Work Rate and Mass of Active Tissue – Cardiac Output



Lewis et al 1983, p1314-

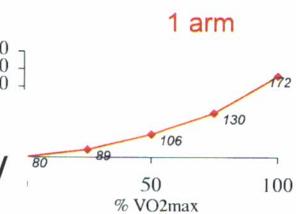
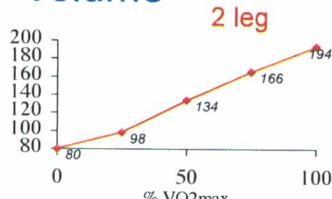
$$\text{Cardiac Output (Q)} = \text{SV} \times \text{HR}$$

$\text{VO}_{2\text{max}}$  - point of oxygen consumption until fatigue.

does depend on  $\text{VO}_{2\text{max}}$

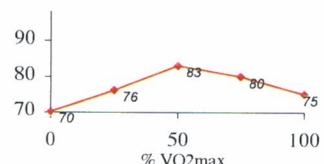
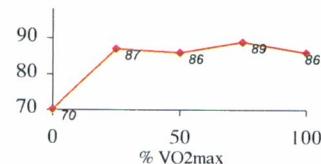
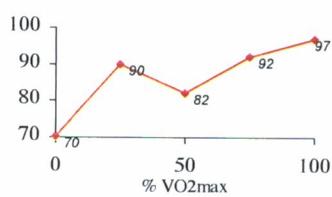
# Cardiovascular Response:

## Work rate and Mass of Active Tissue – Heart Rate & Stroke Volume



### Why does HR increase?

- Withdrawal of PNS activity
- AND
- Increased SNS activity

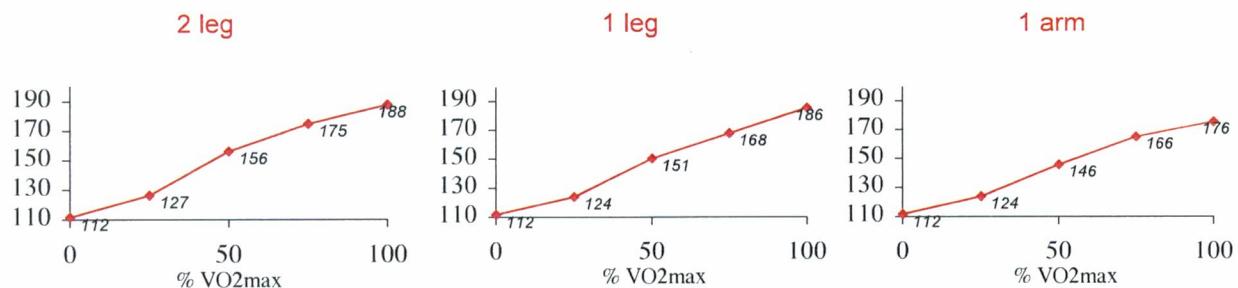


Lewis et al 1983, p1314.

## During near maximal aerobic exercise:

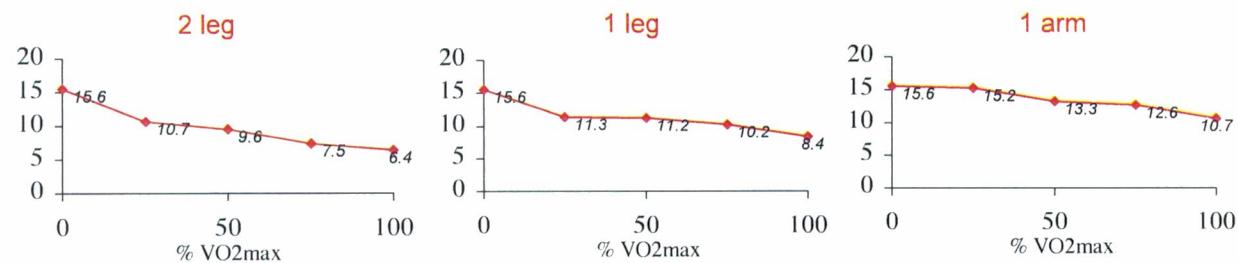
- Cardiac Output reaches maximal levels due to:
  - Near maximal heart rate and,
  - Near maximal stroke volume.

## Cardiovascular Response: Work Rate and Mass of Active Tissue – Systolic Blood Pressure



Lewis et al 1983, p1314-

## Cardiovascular Response: Work Rate and Mass of Active Tissue – Total Peripheral Resistance



Lewis et al 1983, p1314-

# Redistribution of cardiac output during exercise

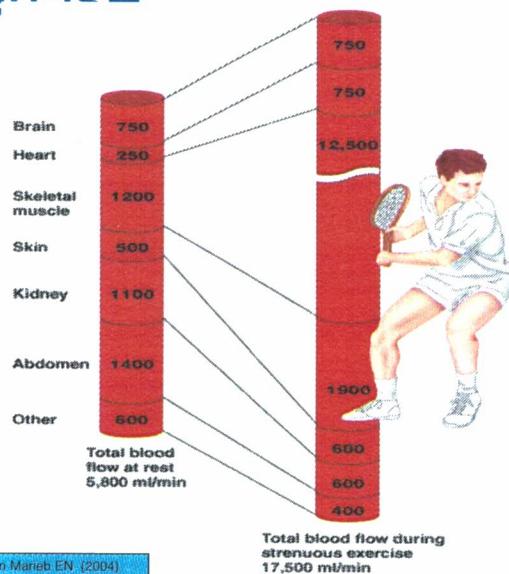
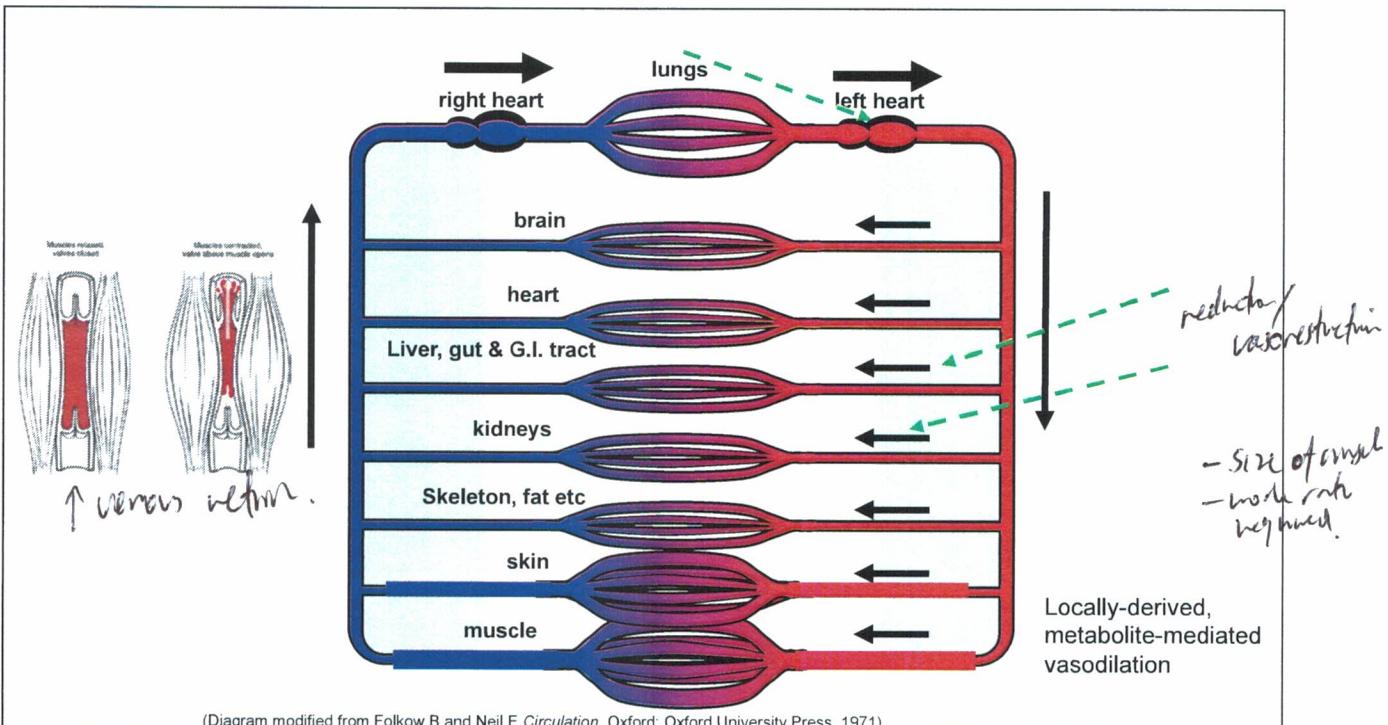


Figure 12-12 in Marieb EN (2004)  
Human Anatomy & Physiology, 6th  
Ed., Pearson Education, San Francisco

## Reasons for blood flow changes:

- Heart and skeletal muscle:** mainly local metabolic factors causing vasodilation
  - In the **heart**, blood flow occurs mainly during ventricular diastole (coronary vessels are compressed during ventricular systole)
- Skin:** mainly decrease in sympathetic vasoconstrictor effects, plus effects of bradykinin in sweat, both causing vasodilation, as part of thermoregulatory reflexes
- Kidney and abdominal viscera:** mainly increase in sympathetic vasoconstrictor activity
- Brain:** no change, because cerebral blood flow mainly affected by local metabolic activity (i.e. neural activity), which does not change as a result of exercise

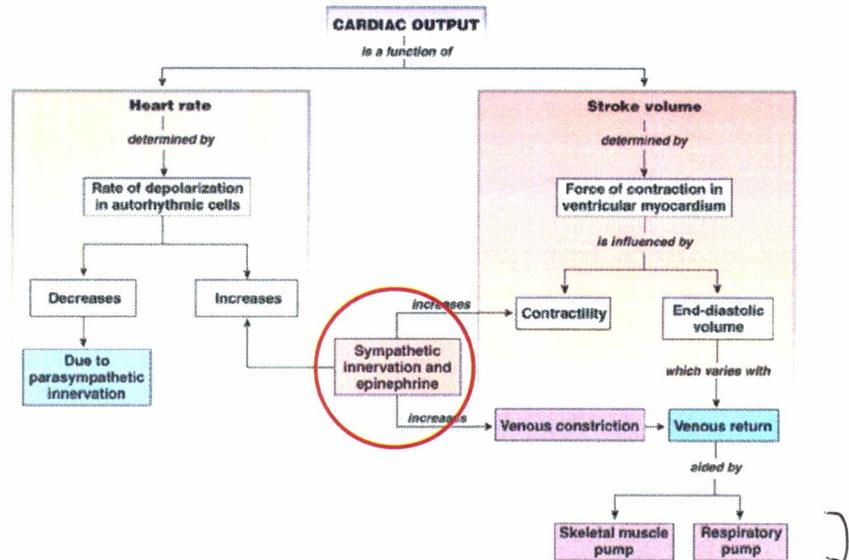


# Mechanisms for control of regional blood flow

- LOCAL CONTROL

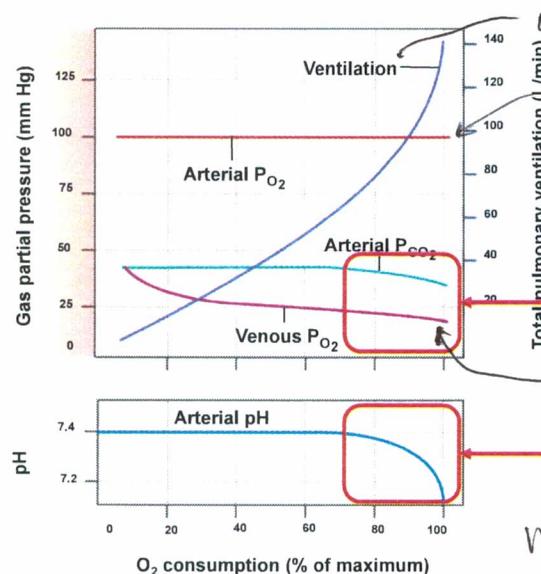
- Autoregulation: constant blood flow with changing pressures (e.g. kidneys, brain, heart)
- Active hyperemia: blood flow is proportional to metabolic activity (e.g. skeletal muscle)
- Reactive hyperemia: increased blood flow in response to a period of decreased blood flow (e.g. Skeletal muscle, cardiac muscle)
- Myogenic hypothesis: when vascular smooth muscle is stretched it contracts
- Metabolic hypothesis: as a result of metabolic activity the tissues produce vasodilator metabolites ( $H^+$ ,  $K^+$ , lactate, adenosine,  $CO_2$ )

both



Copyright © 2007 Pearson Education, Inc., publishing as Benjamin Cummings.

Arterial blood gases and pH remain steady with submaximal exercise.



box depicts normoventilation maintains P<sub>O<sub>2</sub></sub> (normal arterial) and P<sub>CO<sub>2</sub></sub> (normal venous).

Hyperventilation occurs due to more oxygen (muscle oxygenate more).

Lactic Acid Production not much change but used by heart.

→ lactic acid of fatigue → hyperventilation reduces CO<sub>2</sub> which is a buffer, reduces buffering capacity, lactic acidification.

## Central Control during Exercise

Mobilisation of Stored Substrates

## Substrates and ATP Generation

Intramyocellular vs extramyocellular pools

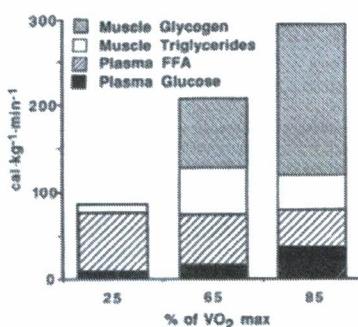
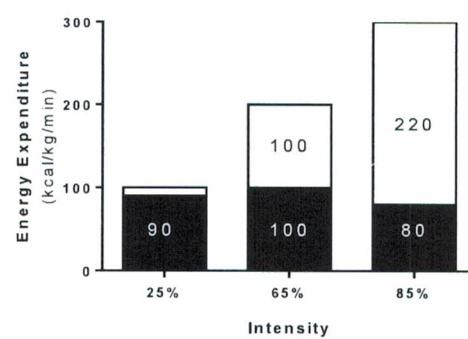


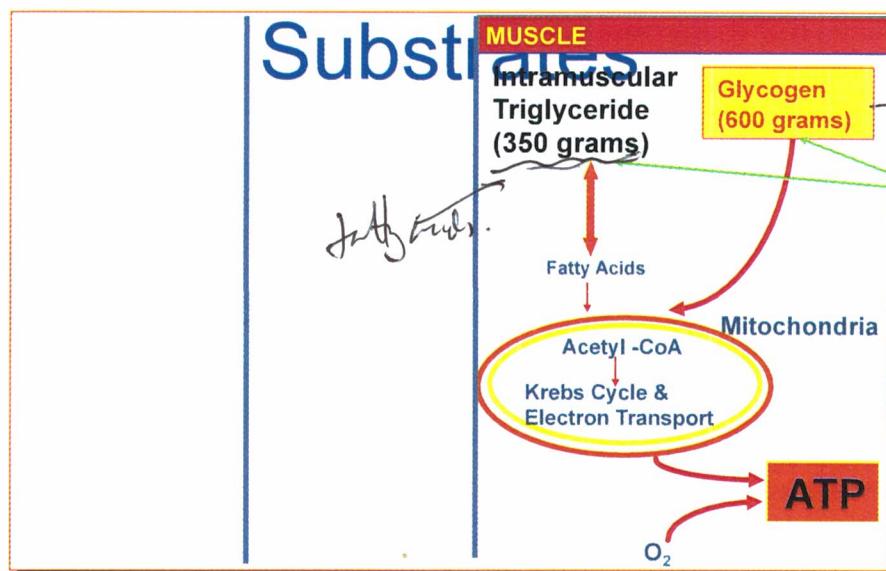
Fig. 8. Maximal contribution to energy expenditure derived from glucose and FFA taken up from blood and minimal contribution of muscle triglyceride and glycogen stores after 30 min of exercise, expressed as function of exercise intensity. Total amount of calories (cal) available from plasma does not change in relation to exercise intensity.

Romijn et al, AJP-Endo 1993



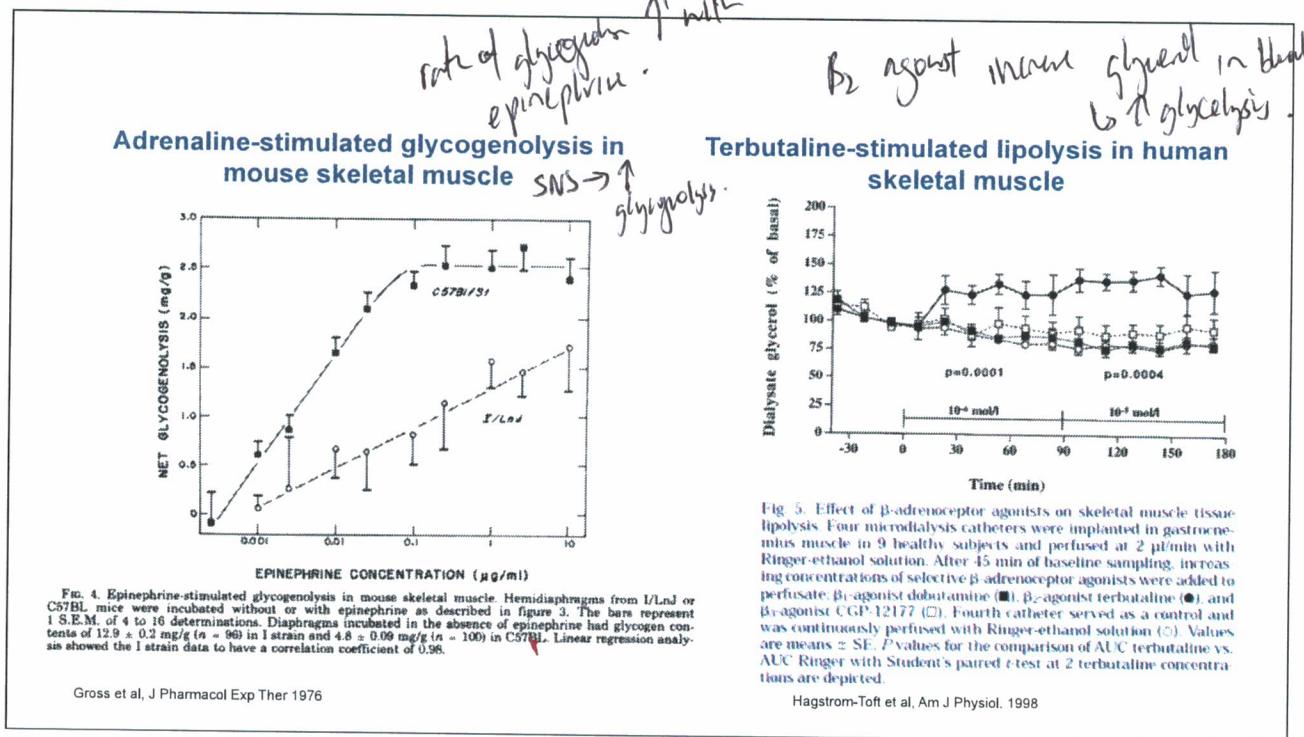
fat is only  
contribution.

## Mobilisation of Stored Substances

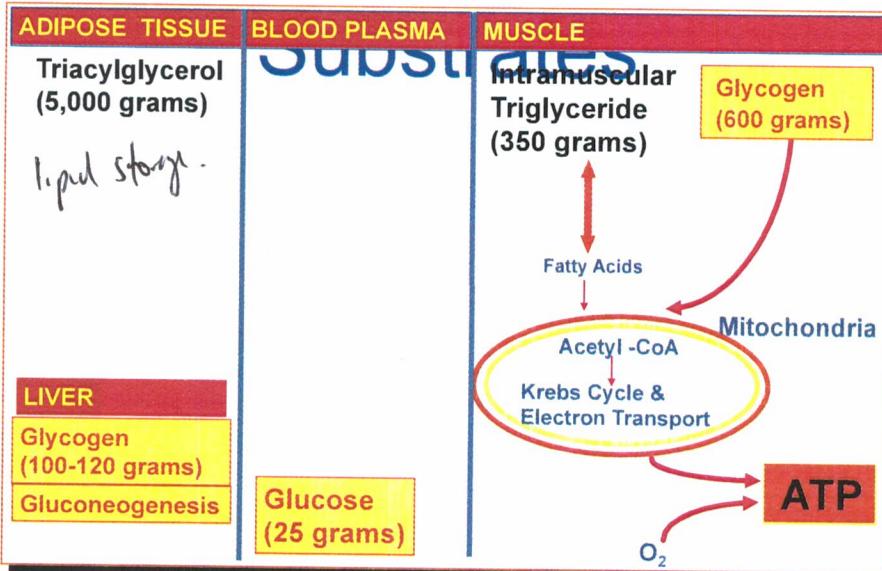


SNS  $\Rightarrow$  lipolysis & glycogenolysis stimulated.

26/05/16



## Mobilisation of Stored Substances



liver works  $\rightarrow$  hepatic glycogen + lactate & make glucose from other sources.

# Substrates and ATP Generation

## Changes over time

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Arterial Concentrations of Glucose, Lactate, Pyruvate, Glycerol, Insulin, and Glucagon  
at Rest and During Prolonged Exercise\*

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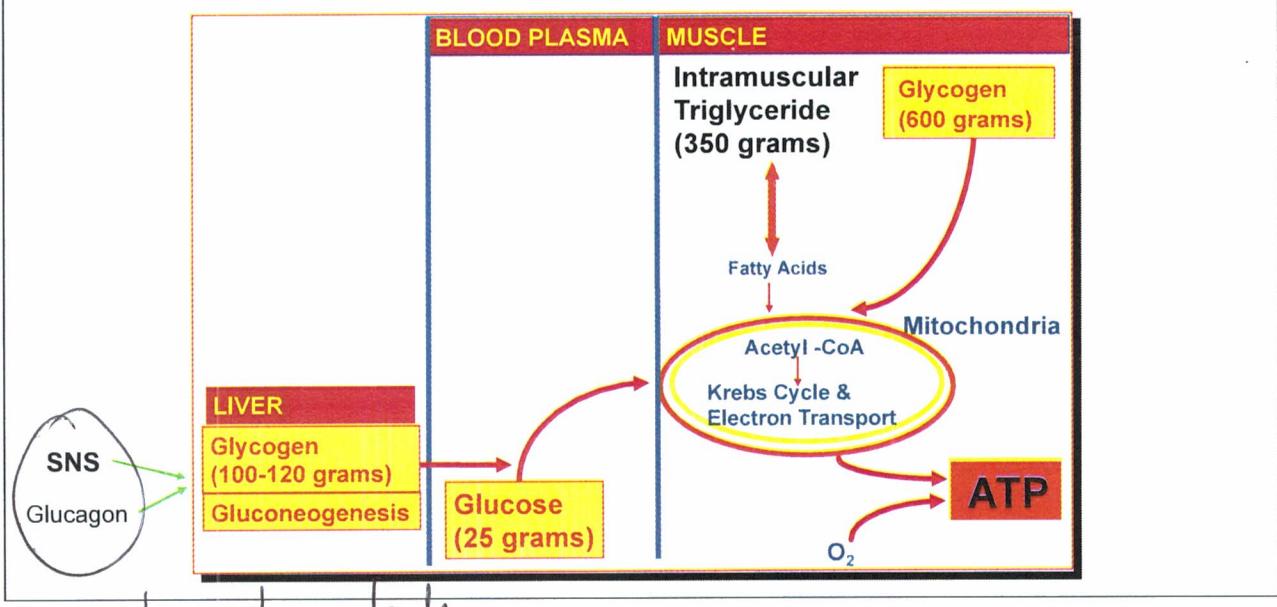
\* Data presented as mean±SEM.

‡ Data for the resting state represent the mean of two to three observations at 5- to 10-min intervals in each subject.

Ahlborg et al, J Clin Invest 1974

glucose levels  
maintained

## Mobilisation of Stored



# Substrates and ATP Generation

## Changes over time

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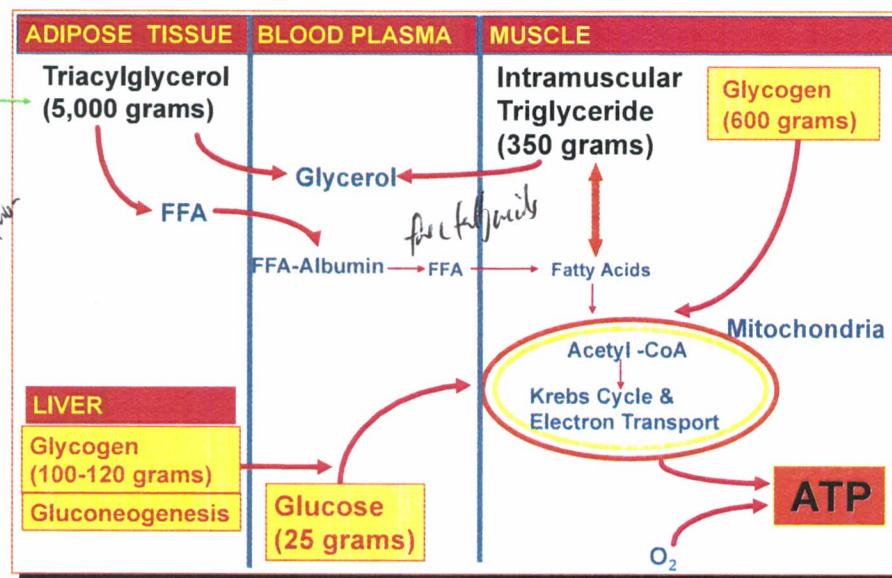
\* Data presented as mean±SEM.

† Data for the resting state represent the mean of two to three observations at 5- to 10-min intervals in each subject.

mean slightly  
due to hypoglycemia

Ahlborg et al, J Clin Invest 1974

## Mobilisation of Stored



# Substrates and ATP Generation

## Changes over time

TABLE III  
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at Rest and During Prolonged Exercise\*

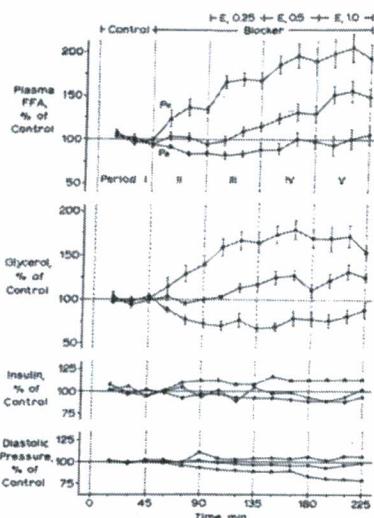
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Lactate, mmol/liter	1.06±0.13	1.31±0.11	1.32±0.09	1.38±0.13	1.80±0.28
Pyruvate, mmol/liter	0.068±0.006	0.087±0.008	0.091±0.009	0.092±0.010	0.109±0.012
Glycerol, mmol/liter	0.04±0.01	0.19±0.03	0.25±0.03	0.39±0.04	0.48±0.05
FFA, mmol/liter	0.66±0.06	0.78±0.07	0.93±0.12	1.57±0.15	1.83±0.18
Glucagon, pg/ml	75±15	76±16	99±17	201±67	408±103
Insulin, µU/ml	13.9±1.9	12.3±1.6	10.0±1.4	7.2±1.9	6.2±1.4

\* Data presented as mean±SEM.

‡ Data for the resting state represent the mean of two to three observations at 5- to 10-min intervals in each subject.

Significant increase  
6 vertice.

Ahlborg et al, J Clin Invest 1974



Epinephrine + phentolamine ( $\alpha$ -inhibitor)

Epinephrine alone  $\uparrow$  plasma FFA. (not due insulin).

Epinephrine + propranolol ( $\beta$ -inhibitor)

( $\beta$  block lipolysis)

FIGURE 2 The effect of graded quantities of epinephrine (E) alone (closed circles), epinephrine plus propranolol (Pr, diamonds, 0.08 mg/min) and epinephrine plus phentolamine (Ph, triangles, 0.05 mg/min) on the plasma-free fatty acids (FFA), glycerol, insulin and diastolic blood pressure of 10 normal subjects. Each point is the mean of 10 values; the horizontal lines above and below the points are the standard errors of the means.

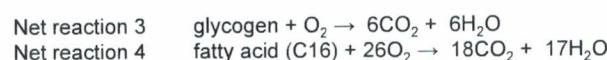
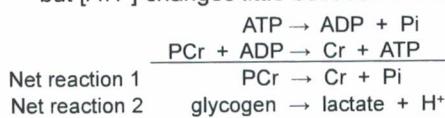
Burn et al, J Clin Invest 1974

# Potential Sources of Fatigue #1

$\uparrow$  Symp. Nerv. activity.  
 $\hookrightarrow$   $\uparrow$  Blood flow &  $O_2$  delivery  
 $\hookrightarrow$  fatigue & glucose level.

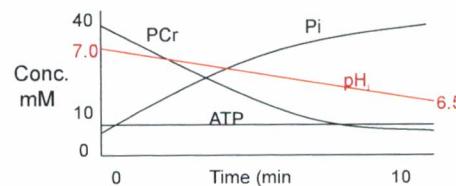
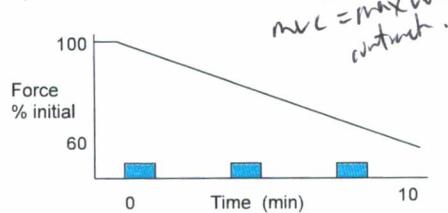
## Metabolic changes during fatigue

Fatigue occurs when ATP breakdown exceeds ATP resynthesis  
but [ATP] changes little because of PCr breakdown



Initial contrib - phosphocreatine  
 over time - glucose  $\rightarrow$  lactate  
 ATP

Data from humans performing intermittent maximal voluntary contractions (3 15s MVCs) under ischaemic conditions (first dorsal interosseous muscle).

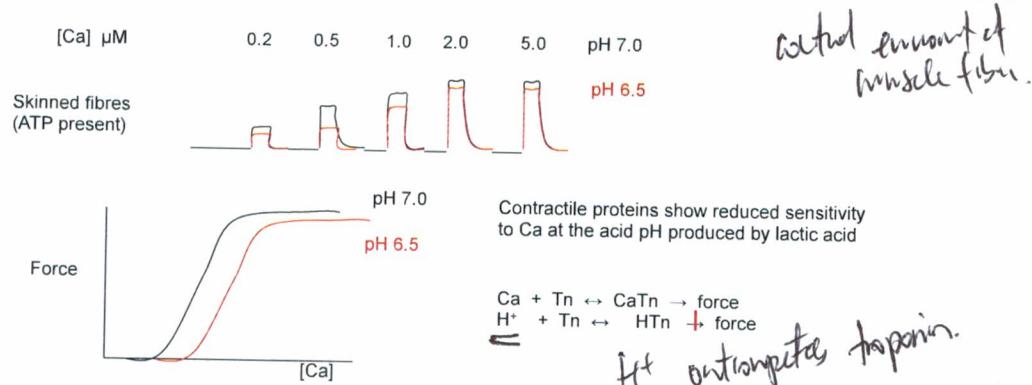


So, PCr, Pi & H are candidates for causing fatigue

PCr decreases  $\downarrow$   
 fatigue,  
 ATP don't change.  
 Pi reduced.

## Lactic acid theory of muscle fatigue

To test whether measured degree of intracellular acidosis can explain fatigue by means of effects on myofibrillar proteins, test with skinned fibres.

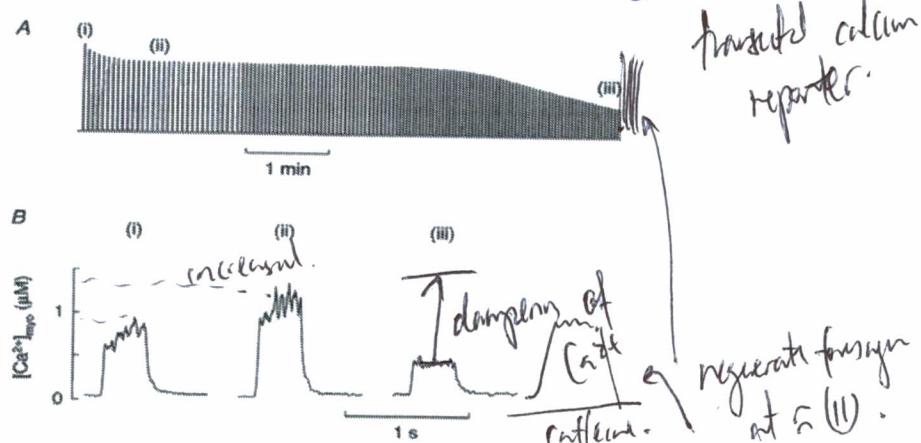


### Problems with lactic acid theory

1. Fatigue often occurs without acidosis; muscles have an active lactate transporter
2. Skinned fibre experiments shown above usually done at room temp. When repeated at 37 °C acidosis has only a very small effect
3. If intact fibres at 37 °C are made acid, the force does not fall

*lactate near muscle membrane  $\Rightarrow$  intracellular pH does not change*

## Failure of calcium release causes fatigue



Conclusion. Caffeine increases Ca release and overcomes final phase of fatigue.  
Final phase of this type of fatigue is caused by failure of Ca release from SR

## Next Time

- The contribution of diet/nutritional alterations to prevent fatigue.
- The adaptations in the cardiovascular system and metabolic pathways in skeletal muscle to aerobic exercise training.

## Lecture 3 - Cardiovascular and Metabolic Adaptations to Exercise Training and review



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## Learning Objectives



- The contribution of diet/nutritional alterations to prevent fatigue.
- The adaptations in the cardiovascular system and metabolic pathways in skeletal muscle to aerobic exercise training.

## Potential Sources of Fatigue #2

Role of Diet



### Nutritional factors causing 'fatigue' during exercise

#### Considerations

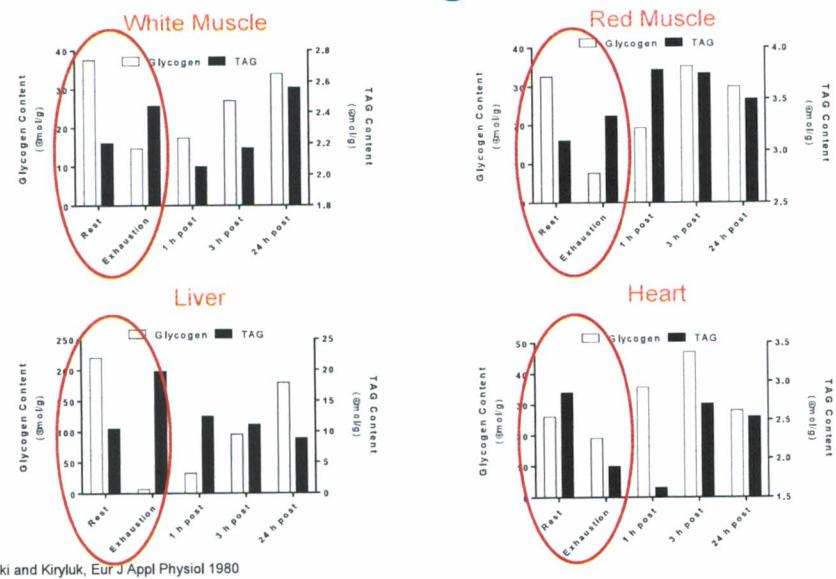
- Duration and intensity of the event.
- The environmental conditions (temp, humidity).
- Fitness of the individual (acclimatisation).

#### Metabolic Causes

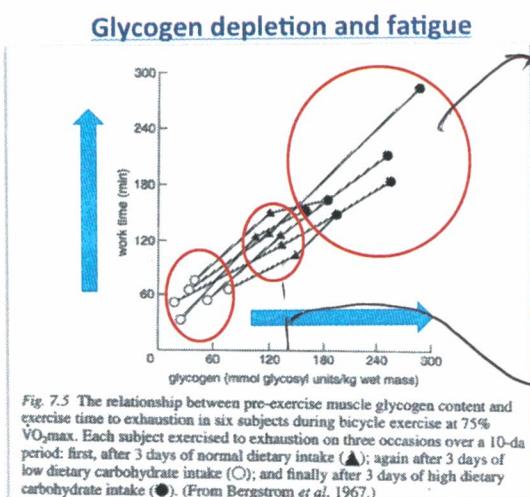
- Muscle glycogen depletion.
- Low blood sugar (CNS fatigue).
- Dehydration.
- Hyponatraemia (low sodium).
- GI discomfort.

reduces blood supply  
circulation

## Effect of Treadmill Running on Substrate Levels in Rats



## CHO depletion causes fatigue

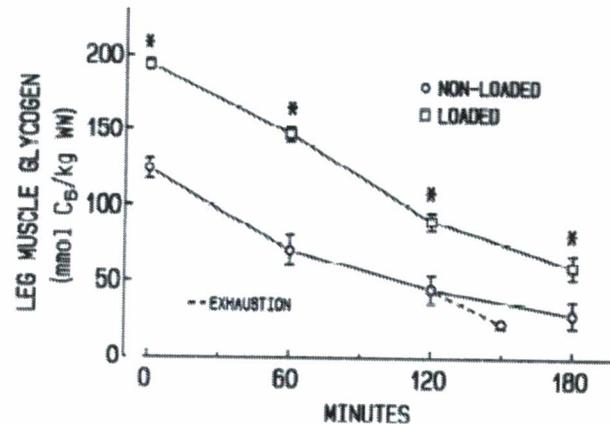


- Increase muscle and liver glycogen stores.
  - Delay the onset of fatigue b/c more to burn.
- modest dietary intake.*
- more glycogen / longer work.*
- higher performance.*
- vs more fuel to burn*

## Effectiveness of CHO Loading for exercise lasting > 90 min

15 male endurance-trained cyclists who rode for 180 min at 70% of maximal O<sub>2</sub> consumption

CHO-load – 600g/day for 3 days with energy intake of both groups being similar but, of course, differed in composition.



Bosch et al. J Appl Physiol. 1993 Apr;74(4):1921-7

glycogen decomp.  
products are  
similar,  
which deploys  
similar.

## Effectiveness of CHO Loading for exercise lasting > 90 min

### Maintenance of blood glucose

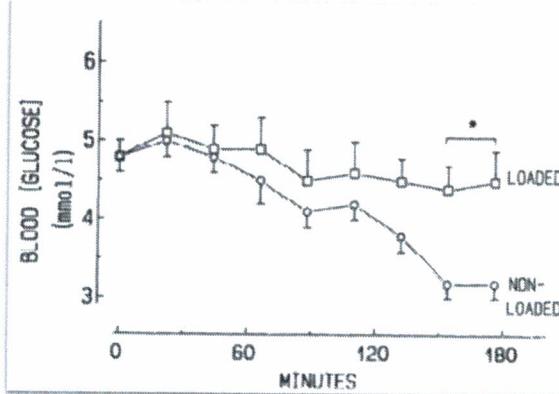
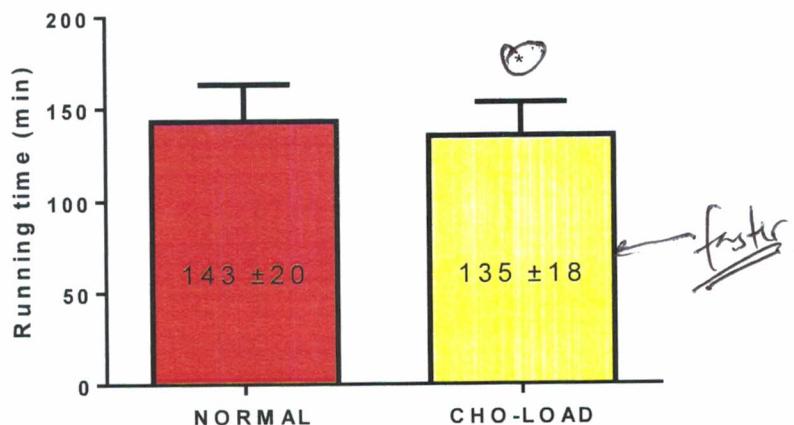


TABLE 1. Characteristics of subjects

	carbohydrate loaded CL	non loaded NL	P (CL vs. NL)
Age, yr	24±3	27±2.5	NS
V <sub>O<sub>2max</sub></sub> , l/min	3.6±0.2	3.7±0.2	NS
Peak work rate, W	315±25	325±20	NS
Mass, kg	73.5±4.0	70.9±4.5	NS
FFM, kg	63.4±3.1	60.7±3.7	NS
%Body fat	13±1.0	14±1.0	NS
Muscle glycogen, mmol/kg wet wt	194±4	124±7	0.001
No. completing 180 min of exercise	7 of 7 180	4 of 8 180* 150*	0.001
Exercise time to exhaustion, min			0.001

Values are means ± SE; n = 7 carbohydrate- (CHO) loaded (CL) and 8 non-CHO-loaded (NL) subjects, except \* n = 4. V<sub>O<sub>2max</sub></sub>, maximal O<sub>2</sub> consumption; FFM, fat-free mass.

## THE EFFECT OF CHO-LOADING ON 30 km RUNNING PERFORMANCE



Karlsson J & B Saltin. *J. Appl. Physiol.* 31: 203-206, 1971.

### In Summary

In prolonged activities, usually – unless at very high intensity and duration – the following occurs:

- Whole body stores of lipids are NOT substantially depleted
  - Actually, the resulting levels may be slightly increased due to increased flux
- Intramyocellular [ATP] does not alter substantially
- Blood glucose does NOT fall substantially
  - Can associate with fatigue
- Muscle and liver glycogen stores are substantially depleted
  - Increasing the starting amount can improve exercise performance for events lasting >90 mins

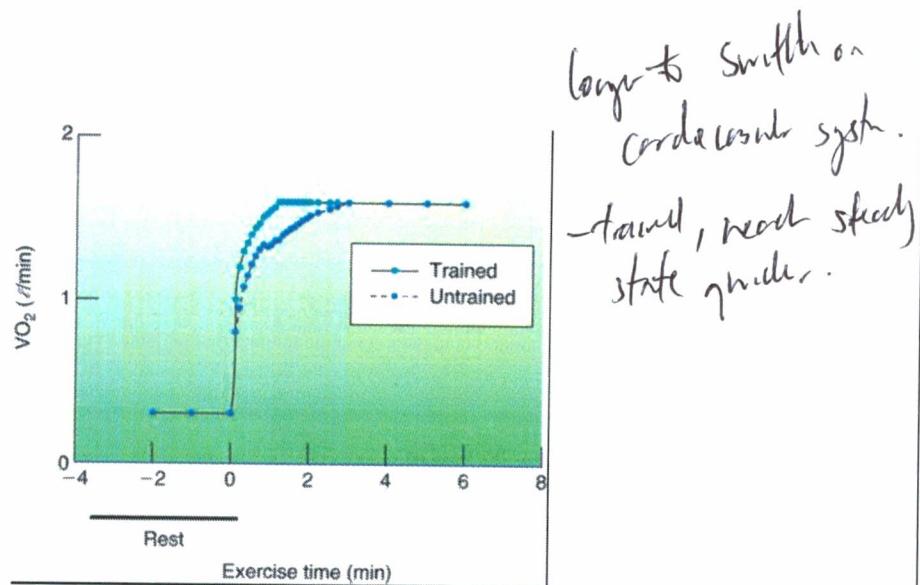
enhance performance, delay fatigue  
by diet.

shorter exercise period,  
no fatigue effect,  
only long time  
block (2h).

triacylglycerol end why higher

# Adaptation to Exercise Training

Cardiovascular System



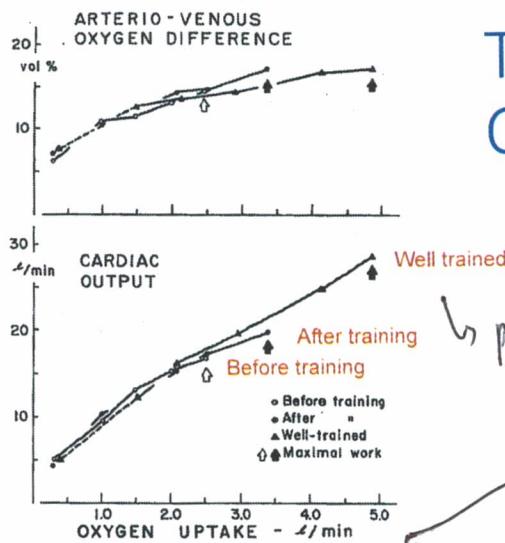


Figure 4 — Arterio-venous oxygen uptake and cardiac output in relation to the oxygen uptake in three previously sedentary subjects, who trained for 55 days (41). Included are also the mean values from a cross-sectional study on six subjects who had trained for several years (three studied by Astrand et al. (3) and three by Saltin (38)).

## Training Increases Cardiac Output

Due to ventricular hypertrophy

↳ push further, higher cardiac output  $\Rightarrow$  weaker heart & harder work, greater oxygen uptake. can push over

Saltin, Med Sci Sports 1969

### Effect of Physical Training on Hemodynamic Response during Submaximal and Maximal Exercise in 11-13-Year Old Boys

Exercise training – 34 sessions of physical conditioning, 3 times per week for 1h/session

$$\text{Cardiac Output (Q)} = \text{SV} \times \text{HR}$$

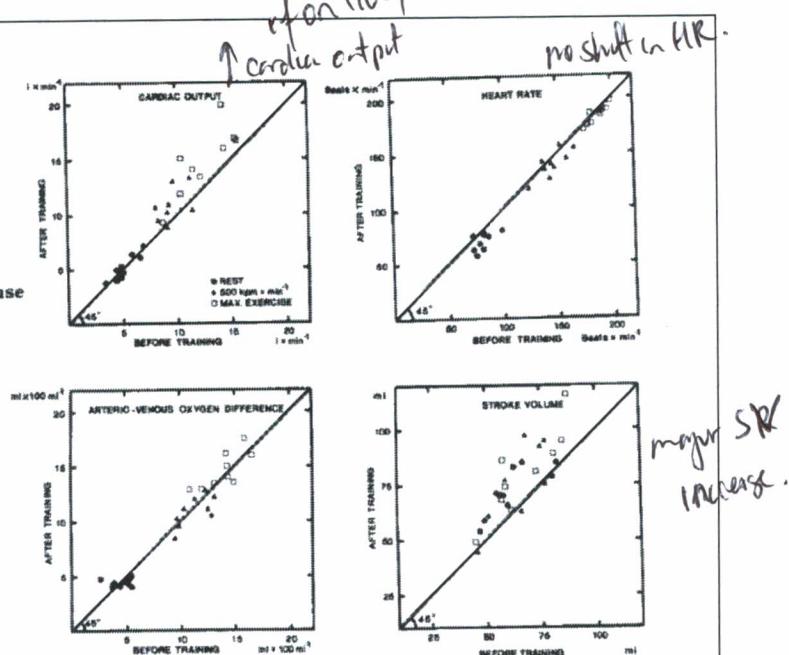


Fig. 2. Individual values for cardiac output, heart rate, arterio-venous oxygen difference and stroke volume at rest (supine position) submaximal ( $500 \text{ kpm} \times \text{min}^{-1}$ ) and maximal exercise.

Eriksson and Koch, Acta Physiol Scand 1972

$\uparrow \text{S.V} \Rightarrow \text{hypertrophy}$

# Training and de-training on CVS

TABLE 3. Effects on  $\dot{V}O_{2\text{max}}$  of 10 wk training and 15 wk training at one- or two-thirds reduced intensities

	$\dot{V}O_{2\text{max}}$	Before training	After 10 wk Training	Reduced Training Intensity	
			3 wk	10 wk	15 wk
<i>One-third reduced intensity group</i>					
Cycling	1-min <sup>-1</sup>	3.15 ±0.30	3.60* ±0.31	8.44* ±0.32	3.33*† ±0.29
	ml·kg <sup>-1</sup>	40.8 ±1.2	49.0* ±1.7	46.5* ±2.0	44.8*† ±1.7
Treadmill	1-min <sup>-1</sup>	3.45 ±0.34	3.82* ±0.33	3.68* ±0.36	3.55*† ±0.35
running					3.66*†
	ml·kg <sup>-1</sup>	44.8 ±1.8	52.0* ±1.7	49.7* ±1.8	47.4*† ±1.8
<i>Two-thirds reduced intensity group</i>					
Cycling	1-min <sup>-1</sup>	2.88 ±0.35	3.46* ±0.37	3.11*† ±0.38	3.00*† ±0.40
	ml·kg <sup>-1</sup>	39.3 ±1.2	48.6* ±1.1	43.4*† ±1.9	41.4† ±2.2
Treadmill	1-min <sup>-1</sup>	3.18 ±0.34	3.58* ±0.34	3.30† ±0.35	3.19† ±0.35
running					3.24†
	ml·kg <sup>-1</sup>	49.5 ±1.1	50.1* ±0.7	46.3† ±1.5	44.4† ±1.2

Values are means ± SE. \* Significantly different from before training; † Significantly different from 10 wk training.

TABLE 5. Resting heart rate and left ventricular dimensions in response to training and reduced training intensities

Group	Variable	Before Training	After 10 wk Training	After 15 wk Reduced Intensity
One-third reduced intensity (n = 6)	HR, beats/min	66.3±4.4	58.2±3.2	61.3±4.5
	LVID <sub>d</sub> , cm	4.75±0.25	5.06±0.24*	4.97±0.24
	IVS, cm	0.88±0.06	0.87±0.05	0.80±0.05
	LVPW, cm	0.73±0.05	0.85±0.06	0.73±0.05
	% FS	36.0±2.2	38.8±2.2	38.4±1.3
	Mass, g	69.7±9.1	82.9±10.0*	71.4±9.6
Two-thirds reduced intensity (n = 4)	HR, beats/min	60.0±4.3	54.0±2.2	67.8±4.9
	LVID <sub>d</sub> , cm	5.08±0.30	5.18±0.23	5.18±0.23
	IVS, cm	0.88±0.03	0.93±0.13	0.86±0.06
	LVPW, cm	0.80±0.09	0.80±0.11	0.78±0.08
	% FS	37.8±4.7	37.5±3.8	36.9±2.7
	Mass, g	81.4±13.2	87.8±17.9	81.7±13.4
Combined group (n = 10)	HR, beats/min	63.8±3.2	56.5±2.1*	63.9±3.3†
	LVID <sub>d</sub> , cm	4.88±0.19	5.10±0.16*	5.05±0.17
	IVS, cm	0.88±0.04	0.89±0.05	0.83±0.04
	LVPW, cm	0.75±0.05	0.83±0.05	0.75±0.04
	% FS	36.1±2.2	38.3±1.9	37.8±1.3
	Mass, g	74.3±7.4	84.8±8.7*	75.5±7.6†

Values are means ± SE. HR, heart rate; LVID<sub>d</sub>, left ventricular internal dimension in diastole; IVS, intraventricular septum; LVPW, left ventricular posterior wall; FS, fractional shortening. \* Significantly different from before training. † Significantly different from 10 wk training. FS and mass were calculated as described in METHODS.

Hickson et al, J Appl Physiol 1985

left ventricle hypertrophy

Increased Haemoglobin =  $\uparrow O_2$

$\uparrow V_{O_2 \text{ max}}$   
with exercise.

Table 1.

Amount of hemoglobin and blood volume of physically trained and not specially trained individuals.

Material	Sex	Age mean	Num- ber of indiv.	Body weight kg.	He- mogl. gr. Mean	Hb/kg. bodyw. Mean ± standard error of mean	Rel. Hb.	Blood volume litres
Untrained..	women	37.6	92	65.5	555	0.86 ± 0.013	88	4.070
Trained ....	women	26	8	64	800	1.25 ± 0.05	93	5.670
Untrained..	men	24	174	70	805	1.16 ± 0.01	99	5.250
Trained A..	men	36	14	73	995	1.37 ± 0.03	98	6.680
Trained B..	men	27	23	72	1130	1.58 ± 0.03	99	7.450

Kjellberg et al, Acta Physiol Scand 1949

↑ weight in trained.

## Specific Training alters $\dot{V}O_2$ Max/Peak

TABLE 2. Comparison of pre- and post-training  $\dot{V}O_{2 \text{ max}}$  and associated maximum measures

	Variable	Treadmill Test				Bicycle Test			
		Pre	Post	Diff	t	Pre	Post	Diff	t
Treadmill group (N = 20)	$\dot{V}O_{2 \text{ max}}$ , ml/min	3,957 ± 383	4,226 ± 305	269	9.61*	3,507 ± 283	3,750 ± 296	243	7.17*
	HR <sub>max</sub> , beats/min	194 ± 8.2	188 ± 6.2	6.0	5.18*	190 ± 8.9	184 ± 8.6	6.0	5.05*
	$V_E$ <sub>max</sub> , l/min BTPS	156.6 ± 16.0	163.1 ± 13.3	6.5	2.71†	147.4 ± 13.4	154.2 ± 15.8	6.8	2.70†
	R <sub>max</sub>	1.11 ± 0.05	1.07 ± 0.04	0.04	4.00*	1.12 ± 0.05	1.07 ± 0.04	0.05	4.07*
Bicycle group (N = 20)	$\dot{V}O_{2 \text{ max}}$	4,023 ± 529	4,128 ± 488	105	2.64†	3,502 ± 475	3,774 ± 414	272	5.30*
	HR <sub>max</sub>	198 ± 5.6	192 ± 5.6	6.0	5.29*	195 ± 7.4	190 ± 6.5	5.0	2.87*
	$V_E$ <sub>max</sub>	152.1 ± 20.6	154.5 ± 20.9	2.4	0.87	146.4 ± 18.3	157.7 ± 21.3	11.3	3.28*
	R <sub>max</sub>	1.09 ± 0.04	1.07 ± 0.02	0.02	3.33*	1.11 ± 0.05	1.08 ± 0.04	0.03	2.88*
Control group (N = 20)	$\dot{V}O_{2 \text{ max}}$	3,942 ± 455	3,911 ± 403	31	0.75	3,469 ± 425	3,398 ± 325	71	1.44
	HR <sub>max</sub>	194 ± 10.2	193 ± 10.1	1.0	0.67	192 ± 10.8	189 ± 8.1	3.0	2.01
	$V_E$ <sub>max</sub>	153.9 ± 17.7	153.6 ± 15.8	0.3	0.09	149.4 ± 20.9	155.3 ± 20.6	4.1	1.81
	R <sub>max</sub>	1.11 ± 0.04	1.10 ± 0.04	0.01	1.14	1.12 ± 0.06	1.11 ± 0.06	0.01	0.93

Values are means ± SD.

\* Significant at  $P < 0.01$

† Significant at  $P < 0.05$ .

Pecher et al, J Appl Physiol 1974

Overall:

### Training:

- Reduces resting heart rate,
- Increases stroke volume due to ventricular hypertrophy
- Increase [Hb] and blood volume
- Increases maximal cardiac output
- Increases  $\dot{V}O_2$  Max/Peak

reduce R.H.R., ↑ S.V., ↑ max cardiac output,  
ventricular hypertrophy,  $\dot{V}O_2$  max,  
↑ Hb, blood volume.

# Adaptation to Exercise Training

## Metabolic Pathways

### Another “Classic” study

TABLE I  
Muscle glycogen and triacyl glycerol concentrations before and after exercise when the subjects were untrained and trained\*

	Untrained	Trained
	mmol/kg dry wt	
Muscle glycogen		
Before exercise	285	328†
After exercise	82‡	209‡§
Muscle triacylglycerol		
Before exercise	59.2	63.3
After exercise	46.4	37.2‡

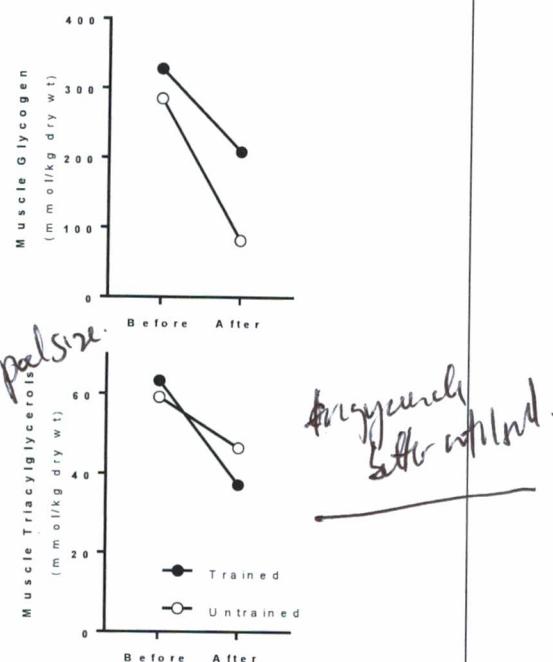
\* Data from reference 27.

† Significantly different from untrained group ( $P < 0.05$ ).

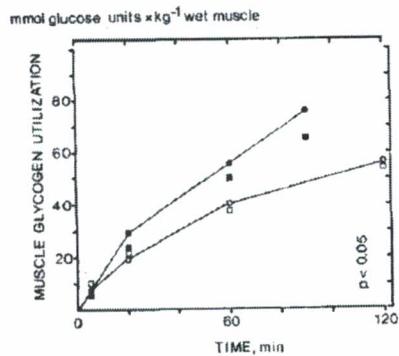
‡ Significantly different from before exercise ( $P < 0.05$ ).

§ The depletion is significantly different from untrained group ( $P < 0.05$ ).

Saltin and Astrand, Am J Clin Nutr 1993



## Training prevents glycogen utilisation



run out of glycogen earlier  
for untrained.

Fig. 2. The relationship between the utilization of muscle glycogen and work time before (●) and after (○) training. The significance of mean differences has been tested as in Fig. 1. Mean values for the 3 subjects who had the same initial content of muscle glycogen before (■) and after (□) training have also been included in the figure.

Karlsson et al, Acta Physiol Scand 1974

## Another “Classic” study

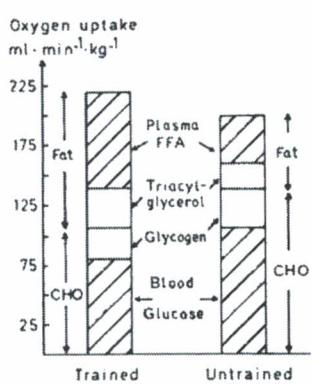
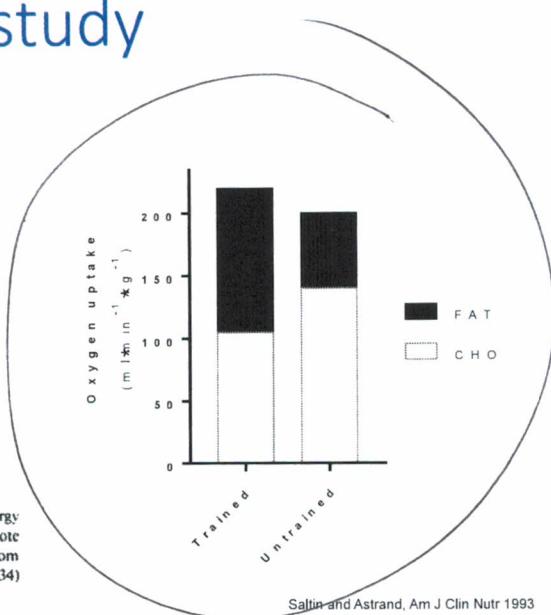


FIG 3. The estimated contribution of various substrates to energy metabolism during exercise when the limb is trained or untrained. Note the greater dependence on plasma FFAs for the trained limb (data from ref 39). Very similar results were obtained in studies by Henriksson (34) and Kiens et al (29).



Saltin and Astrand, Am J Clin Nutr 1993

5 male subjects exercised for 90 mins (before) and 120 mins (after) @ 65%  $\text{VO}_{2 \text{ Max}}$

Exercise training – 21 sessions of physical conditioning, which was characterized by repeated, short (15 s) maximal or close to maximal runs with intervening periods (15 s) of jogging or walking ("interval training"). The total running time at maximum was 6 h.

Karlsson et al, Acta Physiol Scand 1974

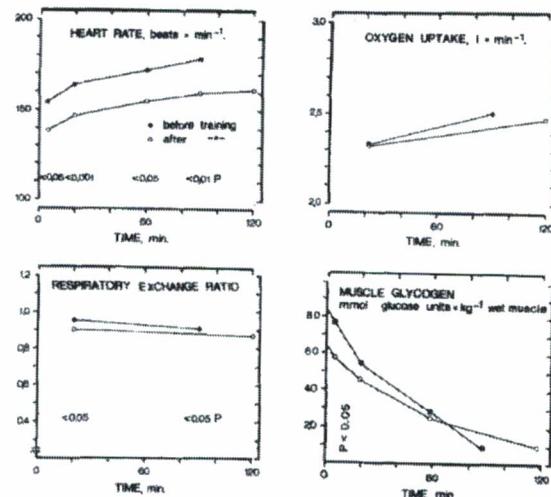


Fig. 1. Mean values for different variables in 5 subjects at rest and during work tests at the same absolute work load (mean oxygen uptake  $2.3 \text{ l} \times \text{min}^{-1}$ ) before and after 8 weeks of interval training. The significance of mean differences at equivalent points of time and between values at 90 and 120 min has been tested by the t-test and the degree of significance has been included in the figure.

↳ happens in mitochondria



## Mitochondrial "Activity"

TABLE 1. Mean ( $\pm$  S.E.) characteristics of trained male (M) and female (F) cyclists and untrained men and women.

Subjects	Sex	N	Age (yr)	Ht (cm)	Wt (kg)	$\dot{V}\text{O}_{2 \text{ max}}$ (ml/kg·min)	Years Competition
Cyclist—A	M	11	24.6 (3.5)	180.0 (1.6)	72.8 (1.4)	67.1 (1.3)	5.6 (2.0)
Cyclist—B	M	11	24.6 (1.6)	175.4 (1.0)	70.4 (2.3)	57.1 (2.9)	3.1 (0.8)
Cyclists	F	7	20.1 (3.1)	165.0 (1.8)	55.0 (2.1)	50.2 (2.9)	4.2 (1.3)
Untrained	M	19	27.4 (2.4)	178.4 (2.4)	82.3 (3.1)	38.2 (1.8)	
Active	F	10	22.2 (1.0)	163.0 (1.5)	60.2 (3.9)	41.5 (1.6)	

TABLE 4. Mean ( $\pm$  SE) muscle succinate dehydrogenase (SDH), malate dehydrogenase (MDH), phosphorylase (PH) and lactate dehydrogenase (LDH) activities ( $\mu$  moles/g/min) of trained male and female cyclists and untrained men (M) and women (F).

Subject	Sex	SDH	MDH	PH	LDH
Cyclist—A	M	20.6 (1.6)	530 (14)	7.6 (0.5)	701 (32)
Cyclist—B	M	18.1 (1.9)	590 (22)	5.8 (0.5)	687 (19)
Cyclist	F	12.9 <sup>a</sup> (2.4)	545 (49)	8.6 <sup>a</sup> (1.7)	756 <sup>a</sup> (51.8)
Untrained	M	6.4 <sup>a</sup> (0.6)	227 <sup>a,c</sup> (22)	8.6 (0.8)	843 (33)
Active	F	8.2 <sup>a,b</sup> (1.0)	412 <sup>a,b</sup> (31)	6.8 (0.6)	764 <sup>a</sup> (31)

<sup>a</sup> = mean significantly different  $P < .01$  from combined means for cyclist A and B.

<sup>b</sup> = mean significantly different ( $P < .01$ ) from mean for female cyclists.

<sup>c</sup> = mean significantly different ( $P < .01$ ) from mean for active females.

Succinate dehydrogenase (Complex II) - succinate to fumarate  
Malate dehydrogenase - malate to oxaloacetate  
• Both are mitochondrial enzymes

Burke et al, Med Sci Sports 1977

influx in mitochondrial mm<sup>2</sup>  
not become enzyme more active  
↑<sup>12</sup>

## Mitochondrial ATP Production

TABLE 1. Heart rate, lactate concentration in blood, and maximal  $O_2$  uptake determined at different work loads before and after training and after detraining

	Work Load	Before Training	After Training	After Detraining
Heart rate, beats/min	100 W	125±7	121±6	120±7
	150 W	147±6	141±8*	140±7†
	Max	187±10	190±10	186±11
Lactate concn in blood, mmol/l	100 W	2.5±1.3	1.9±0.3	1.6±0.4
	150 W	3.7±1.5	2.5±0.8*	2.5±1.2†
	Max	10.9±2.0	12.6±2.2	11.4±2.8
Maximal $O_2$ uptake, l/min	Max	3.29±0.37	3.61±0.40*	3.37±0.34†

Values are means  $\pm$  SD;  $n = 9$  men. Max, maximal work load. Significant differences with ANOVA ( $P < 0.05$ ) between \* before and after training, † after training and after detraining, and ‡ before training and after detraining.

Wibom et al, J Appl Physiol 1992

$V_O_2$  my dobs  
w/training

TABLE 2. Mitochondrial ATP production rates before and after detraining

Substrate	Before Training	After Training	After Detraining
PPKM	7.5±1.6	12.4±1.4*	10.2±1.1†‡
T+A	6.4±1.5	10.5±1.0*	8.5±1.3†‡
$\alpha$ -KG	4.8±1.1	7.9±1.0*	6.5±0.8†‡
PC+M	2.43±0.86	4.27±0.59*	3.74±0.63†‡
P+M	2.24±0.68	3.20±0.63*	2.40±0.40†‡
S+R	2.39±0.53	3.84±0.57*	2.70±0.30†‡

Values are means  $\pm$  SD, are related to muscle mass, and are in mmol ATP·min $^{-1}$ ·kg muscle $^{-1}$  (25°C);  $n = 9$  men. PPKM, pyruvate + palmitoyl-L-carnitine +  $\alpha$ -ketoglutarate + malate; T+A,  $N,N,N^1,N^1$ -tetramethyl-1,4-phenyldiamine + ascorbate;  $\alpha$ -KG,  $\alpha$ -ketoglutarate + malate; PC+M, palmitoyl-L-carnitine + malate; P+M, pyruvate + malate; S+R, succinate + rotenone. Significant differences with ANOVA ( $P < 0.05$ ) between \* before and after training, † after training and after detraining, and ‡ before training and after detraining.

add in expt,

$V_O_2$  constant, enough energy  
(constant)  $\rightarrow$  produce  
ATP for rest of body.

## Overall, training:

- Increases “efficiency” of oxygen consumption,
- Increases basal glycogen content
- Reduces the rate of glycogen consumption,
- Lowers RER/RQ, indicating increased FAO,
- Increases  $VO_2$  Peak/Max
- Increases mitochondrial number and size.

# Adaptation to Exercise Training

Skeletal muscle hypertrophy

## Exercise-induced hypertrophy – in elderly men

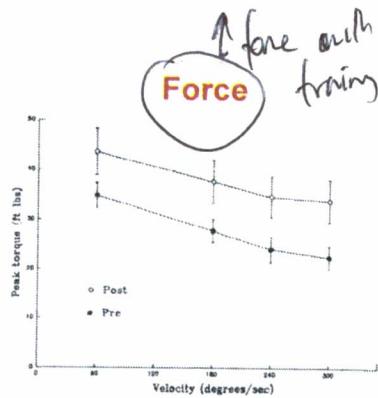


FIG. 1. Peak torque of elbow flexors (means  $\pm$  SE of 5 elderly males) was determined on an isokinetic dynamometer at velocities of contraction between 60 and 300°/s before (pre) and after (post) 12 wk of heavy-resistance training. Posttraining peak torque values were significantly greater at all tested velocities compared with pretraining values.

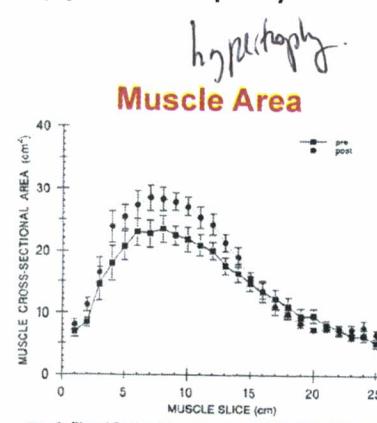


FIG. 2. Plot of flexor cross-sectional area (CSA) digitized from serial magnetic resonance imaging scans (right proximal to left distal) before (pre) and after (post) 12 wk of heavy-resistance training in 5 elderly males. Area under curve, muscle volume of elbow flexors (biceps brachii and brachialis). Note that contiguous slices have different CSAs.

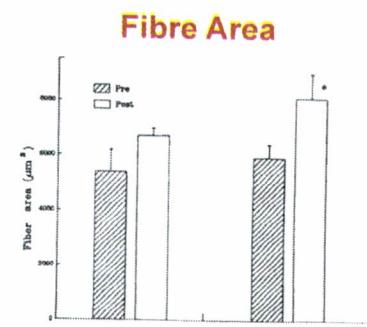


FIG. 3. Type I and type II fiber areas from biceps brachii of 5 elderly males (means  $\pm$  SE) were determined from histological cross sections stained for myosin ATPase before (pre) and after (post) 12 wk of heavy-resistance training. Minimum of 200 fibers from each type were analyzed. \*  $P < 0.05$ , pre- vs. posttraining fiber areas.

## Exercise-induced hypertrophy

Specifying on  
increased force  
to muscle.

TABLE 1. Subject characteristics

Subject Group	n	Age, yr	Height, cm	Weight, kg
Sedentary controls	7	24.8±3.4	176.9±5.3	75.6±10.4
Active controls	6	24.7±1.5	175.6±4.7	78.4±7.6
Strength athletes	6	26.9±1.2	177.7±3.7	98.8±7.7
Endurance athletes	6	25.8±1.4	176.7±5.7	69.9±3.8

Values are means ± SD. Significant differences were found in body weight among the subject groups.  $P < 0.05$  for active controls compared with endurance athletes.  $P < 0.01$  for sedentary controls compared with strength athletes, active controls compared with strength athletes, and strength athletes compared with endurance athletes.

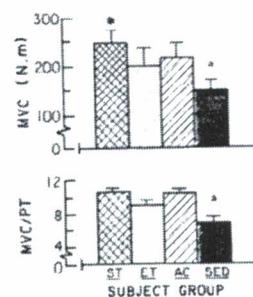


FIG. 5. Maximal voluntary torque (MVC) and ratio of MVC to peak twitch torque (PT) of triceps surae complex in strength-trained (ST), endurance-trained (ET), active control (AC), and sedentary control (SED) subjects. \*Significant differences between ST and all other groups at  $P < 0.05$ . \*Significant differences between SED and all other groups at  $P < 0.05$ .

Alway et al, J Appl Physiol 1988

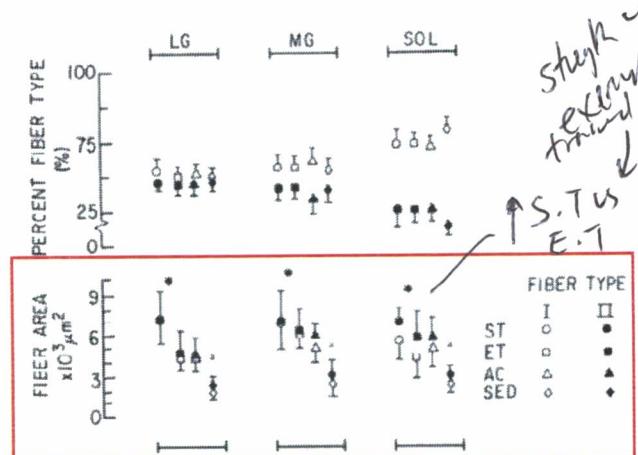


FIG. 6. Percent fiber type and fiber area in type I fibers (open symbols) and type II fibers (filled symbols) of lateral gastrocnemius (LG), medial gastrocnemius (MG), and soleus muscles of strength-trained (ST), endurance-trained (ET), active control (AC), and sedentary (SED) subjects. Data are means ± SD averaged from 200 type I and 200 type II fibers from each subject. Percent fiber type is calculated from all fibers obtained in biopsy specimen. \*Significant difference between ST and all other groups at  $P < 0.05$ . \*Significant differences between SED and all other groups at  $P < 0.05$ .

### How?

- May involve exercise-induced muscle damage,
- Does involve increased protein synthesis, reduced protein breakdown
- Myofibrils thicken
- Increased number of sarcomeres
- Or more simply - the synthesis of more muscle proteins

Alway et al, J Appl Physiol 1988

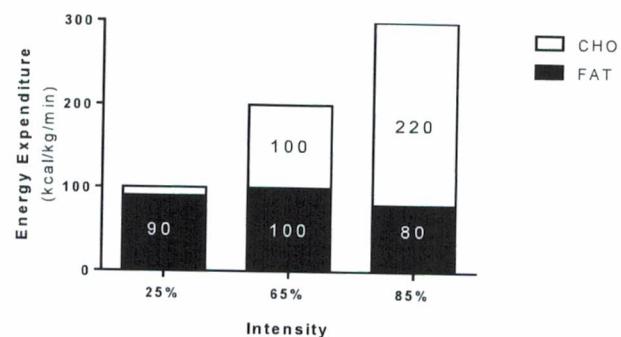
So what are the key take-home messages?

## Exercise

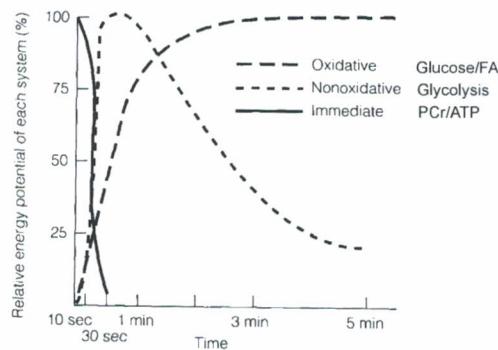
ATP consumed during:

- Contraction – for power stroke
- Relaxation –  $\text{Ca}^{2+}$  clearance

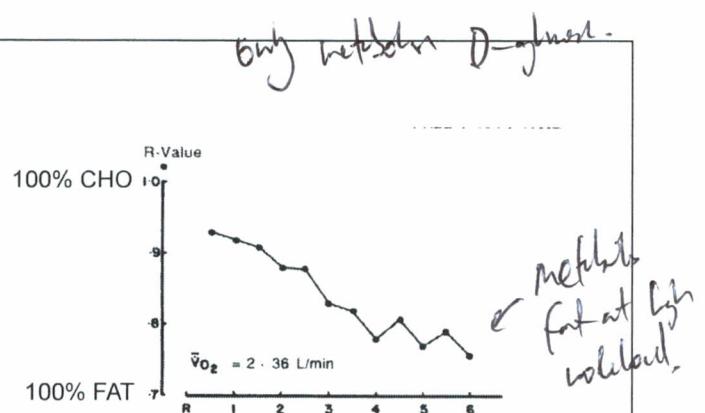
Reaction	ATP change per glucose
Anaerobic glycolysis	2
Aerobic glycolysis + oxidation	36
Reaction	ATP change per palmitate (C16:0)
Fatty acid/ $\beta$ -oxidation	17 per cycle
8 cycle – 2 ATP (C16:0 to C16:0-CoA)	129



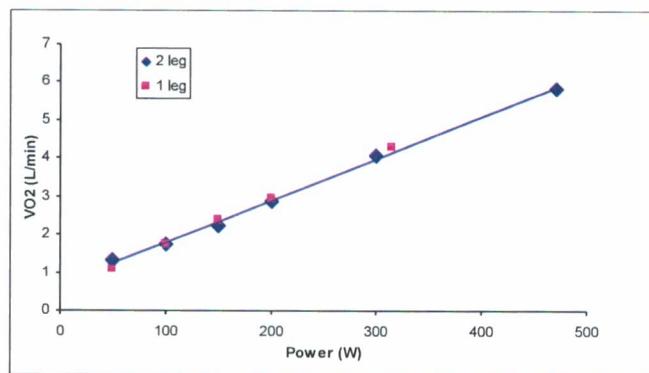
# Metabolism



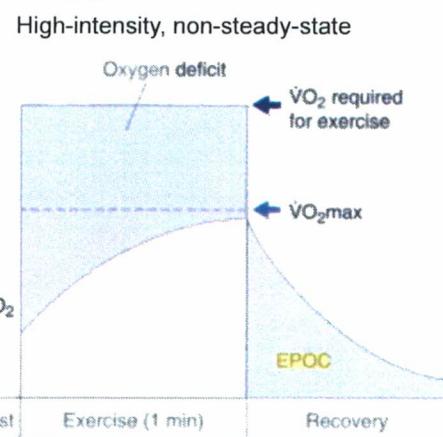
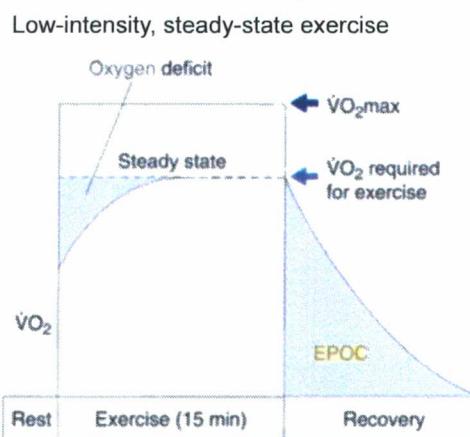
**Figure 3-1** Energy sources for muscle as a function of activity duration. Schematic presentation showing how long each of the major energy systems can endure in supporting all-out work. Source: Edington and Edgerton, 1976. Used with permission.



- Glucose Oxidation
  - $\text{Glucose} + 6\text{O}_2 \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O}$
- FA Oxidation
  - Fatty acid (C16) + 26O<sub>2</sub> → 18CO<sub>2</sub> + 17H<sub>2</sub>O
- RQ/RER = VCO<sub>2</sub>/VO<sub>2</sub>



## EPOC - Excess post-exercise oxygen consumption



EPOC – PCr replenishment, lactate metabolism, HR recovery, plus other processes

<http://archive.yeahmanh.com.s97240.gridserver.com/wp-content/uploads/2009/05/nsca-e poc.jpg>

## Getting Oxygen to Working Muscle

### Oxygen:

1. Ventilation,
2. Diffusion,
3. Transport of  $O_2$  to the tissues,
4. Increased blood flow,
5. Uptake of  $O_2$  by muscle cells

### Metabolites:

1. Sympathetic-stimulated breakdown of TAG and Glycogen

### Blood Flow:

1. Increase in cardiac output
  1. Primarily due to HR
2. Local metabolite-mediated vasodilation, systemic vasoconstriction

# Exercise Physiology

multiple systems  
achieve a  
single goal.

Prime example of multiple systems – CardioRespiratory, Skeletal, Endocrine – working together to support performance.

From an experimental perspective – exercise is a modality which provides insight into the dynamic range of organ systems.

## Implications – where to from here?

- Alter Metabolism is a Characteristic of:
  - Type 2 Diabetes and Obesity,
  - Cardiovascular Disease, in particular Heart Failure
  - Cancer – metabolism is changed in cancer
- Exercise as a Therapeutic

### **Worksheet: CV Review Lecture**

#### **Activity 1:** Sample SAQ.

- You have been on a long plane flight and your legs are swollen and puffy. Can you explain why?

10 marks – 10 minutes.

#### IMPORTANT EQUATIONS

- $CO = HR \times SV$
- $MAP - RAP = CO \times TPR$
- $MAP = CO \times TPR$  (if  $RAP = 0$  which is a reasonable approximation if value not given)
- $MAP = HR \times SV \times TPR$
- $MAP = DP + 1/3 (SP - DP)$
- $PP = SP - DP$
- $J = -PS (C_o - C_i)$
- $(\Delta P) = P_1 - P_2 = QR$
- $R = kl/r^4$  (Poiseuille's Law)
- $Velocity V = Q/A$  ( $Q$  = flow,  $A$  = cross sectional area)
- Fluid flow outwards =  $k \{sum (outward forces) - sum (inward forces)\}$
- Fluid flow outwards =  $k \{(P_c + p_{IF}) - (P_{IF} + p_p)\}$ .

**Remember:** The socrative quizzes will continue through StuVac and the exam period – Monday thru Sunday – one quiz each day. Don't forget..... Room 1800800 Good luck!

*Sharon*