Physiology 1A

Microcirculation and Integrated Cardiovascular Physiology

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From this lecture you should

- Understand the roles of arterioles, capillaries and venules in the microcirculation
- Appreciate the mechanisms of substance exchange at the capillary level: diffusion, filtration and pinocytosis
- Understand the Starling forces and equation controlling and balancing the net movement of fluid in and out of capillaries
- Standfield Ch. 14.5 pp. 409-416
- Appreciate the role of the lymphatic system in retrieving tissue fluid – Standfield p. 419.
- Understand the integrated cardiovascular response to exercise – Standfield p . 428

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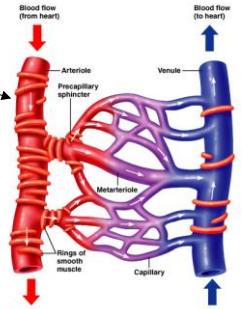
Microcirculation

Controls uptake of nutrients into tissues and collection of metabolic waste

Constricts / dilates to control capillary bed perfusion



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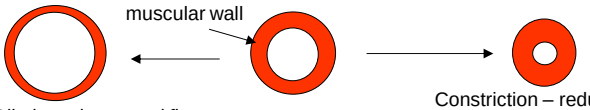
Consists of:

Arterioles - resistance vessels

- diameter 5 - 100 μm
- control blood flow into capillaries



Dilation – increased flow

Myogenic (decreased pressure)
Flow-mediated
Metabolites (e.g. adenosine)
Bradykinin

Constriction – reduced flow

Myogenic (increased pressure)
Sympathetic stimulation
Adrenaline (not muscle/coronary)
Angiotensin II

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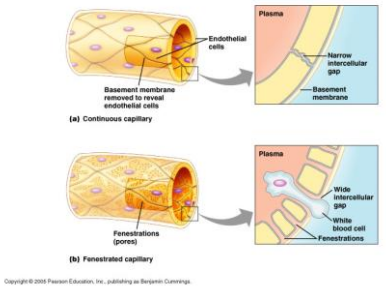
Capillaries - exchange vessels
- diameter 5 - 10 μm
- control nutrient / waste exchange
- single layer of endothelial cells attached to a basement membrane.



Two basic types:
Continuous (most tissue)

Fenestrated (kidney, intestine, endocrine tissue)

Also specialized types:
Discontinuous (large gaps in wall; liver, spleen, bone marrow)
Blood-brain barrier.

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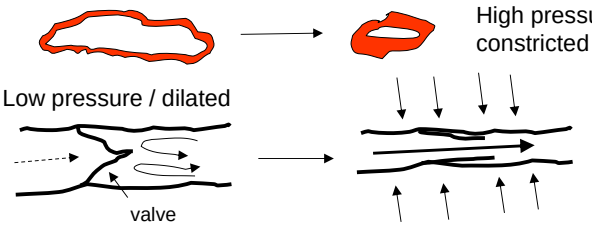
Venules - capacitance vessels
- 20 - 200 μm
- constrict in response to:
  - sympathetic stimulation
  - adrenaline
  - 'muscle' and 'abdominal pumps'



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Trans-capillary exchange

Exchange of nutrients and metabolites across capillary membrane may occur by three processes:

Diffusion - <u>most important</u> (98% of all exchange)

Filtration - water

Pinocytosis - least important overall. Key for some molecules

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Diffusion

Rate of diffusion depends upon:
- capillary permeability to the substance (P)
- capillary surface area (S)
- concentration gradient
  ($C_{outside} - C_{inside}$)

Fick's Law (for capillaries):
rate of diffusion $J = -PS(C_o - C_i)$

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Highly permeable substances:

- lipid-soluble (includes O_2, CO_2)

Moderately-permeable:

- small, charged particles (e.g. water, ions)
- some diffusion, more through <u>pores</u>

	Relative pore permeability	
	Water	1.0 (300 ml/min/100g tissue)
	NaCl	0.96
Increasing Size ↓	Urea	0.80
	Glucose	0.6
	Sucrose	0.4
	Inulin (polysacc.)	0.2
	Myoglobin	0.03
	Hemoglobin	0.01
	Albumin	0.001

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Poorly permeable

- large, charged particles (e.g. protein)
- 'cut off' MW ~ 60,000

Filtration

Determined by rate and direction of water passage through pores / fenestrations.

Filtration is, in turn, determined by various forces acting on fluid within capillary: 'Starling forces'

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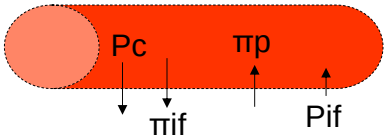
Starling Forces, Net Filtration Pressure and Starling Equation in trans-capillary exchange:

'Outward' forces driving filtration:
Hydrostatic pressure of blood in capillary (Pc)
Interstitial fluid colloid osmotic pressure (πif)



'Inward' forces driving absorption:
Hydrostatic pressure of interstitial fluid (Pif)
Plasma colloid osmotic pressure (πp)

Net filtration pressure (NFP) = [(Pc + πif) – (Pif + πp)]

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<u>Starling Equation:</u>

Volume flux across capillary wall (Jv) = k[(Pc + πif) - (Pif + πp)]

k (in Starling equation) is filtration co-efficient; reflects differing permeability of capillaries to water (no., size of pores).

As sum of forces [(Pc + πif) – (Pif + πp)] is (NFP), therefore

Jv = k x NFP

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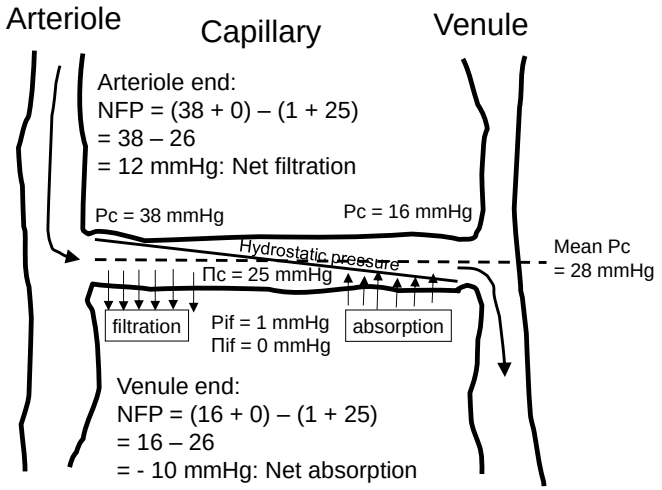

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Hydrostatic (blood) pressure in capillary is key factor.

'Ideal' capillary:

- some only filter (e.g. glomerulus)
- some only absorb (e.g. intestinal)

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NFP using mean Pc:

NFP = (28 + 0) – (1 + 25)
= 28 – 26
= 2 mmHg

Overall outwards pressure. Fluid 'escapes'.
2 - 3 L / 24 h.

Collected by lymphatic vessels.

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Pinocytosis

Vesicles

Transport of large, lipid-insoluble molecules

Venous end, muscle > lung > brain

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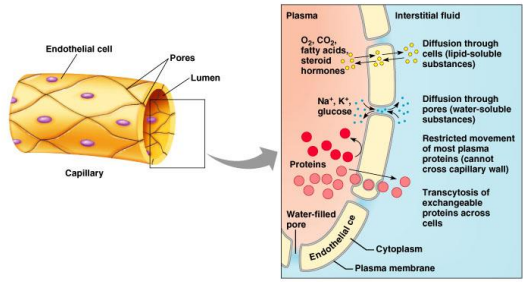
Movement of substances across capillary wall - summary



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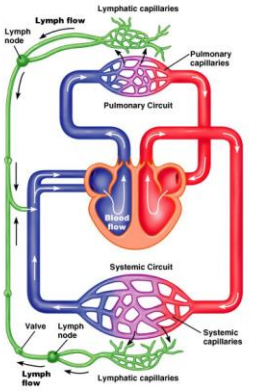
Lymphatic System



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Lymphatic Vessels

Closed-end, highly permeable. Structure a 'cross' between capillaries and veins:

-large gaps between endothelial cells

- anchored to surrounding cells by filaments. Pull vessel open / push fluid along.

Widely distributed.

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Formation of Lymph

2 ml/min leaves capillaries: 2-3 L in 24h.

Lymph fluid has less protein than plasma (lower oncotic pressure) but large gaps between cells means can re-absorb protein from tissue fluid: capillaries can not re-absorb protein.

Lymph nodes remove large foreign particles entering lymphatics: bacteria, etc.
Lymph fluid returns to circulation at vena cava level

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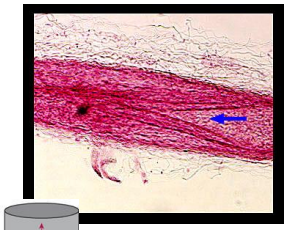
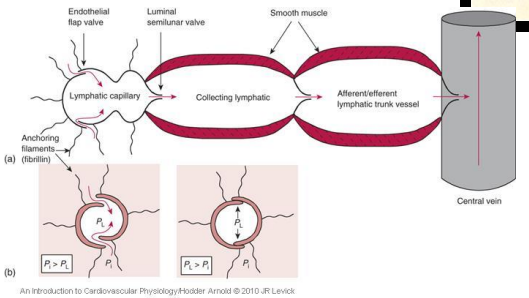
Lymphatic transport mechanisms. (a) Interstitial fluid enters the initial lymphatic through the intercellular cleft flap valves down a pressure gradient. Each muscular segment then pumps lymph into the next segment and ultimately into the venous system. (b) Proposed operation of initial lymphatic endothelial junctions as flap valves (see text). P_i, interstitial pressure; P_L, lymph pressure.





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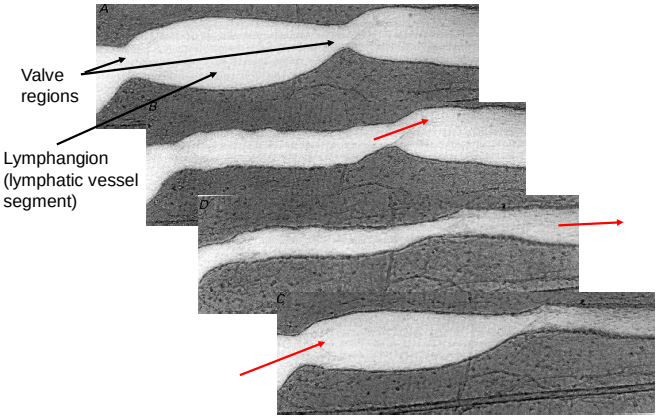
Spontaneous contraction of guinea-pig mesenteric lymphatic segments like a series of mini-hearts



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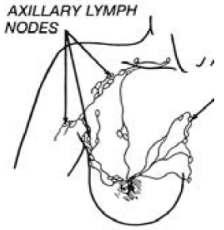
3. Immune Surveillance

- All collecting vessels pass through lymph nodes.
- Lymph nodes vary in size from 1 to 10mm diameter.
- Lymph nodes are found throughout the lymphatic system for example in the neck, armpits, trachea, GIT, groin, abdominal cavity and pelvic area.
- Lymph nodes are organised in clusters for example there are 35-45 lymph nodes in the armpits



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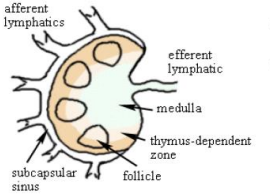
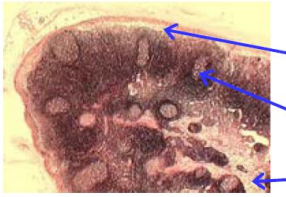
Lymph node histology



- Lymph nodes are encapsulated
- Lymph enters the lymph node through the afferent lymphatics, is filtered through the follicle and then leaves the node by the efferent lymphatics.



Afferent lymphatic flows into the subcapsular sinus

Follicle

Efferent lymphatic

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Anything increasing capillary filtration will increase lymph formation and flow:

- capillary pressure
- permeability
- increase in interstitial fluid oncotic pressure (protein leak / accumulation).

Block of lymphatics: lymphatic oedema or lymphoedema

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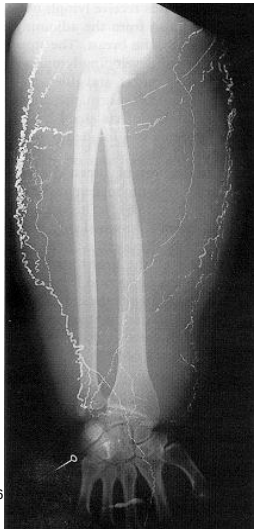
Lymphangiograph,
6 months after axillary node removal for malignant melanoma.

Note dilatation & tortuousity of obstructed lymphatic trunk vessels



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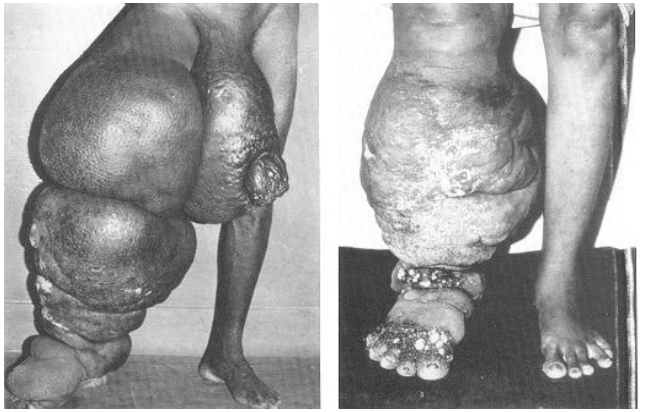
Leg & genital lymphoedema;
'elephantiasis' due to filariasis.



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Integrated Control of the Cardiovascular System

How do systemic and local mechanisms operate together to manage specific circulatory requirements?

Consider specific situation: - exercise

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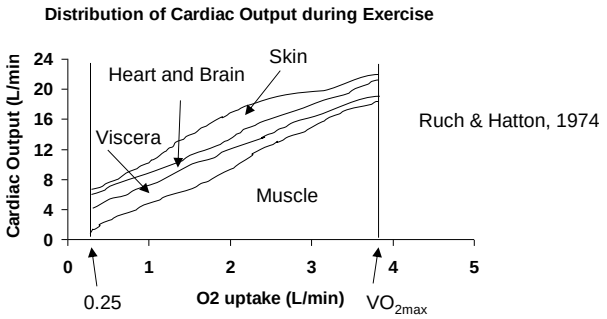
Exercise



Ruch & Hatton, 1974

Greatly increased cardiac output (4 -5 times)
Nearly all of increase directed to muscle

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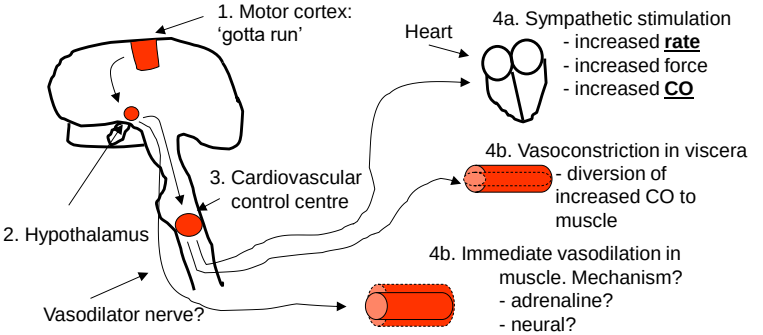
Cardiovascular response to exercise consists of 'early' and 'delayed' components.
<u>Early</u> integrated response is initiated by the CNS:



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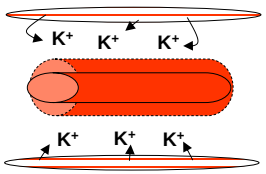
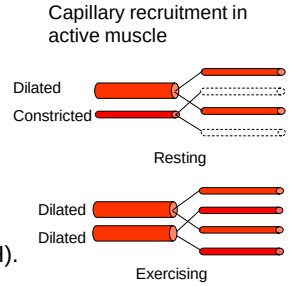
<u>Delayed</u> integrated response involves local regulation of flow, baroreceptor and muscle reflexes, temperature control.

<u>1. Metabolic dilation</u>



Working muscle releases K^+ (also adenosine, lactate, CO_2, decrease pH).
Vasodilation - increased flow
- capillary recruitment



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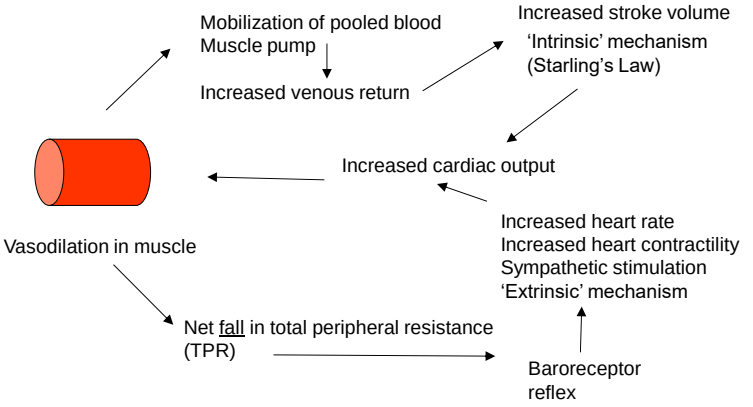
<u>2. Sustained increased in cardiac output</u>



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Other factors in delayed, integrated response to exercise:

Local histamine release
- vasodilation
- increased capillary permeability – increased lymph flow

Adrenaline release
- increased cardiac output
- dilation of coronary, muscle vessels

Stretch receptors in muscle - reflex activation of CV centre

Temperature increase
- dilation of skin vessels
- sympathetic stim. of sweat glands

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Summary

Blood flow through capillaries is chiefly regulated by the contraction and relaxation of arterioles (resistance vessels).

Capillaries consist of a single layer of endothelial cells.

Movement of water and small solutes between the vascular and interstitial fluid compartments occurs through capillary pores mainly by diffusion, but also filtration. Absorption may also occur.

Lipid-soluble substances, such as CO_2 and O_2, pass directly through the lipid membranes of the capillary and the ease of transfer is directly proportional to the lipid solubility of the substance.

Capillary filtration and absorption are described by the Net Filtration Pressure (NFP) equation: NFP = [(Pc + πif) – (Pif + πc)]. Filtration occurs when the sum is positive; absorption when negative.

Large molecules move across the capillary wall in vesicles, a process called pinocytosis

Fluid and protein which escapes the capillaries is collected by lymphatic vessels and returns to the circulation.

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- The cardiovascular response to exercise involves an early preparatory response to increase cardiac output and direct blood flow to muscle beds, later on local dilation caused by metabolites and adrenaline helps to maintain blood flow to muscle and high cardiac output. Venous muscle pumps assist with increased venous return.

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