By Adam Hollingworth

3.Dynamics of Blood Flow

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Intro

- Flow created by:
  - Pumping of heart
  - Diastolic recoil
  - Muscle pump
  - -ve thorax pressure in resp
- Resistance to flow:
  - Diameter of vessels
  - Viscosity
- Flow regulated by:
  - Local chemical
  - General neural & humoral mechanisms

Vessels

Vascular Smooth Muscle

- vital in regulating vessel diameter
- contraction produced by myosin light chain mechanism
- prolonged contraction determining tone produced by latch bridge mechanism
- calcium effects on contraction:
  - Ca influx via voltage gated Ca channel ⇒ ↑Ca [in] ⇒ contraction
  - Also ↑Ca [in] ⇒ ↑Ca release from SR via Ca sparks ⇒ ↑↑Ca [in] which interacts with β1 subunit on Ca activated K channels in cell membrane (BK channels) ⇒ BK opening ⇒ fast K efflux ⇒ ↑membrane potential ⇒ shutting of voltage Ca channels ⇒ relaxation

  ↳neg feedback system for homeostasis

  ↳sensitivity of β1 subunit to Ca sparks controls vascular tone

Arteries & Arterioles

- Out ⇒ in:
  - Outer CT
  - Adventitia
  - External elastic lamina
  - Middle layer smooth mm
  - Media
  - Intima:
    - Internal elastic lamina
    - Endothelium
- Large diameter arteries = ↑elastic tissue
- Arterioles = ↓elastic tissue; ↑↑smooth muscle
- Smooth mm in arterioles innervated:
  - NA nerve fibres ⇒ VCs
  - Cholinergic fibres ⇒ VD (only in some instances)

Capillaries

- Arterioles ⇒ metarterioles ⇒ capillaries
- Pre capillary sphincters

  ↳not directly innervated BUT do respond to circulating VC substances
- Capillary diameter
  - 5um artery end
  - 9um venous end

  ↳when dilated allow rbc through in single file
- capillary walls 1cell thick (1um)

- transport across endothelium:
  - junctions between cells:
    - in general - permit molecules 10nm
    - brain – tighter junction
    - intestine – cytoplasm of cells themselves have fenestrations – 20-100nm wide
    - liver sinusoidal capillaries 600-3000nm
  - active vesicular transport
- pericytes:
  - live around capillary ECs
  - release vasoactive substances
  - synthesise BM
  - regulate flow inbetween ECs especially in presence of inflam

Lymphatics

- many valves
- no fenestrations
- open junctions between ECs

A/V Anastomoses

- seen in fingers, palms, ear lobes
- thick muscular walls
- innervated ++ by VC nerve fibers

Venules & Veins

- little smooth mm
  ↳but NA nerves and circulating VCs (eg endothelins) ⇒ VC
- valves from folded intima of limb veins
  ↳not present in v small veins, great veins, veins from brain & viscera

Angiogenesis

- VEGF vital

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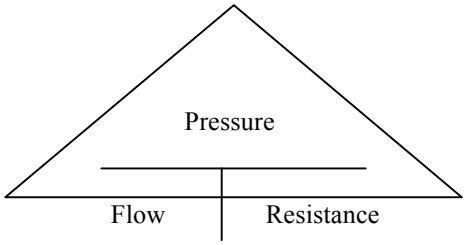
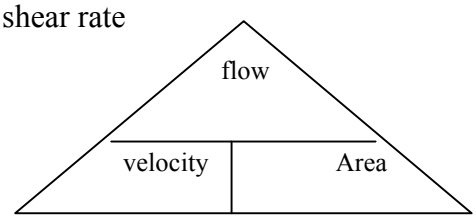
BioPhysics

Equations

- Ohms:
- Flow (mL/s), pressure (mmHg) , resistance (R unit):



- Shear stress = viscocity x shear rate
- Velocity, flow, area:



- Poiseuille-Hagen Formula

$$R = \frac{8 \times \text{viscocity} \times \text{length}}{\pi \times r^4}$$

- Reynolds Number:

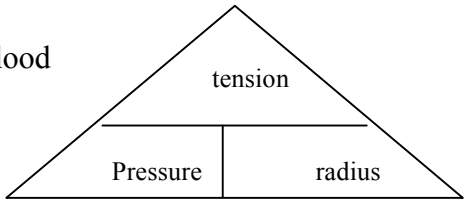
$$Re = \frac{2rvd}{n}$$

r = radius
v = velocity
d = density
n = viscocity

- Law of laplace:

$$\text{Tension} = \frac{\text{Pressure} \times \text{radius}}{2 \times \text{Wall thickness}}$$

Or in a blood vessel:



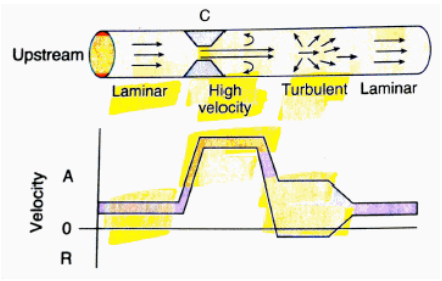
- pulse pressure = systolic – diastolic pressure
- mean pressure = diastolic pressure + 1/3 of pulse pressure

Flow, Pressure, Resistance

- flow = pressure / resistance
- Pressure = mean intraluminal pressure at arterial end – pressure at venous end

Laminar Flow

- Velocity is greatest in center of stream
- Laminar flow occurs up to critical velocity ⇒ turbulent flow
- ↑Probability of turbulence related to
  - ↑velocity
  - ↓diameter – as will cause ↑velocity
  - ↓viscosity eg anaemia
- Re number = probability of turbulence
  - ↳<2000 = no turbulence
  - >3000 = nearly always turbulent



Shear Stress

- Shear stress = viscosity x shear rate
- ↑shear stress ⇒ marked change in gene expression by EC eg VCAM-1, TGF-B, endothelin 1

Average Velocity

- velocity = flow / area of conduit
- rules:
  - ↑velocity ∝ ↓area
    ↳works same in system of parallel tubes

Flow & Radius

Laminar Flow

- poiseuille-Hagen Formula:

$$R = \frac{8 \times \text{viscocity} \times \text{length}}{\pi \times r^4}$$

↳∴ ↑ blood flow & ↓resistance to radius ^{4}

- eg
  - flow through vessel: doubled by ↑19% radius
  - resistance in vessel: decr to 6% of original with radius x2

Turbulent Flow

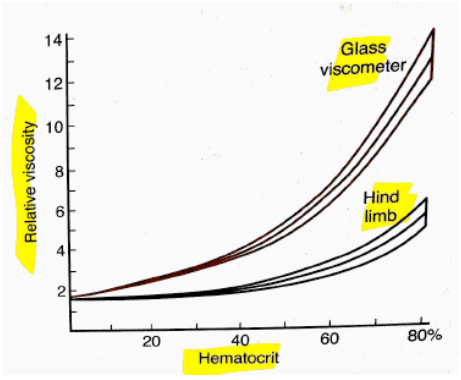
- equation:

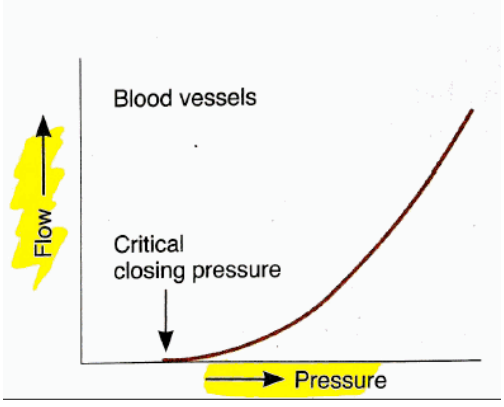
$$\frac{\text{density} \times \text{length}}{\pi \times r^5}$$

Viscosity & Resistance

- resistance to flow determined by:
  - radius (most)
  - viscosity
- viscosity depends mostly on haematocrit ie % volume of blood occupied by rbcs
  ↳also on composition of plasma & resistance of rbcs to deformation
- in vivo effect of viscosity different to poiseuille-Hagen formula:
  - large vessels – ↑haematocrit ⇒ ↑↑viscosity
  - small vessels <100um – haematocrit small effect as cells flow in single file through capillary anyway

  ↳∴ haematocrit only effects resistance in extremes eg anaemia or polycythaemia





Critical Closing Pressure

- ↓ing pressure small blood vessel – will get to a point where no blood flows even though pressure > 0
  ↳= critical closing pressure

Law of Laplace

- Tension in wall of cylinder is equal to the product of transmural pressure & the radius divided by wall thickness:

$$\text{Tension} = \frac{\text{Pressure} \times \text{radius}}{\text{Wall thickness}}$$

- Transmural pressure = pressure inside cylinder – pressure outside
  - ↳but pressure outside body is low so pressure inside can simply be used
- ∴ law can be changed to:

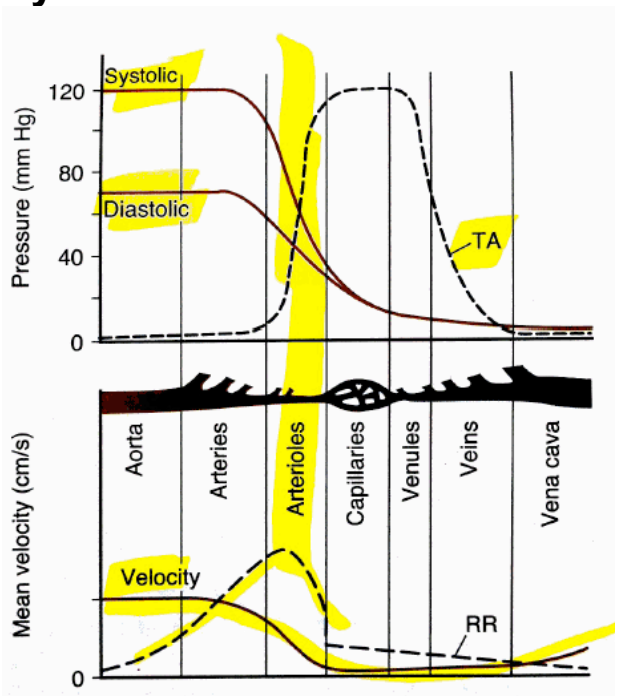
$$\text{Pressure} = \frac{\text{tension}}{\text{Radius}}$$

- ∴↓radius of blood vessel, the ↓tension required to balance distending pressure
- demonstrates problems with dilated hearts:
  - ↑radius of vent chamber means ↑tension required to generate any pressure

Resistance & Capacitance Vessels

- veins normal state is collapsed
  - ↳∵ large amount of blood added to veins before they distend & ↑volume ⇒ ↑pressure
- arterioles = resistance vessels
- veins = capacitance vessels
- Vasodilation/-constriction: - refers to arterioles (ie chief site of vascular resistance) → ↓↑SVR
- Venodilation/-constriction**:** - refers to veins (ie the capacitance vessels) → ↑↓VR
- distribution:
  - 65% veins (55% in supine)
  - 15% central blood volume (25% in supine) – heart & lungs
  - 13% arteries
  - 2% arterioles
  - 5% capillaries

Systemic Circulation



TA = total area

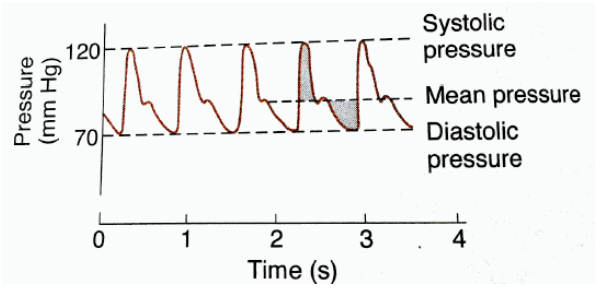
RR = relative resistance

Velocity & Flow of Blood

- proximal aorta flow:
  - phasic – forwards and backwards (too close aortic valve)
- other vessels flow is continuous due to elastic recoil of vessels
  ↳but still pulsatile – otherwise gradual ↑in resistance

Arterial Pressure

- pulse pressure = systolic – diastolic pressure
- mean pressure = diastolic pressure + 1/3 of pulse pressure



Gravity

- pressure in vessels below heart ↑ed & above is ↓ed
- gravity = 0.77mmHg/cm difference

Bernoulli's Principle

- sum of the kinetic energy of flow and the potential energy is constant:
  - pressure drop due to energy lost when overcoming resistance is lost as heat
  - pressure drop due to potential energy conversion to kinetic energy in narrow vessel is reversed when narrowing passed
    ↳= greater velocity of flow ⇒ ↓ed lateral pressure distending its walls
    ↳∴ narrowed vessels ⇒ ↑velocity ⇒ ↓ distending pressure
    ↳∴ narrowed atherosclerotic plaque is self sustaining

Auscultation

- Kororkoff sounds produced by turbulent flow caused by narrowing of vessel ⇒ >critical velocity
- Diastolic pressure correlates best when sound becomes muffled in
  - Post exercise
  - Children
  - AR
  - Hyperthyroid

  ↳otherwise when turbulent flow ceased.
- Cuff near systolic pressure – only intermittent high velocity jets through vessel at peak systole
- Cuff near diastolic pressure = constricted vessel ⇒ continuous turbulent flow

Normal Blood Pressures

- Sleep ⇒ ↓20mmHg
- Pulse pressure ↑s with age – diastolic pressure ↓s at middle age as arteries become stiff

The Microcirculation

- By definition =
  - Smallest arterioles
  - Metarterioles
  - Precapillary sphincters
  - Capillaries
  - Small venules
- ~25 billion capillaries in body
- many are closed for long periods ie skeletal mm
  ↳ ~1/4 open at ret ie recruited when needed
- skin has AV shunts for specialised functions (temp control)
  ↳ ∴ does not contribute to gas exchange and waste product removal
- cap flow is intermittent due to regular contraction/relax of precapillary sphincters
  ↳ called vasomotion
  ↳ local hypoxia = most impt factor ⇒ spincter relaxation

Function of Microcirculation

- systemic capillaries contain ~5% blood volume in close contact with tissue cells ∴ function =
  - transfer/exchange of water, electrolytes, gases, nutrients, wastes & heat

Capillary Pressure & Flow

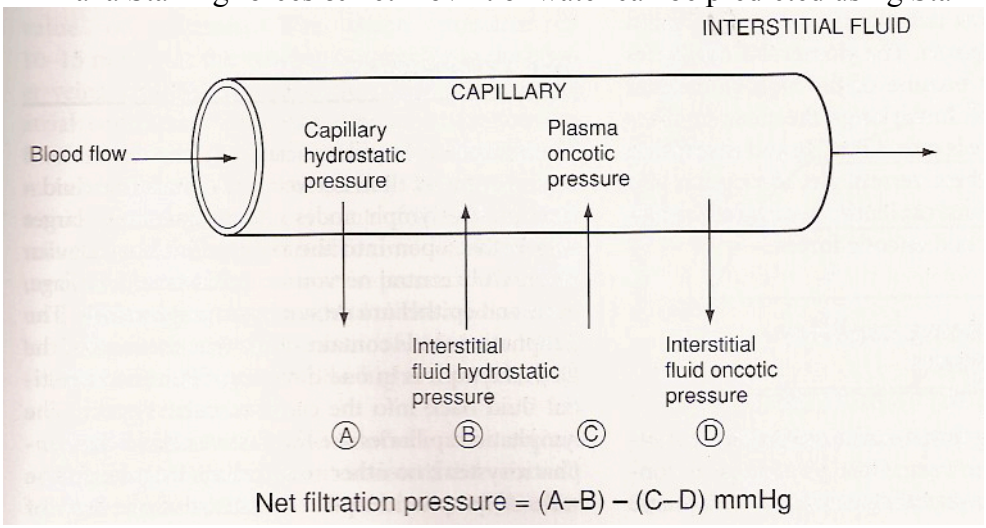
- Capillaries are short but blood moves v slow as large cross sectional area
  ↳transit time art to ven end = 1-2sec

Equilibration with Interstitial Fluid

- Transfer/exchange across capillary wall:
  - Non water movement:
    - Electrolytes & other small molecules – cross via pores & intracellular gaps
    - Lipid soluble (incl O2 & CO2) cross directly through thin endothelium
    - Proteins & other larger molecules – diff to cross membrane:
      - Pinocytosis OR
      - Endo/exocytosis
  - Water:
    - Diffusion:
      - Large amount (~80 000 litres/day) ie much larger than daily CO of ~8000/d
      - Occurs in both directions & does **not** = any net water movement across cap wall
        ↳ cos in norm conditions no osmotic gradient across cap wall
    - Filtration – see notes below

Filtration of Water

- Separate to diffusion being actually ultrafiltration (plasma proteins do not cross)
- Ultrafiltration occurs due to balance of:
  - Hydrostatic pressure
  - Osmotic pressure
  ↳ aka Starling forces & net movmt of water can be predicted using Starling's equation



- Depends on balance:
  - Hydrostatic pressure gradient
    - = Pressure in capillary (P_c) – pressure in interstitial fluid (P_i)
  - Osmotic pressure gradient:
    - = osmotic pressure in capillary (π_c) – osmotic pressure of interstitial fluid (π_I)
- pressures vary:
  - by tissue
  - along length of capillary - NET movement:
    - outward - arterial end
    - inward – venous end

Net driving pressure = α [$(P_c - P_i)$ - $(\pi_c - \pi_I)$]

- 2 more additional factors added:
  - reflection coefficient (σ) = leakiness for proteins
  - filtration coefficient (K) = leakiness for water

$= K \times [(P_c - P_i) - \sigma(\pi_c - \pi_I)]$

Reflection coefficient (σ)

- = correction factor applies to measured oncotic pressure gradient across cap wall
- needed to correct equation:
  - because of small leakage of proteins ∴ π_I = would otherwise be artificially high
  - not all protein present in capillary is effective at exerting an oncotic pressure ∴ π_c would otherwise be artificially high
  - ↳ ∴ both factors ↓actual oncotic pressure gradient
- value is from 0 to 1 depending on tissue:
  - CSF & Kidney (glomerular filtrate): both have v low proteins ∴ σ = close to 1
  - Liver: ∴ σ = closer to 0 because of:
    - v high protein amount
    - proteins pass through very leaky hepatic sinusoids easily

Filtration Coefficient (K)

- net fluid flux due to filtration is proportional to NET driving pressure
- K = constant of proportionality in the flux equation
- K depends on 2 components:
  - Area of capillary walls
  - Permeability of capillary walls to water (aka hydraulic conductivity)
  - ↳∴ K = area x hydraulic conductivity
- Eg leaky capillary would have high K

NET Fluid Flux

Complete equation:

$= K \times \Delta P$

$= K \times [\Delta P_{hydrostatic} - \sigma.\Delta\pi]$

$= K \times [(P_c - P_i) - \sigma(\pi_c - \pi_I)]$

Typical Starling Values (CVS Capillaries)

	Arteriolar end	venous end
P_c	25mmHg	10
P_i	0	0
(P_{total})	(25)	(10)
π_c	20	20
π_I	5	5
(π_{total})	(20)	(20)
net filtration P	+10	-5

- Along length of cap only pressure that drops is hydrostatic pressure
- Body as a whole:
  - NET ultrafilration of ~ 20ml/min ⇒
    - 18ml/min reabsorbed by capillaries

  - 2ml/min removed by lymph ie 2-4litres /day into lymph
- Starling equation limited value in practise as needs measurement of 6 unknowns
- ∴ more useful to describe NET fluid movement in diff capillary beds

Kidney (glomerulus) Starling Forces:

○ In Glomerulus (ie GFR) NET excess ~ 180litres/day

↳ different lies in reabsorption in kidney tubules

- Glomerula specifics:
  - High K
  - High σ ~1.0
  - P_c is high and does not drop much along the length of the capillary.
  - σ_c *increases* along the length of the capillary (large fluid loss (concentration proteins) + high σ_c initially).
    ↳ This ↑ed capillary oncotic pressure is important for the reabsorption of water into the proximal tubule from the peritubular capillaries
  - ∴ = NET outward filtration pressure along whole length of glom capillary

	Aff. Art end	Eff art end
P_{GC}	45mmHg	45
P_{BC}	10	10
π_{GC}	20	35
π_{BC}	0	0
Net filtration P	15	0

(GC = glomerular capillary

BC = Bowman's capsule

Hhydrostatic pressure in the glomerular capillary is affected by the balance b/w afferent and efferent arteriolar tone.)

∴ $GFR = K \times (P_{GC} - P_{BC} - \pi_{GC})$

Cerebral Microcirculation

- most body capillaries are
  - permeable to low mw solutes (ie Na & Cl)
  - impermeable to high mw solutes (aka proteins) (depending on their σ).

  ↳ ∴ it is the large protein solutes which exert an osmotic force across cap wall
  ↳ ie there is a differential inside to outside capillary
- in cerebral capillaries the cap membrane:
  - relatively impermeable to all solutes incl low mw solutes eg Na & Cl
- ∴ low mw solutes exert an osmotic force across cerebral capillary membrane (ie BBB)
- ∴ starling forces in cerebral caps =
  - hydrostatic pressure
  - osmotic pressure (not oncotic) due to effective solutes
- oncotic pressure is small in comparison to huge osmotic pressure exerted by low mw solutes
  ↳ because number and not size is important
  ↳ aka colligative properties
  ↳ other colligative properties = SVp depression, boiling point elevation, freezing point depression
- small leak of these solutes can also be accounted for with a reflection coefficient
  ↳ same as for plasma protein elsewhere
- 1 mOsmole ↑osmotic pressure gradient blood:brain interstitial fluid ⇒ force 17-20mmHg

↳ ∴ small change in plasma tonicity has marked effect on cerebral volume

(tonicity = effective osmolality ie osmoles effective at exerting an osmotic pressure across membrane in question)

Pulmonary Microcirculation

- main function is gas exchange
- features that assist with gas exchange:
  - pulmon capillaries & alveoli have v thin walls
  - large SA for exchange: capillaries in the alveolar walls are seen as a continuous film of flow
  -
  - low pressure pulmon circuit ∴ very low resistance (but pressure sufficient to perfuse apical lung (West zone 2)

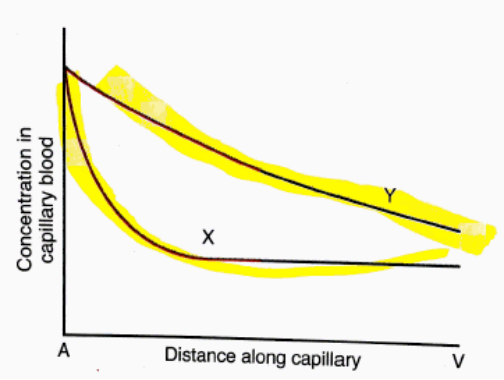
Starling forces in the lung:

	Arteriolar end	venous end
P_c	13 mmHg	6
P_i	0 – slight neg	0 – neg
π_c	25	25
π_I	17	17

- oncotic gradient:
  - reflection coefficient (σ)is low = ~0.5
  - allowing for σ NET oncotic gradient is small ⇒ favour reabsorption
- hydrostatic pressure:
  - capillaries in lung
    - = intra-alveolar vessels:
      - ∴ cap vessel pressure exposed to alveolar pressure
        ↳ = average of zero
    - varies with gravity:
      - ↑pressure @base : apex
      - pressure diff equivalent to height static water column from base to apex (~23mmHg)
    - quickly affected by change in pulmon artery pressure & LAP
      ↳not much buffering
  - alveolar interstitium:
    - slight –ve pressures
    - closer to hilum: interstitial pressure ↑ingly negative
      ↳ this favours flow of fluid from interstitium into pulmon lymphatics
- ∴ overall under norm conditions small NET outward flow of fluid
  ↳ this = pulmonary lymph flow = ~10-20ml/hr
- NET fluid movement outward (into interstitium) should be bad for gas exchange ie pulmon oedema
  ↳ but mechanisms exist to prevent it – (see resp notes 4 blood flow end of section)

Flow Limited vs Diffusion Limited Exchange

- flow limited exchange =
  - small molecules equilibrate near arteriolar end
    ↳∴ to ↑total diffusion need to ↑flow
- diffusion limited exchange =
  - substances don't reach equilibrium during passage through tissues
    ↳∴ ↑flow will not ↑exchange



Y = diffusion limited
X = flow limited exchange

Activating Capillaries

- capillaries activate by VD of precapillary sphincters & metaarterioles:
  - VD – metabolites
  - ↑permeability – noxious stimuli. Effected by:
    - substance P
    - bradykinin & histamine

Venous Pressure & Flow

- CVP ~5mmHg
- Gravity has greater effect on venous pressure than art pressure
- Velocity of flow ↑'s as blood from venules to greater veins
  ↳av 10cm/sec

Venous Return

- Aided by:
  - Inspiration
    - intrathoracic pressure ⇒ -2.5 to -6 mmHg
      ↳CVP inspiration 2mmHg; expiration 6mmHg
      ↳this drop aids venous return
    - diaphragm descends ⇒↑intrabdo pressure ⇒ ↑VR as valves prevent backflow to LL
  - ventricular ejection ⇒ pulling of tricuspid valve down ⇒ sucking of blood into RA
    ↳venous flow is pulsatile near heart
    ↳1 peak = vent systole
    2nd peak = rapid vent filling in early diastole
  - Muscle pump:
    - Quiet standing – venous pressure @ ankle 80-90mmHg
    - Contractions of leg mm ⇒ pressure @ ankle ↓30mmHg
      ↳even if incompetent valves still see benefit as resistance less in larger veins ie proximally

Venous Pressure in Head

- Dural sinuses have rigid walls ∴ no critical closing pressure
- In standing pressure in them is subatmospheric
  ↳pressure ∝ to distance above collapsed neck veins (top head ~ -10mmHg)

Air Embolism

- Disturbs forward movement of blood as air is compressible
- Surface tension of air bubble ⇒ ↑↑resistance to flow
- Rx hyperbaric oxygen - ↓s size of gas emboli

- 5-100mls lethal

Measuring Venous Pressure

- mean pressure vein in ACF = 7.1; CVP ~5mmHg
- convert mm Saline to mm Hg by dividing by 13.6
- CVP:
    - Increased by:
        - Positive pressure breathing
        - Straining
        - Expansion of blood volume
        - Heart failure
    - Decreased:
        - -ve pressure breathing
        - shock

Lymphatics

- in capillaries normally efflux > influx
- remainder into lymph
- 24hr lymph flow/day 2-4L
- lymph divided:
    - initial lymphatics:
        - no valves or smooth mm
        - in intestine & skeletal mm
        - fluid enters through loose junctions between ECs
        - flow created by mm pump & artery pulsations
    - collecting lymphatics:
        - have valves & smooth mm
        - have own peristalsis
        - flow also aided by:
            - mm pump
            - -ve intrathoracic pressure inspiration
            - suction effect high velocity blood in veins which lymph drains into
- 25-50% of total circulating plasma protein filtered and returned to blood via lymph

Interstitial Fluid Volume

- cause of ↑ed volume & oedema:
    - ↑filtration pressure:
        - venular constriction
        - ↑ed venous pressure ie
            - failure,
            - incompetent valves,
            - vein obstruction,
            - hypervoleamia – salt & water retention
    - ↓osmotic pressure gradient
        - ↓plasma protein – cirrhosis, nephrosis
        - accumulation osmotically active substance in interstitium
    - ↑cap permeability:
        - substance P
        - histamine, kinins
    - inadequate lymph flow
- Exercising mm:
    - ↑cap pressure so higher than oncotic pressure through whole cap ⇒ efflux

- osmotically active metabolite accumulates in interstitium ⇒ efflux
- lymph flow cannot keep up

↳∴ mm volume may ↑up 25%

Fluid Volumes

- see chp 1 physiology notes