UNIVERSITY OF JORDAN
DEPT. OF PHYSIOLOGY & BIOCHEMISTRY
Introductory Course In Physiology
Medical Students 2017/2018
Textbook of medical physiology, by A.C. Guyton and John E, Hall,

مقدمة في الفسيولوجيا للطب (0501110)

Lecture (1)

Chapter 5 (pp 57-71) AND Chapter 45 (pp 564-565)
Membrane Excitability

Resting Membrane potential: origin and determinants.
Electrochemical Equilibrium (**Nernst equation**), chord conductance equation and Goldman-Hodgkin-Katz Equation

- In neurons, RMP ranges from –40 to – 90 mV (average –65 mV).
- In RBC, RMP is -7 mV and in smooth muscles -30 mV. In large nerve axon it is -90 mV. In spinal cord motor neurons it is -65 mV.
- Therefore, most our cells are polarized (RMP Range from **+5 to –100** mV).
Nernst Equation:

$$E_x = \left[\frac{RT}{ZF}\right] * \mathrm{Ln}\left[\frac{Ci}{Co}\right]_x$$

E_x= equilibrium potential for x
R= gas constant
T=Absolute temp
Z= valance
F= Faraday's number (number of coulombs per mole of charge)

$$E_x = \pm 61 * \log\left[\frac{Xi}{Xo}\right]$$

- E_K= -94 mV= $(-61 * \log\left[\frac{140}{4}\right]$ = -61*log 35=- 61*1.54=- 94 mV).
- In Spinal cord motor neurons (pp 564) $[K^+]$inside = 120 mEq/l and not 140 and thus EK =- 86 and not -94 mV
- E_{Na}= +61 mV ECa^{++}= +150 mV E_{Cl}= -70 mV.

$$E_{Cl} = -61 * \log\left[\frac{Xo = 107}{Xi = 8}\right] = -70 \text{ mV}$$ because the valance is negative or we can re-arrange the equation as follows:

$$E_{Cl} = +61 * \log\left[\frac{Cli}{Clo}\right]$$

Ohm's Law:

"Flow is a product of driving force and resistance": Flow is directly proportional to driving force and inversely proportional to resistance (R).

- The unit of R is Ohm. Resistance is vague expression, but it tells you how difficult this process is going to occur.

Conductance (**g**) is the reciprocal of resistance (How easy for the ion to cross the membrane.

-). The unit for "g" is $\left[\frac{1}{Ohm}\right]$ or just "mho"

The magnitude of any ionic current is the product of both conductance to that specific ion and the driving force.
The driving force is how far from electrochemical equilibrium of that ion from the membrane potential. In other words, it is the difference between the Em and Nernst Equilibrium potential for that ion (E_x).

$I_x = g_x (E_m - E_x)$

Examples: If Em is **negative** to Ek (-100 – (-94))= -6 mV then inward current is expected (the resultant current is -ve). K^+ is going inside generating a current. The current is going inside the cell with its positive head directed inside the cell and its negative tail directed outside. We record from outside, thus we record the negative tail, and therefore the current is negative. If Em is +ve to Ek (-90 -(-94))=+4 mV then outward current is expected (the resultant current is +ve).

An example is the RMP in spinal cord motor neurons neuronal cell which is equal to -65 mV. The E_k -94 mV and E_{Cl} is -70 mV. If excitatory neurotransmitter opens Na^+ channels and thus makes the RMP makes less negative. If inhibitory neurotransmitter opens Cl- channels it will make RMP more negative: Cl^- enters the cell to make it more –ve → Hyperpolarization…**I**nhibition.. For example, if RMP in these cells is -90 mV, then only excitation occurs…no inhibition.

E_{Na} is +61. If **g**Na are open then Na^+ enters and → **depolarization** …stimulation. If the RMP is not **-65 mV** but for example like cardiac cells is around **-90 mV** then we cannot control the neurons in term of inhibition.

Cord Conductance Equation:

- When membrane potential is constant with respect to time, then all currents sum to zero.

$I_k + I_{Na} + I_{Ca} + I_{Cl}$ = zero ...we will ignore I_{Cl} because it has negative valence. Hence,

$g_K(E_m - E_K) + g_{Na}(E_m - E_{Na}) + g_{Ca}(E_m - E_{Ca})$ = zero….

We know that total conductance gT= gk + gNa + gCa

$$Em = \left[\frac{gK}{gT}\right]_{EK} + \left[\frac{gNa}{gT}\right]E_{Na} + \left[\frac{gCa}{gT}\right]E_{Ca} = \left[\frac{gk * Ek + gNa * E_{Na} + gCa++ * ECa++}{gT}\right]$$

This equation is known as "**Cord Conductance Equation".**
An alternative to this equation is the CONSTANT FEILD EQUATION (GOLDMAN equation or Goldman-Hodgkin-Katz Equation) using a product of permeability coefficient.

$$Em = -61 \log \left[\frac{P_K[K]i + P_{Na}[Na]i + P_{Cl}[Cl]o}{P_K[K]o + P_{Na}[Na]o + P_{Cl}[Cl]i} \right]$$

-At rest, K leak channel allow K to leak 100 times more than Na.
- If the membrane is leaky to K only then RMP would be -94 mV (Nernst)
-Since it is also slightly permeable to Na, the RMP is -86 mV (Goldman)
- But, because Na-Ka pump is electrogenic, the RMP is finally, -90 mV (contribution of -4 mV)
Na-K pump consumes 45% of the body total ATP expenditure.
- Additional channels are voltage-gated Na^+ channels and voltage-gated K^+ channels.
Ca^{++} affecting the RMP:
Decrease in Ca++, duo to hypoparathyroidism or alkalosis (voluntary, organic or hysterical hyperventilation) can lead to (carpo-pedal spasm).
When ECF Ca^{++} is dropped, it uncovers Na^+ channels→ Na^+ enters the cells → increase excitability.
Increase intracellular Ca++ can activate proteases → cell death
In MI or CVA, we give Ca^{++} channel blockers to protect the cardiac and the brain cells from being damaged.
AP duration in nerve cells takes 0.3 mSec (average 1-2 msec)

- ***EPSP and IPSP***

LECTURE (2)

SRAP vs. FRAP

- Transmembrane Potentials…RMP in SA nodal cells and ventricular cells
- Special Types of AP:
    - Cardiac Action Potential (Fast Response AP)
        - Phases: 4 (RMP), 0 (overshoot), 1 (early repolarization), 2 (plateau), 3 (final repolarization)
        - The "m" gate and the "h" gate theory…briefly
    - (Slow Response AP) and the Pacemaker Concept
        - Slow Response AP…Phases: 4, 0, 2, 3

. The Absolute and Relative Refractory Period.
. Calcium Entry Across Sarcolemma

Objectives

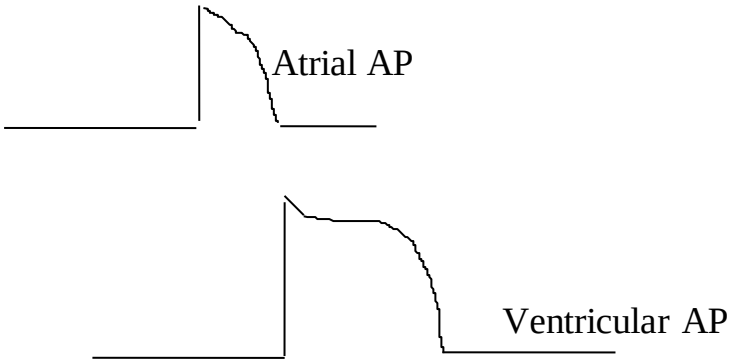
After completing the above two lectures, students should be able to

1. Illustrate the key features of the cardiac action potential and describe the ionic events that underlie its behavior
2. Draw and label an action potential from a ventricular myocardial cell
3. Describe changes in the conductance of various ions involved in the generation of a "fast and slow" type action potential.

HINTS

Cardiac muscle differs markedly from skeletal muscle in a number of ways that are essential for its function. Cardiac muscle cells are connected with each other via low-resistance regions. This permits excitation of one cell to be easily transmitted to its neighboring cells (the concept of Syncytium=cells together). The cardiac muscle action potential is considerably longer than that of skeletal muscle, and the calcium must enter the cell during the action potential for the subsequent contraction to occur. Due to the long action potential, cardiac muscle cannot be tetanized.

Monophasic AP



CONDUCTION SYSTEM OF THE HEART
(pp 116-122)

Lecture Topics

. Pacemakers and the Conduction System
. Natural Excitation of the Heart…Automaticity and Rhythmicity
. Intrinsic Cardiac Rates:
. Overdrive suppression…recovery time

Objectives

After completing this lecture, students should be able to

1. List the characteristics of 'fast' and 'slow' type action potentials.
2. Define a pacemaker potential and explain how it can alter the heart rate
3. Describe the normal pathway for excitation of the heart and explain the electrical events associated with transmission of the excitation process. Include the mechanism responsible for slow transmission through the AV node.

Rate of Firing depends on:

1. Max diastolic potential (inversely proportional). It takes more time to reach threshold potential when it is more -ve. ACh $\rightarrow\uparrow I_K$ and $\downarrow I_f$.
2. Rate of diastolic depolarization during phase (4): directly proportional. Epinephrine $\rightarrow\uparrow I_f$ and $\uparrow I_{Ca}$
3. Threshold potential. Inversely proportional.

. Electrical conduction in the Heart

A. Spread of Depolarization in the Atria

B. Spread of Depolarization via AV Node…AV delay and its significance

C. Spread of Depolarization via the His-Purkinje System…

- Bundle of His…
- Left and Right branches…
- Purkinje cells: broadest cells of the heart (70 μm in diameter) compared to 10-15 μm for ventricular myocardial cells.
  - ↑ gap junctions.
  - abundant sarcomeres,
  - no T-tubules,
  - velocity of conduction 1-4 m/sec.

VENTRICULAR MUSCLE FIBER ACTION POTENTIAL

Fast channels are called so because they open and close fast. Slow Ca-Na channels open slowly and remain open for long time (200 mSec).

FAST RESPONSE AP

Phase (4) (RMP):

-Equals -90 mV.

-Em is constant.

-Inward (Na & Ca) current= outward (K) current.

- gK for K is high but driving force is so small
  Em - Ek = -90 -(-94)=(+4 mV).
- gNa is low but driving force is high
  Em - ENa = -90-61 = - 151 mV as an inward force.

Phase (O):

Overshoot potential is the positive portion.

Because of the activation of gNa, and since driving force is great, Na^+ runs inside the cell causing further depolarization (I_{Na} ... rapid regenerative depolarization occurs (self-sustained) and Em approaches E_{Na}.

Late phase (O) I_{Na} decreases because:

1. Driving force decreases
2. Depolarization causes inactivation of g_{Na}.

The amplitude of AP is the difference in potential between the fully depolarized and the RMP (fully polarized) of the cell interior. This varies largely with $[Na]_o$. If it decreases to around 20 mM, then the cell is no more excitable. (Tetradotoxin: fish toxin TTX) can block fast Na channels (voltage gated channels), but it does not affect I_f in SRAP.

The Gate Theory:

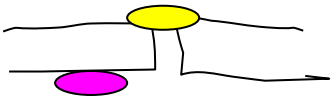
In general, gNa turns on fast and turns off slow.

The m gate (Activation Gate) is fast (0.2 mSec) and it opens when Em become less negative. It opens rapidly when membrane potential gets depolarized (less negative). It remains open unless the Em comes back to a less -ve values.

The h gate (Iinactivation Gate) is slow (1 mSec). It tends to close the channel as Em become less negative. Since it is slow it takes some time before it can close the channel during depolarization. However, if the membrane is slightly depolarized but held at that point (voltage clamp) the m gate is open while the h gate is closed. The end results are the fast Na^+ channels are closed and actually cancelled. The h gate remains closed unless membrane is partially repolarized (Phase 3) which is known as effective refractory period. Midway of phase (3), some of the gNa are already recovered (partial response).

Outside ***m*** gate (activation) rapid (0.2 ms) is closed but ready to open

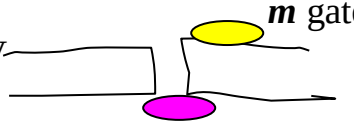
At - 90 mV



Inside ***h*** gate (inactivation) slow (1 ms) is open.

m gate (Open)

At +30 mV



h gate is closed but not ready to open (Closed Inactive)

Effective RP from phase (O) until mid-phase (3).
Relative RP until the end of phase (3).

Phase (1): (I_{to})

Early repolarization. Outward current > inward current.

This phase is seen in Purkenje and epicardial muscle, and less developed in endocardial fibers.

I_{Na} ↓ because of depolarization. gK ↓ because of depolarization but driving force now is great (20-(-100)= +120 as an outward driving force. This would lead to I_K which is larger than I_{Na} causing this initial repolarization (I_{to})

Phase (2) Plateau:

Inward = outward
Depolarization causes two things: **1)** activation of g_{Ca}^{++} (Ca^{++} and Na^+) followed by inactivation of these channels at the end of this phase. This current is so small with amplitude of 1/100 from I_{Na} **2)** activation of I_x(K). At the end of this phase I_x become greater than I_{Ca} leading to repolarization.

The duration of this phase depends on:

1) slow turn on (activation) of I_x.
2) slow turn off (inactivation) of I_{Ca}^{++}.

In skeletal muscle no plateau because:

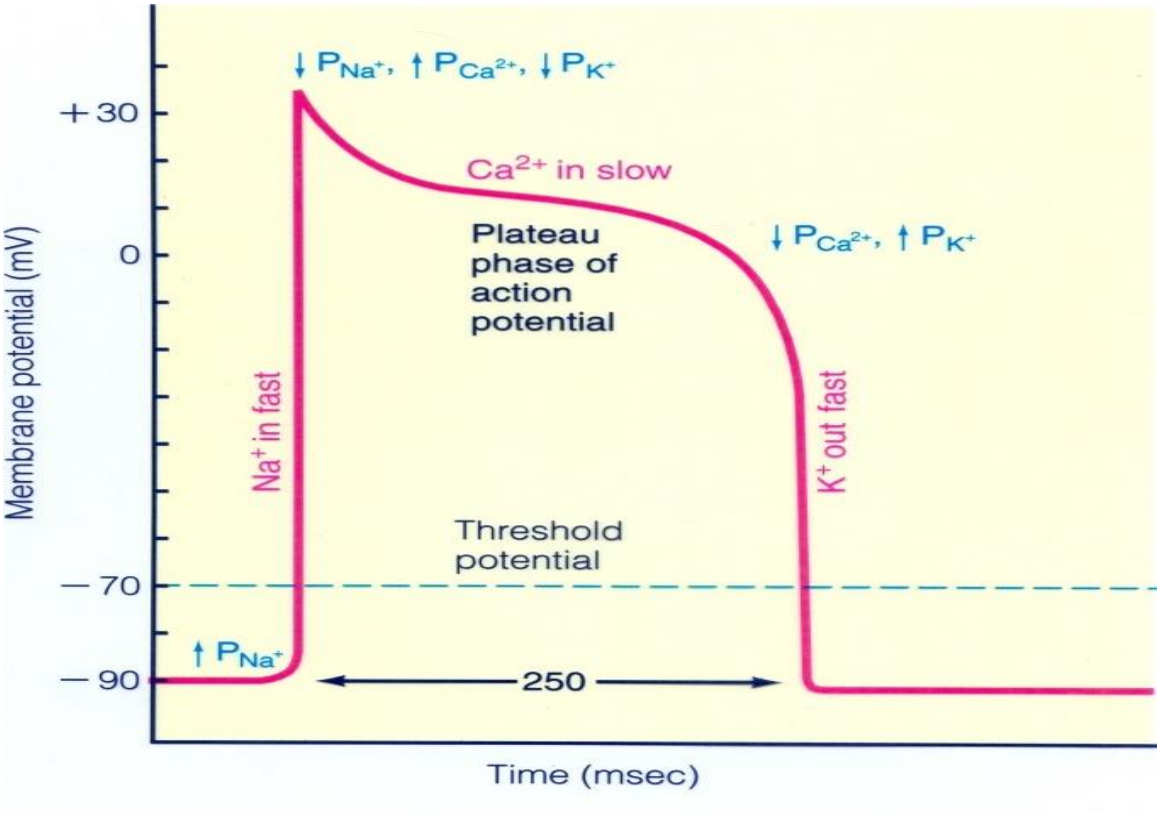
- No I_{Ca}^{++}
- g_K does not decrease during depolarization while here it turns off.

Phase (3):

Final repolarization. $I_{out} > I_{in}$. (↑ gK: ↓ gCa : ↓ gx)

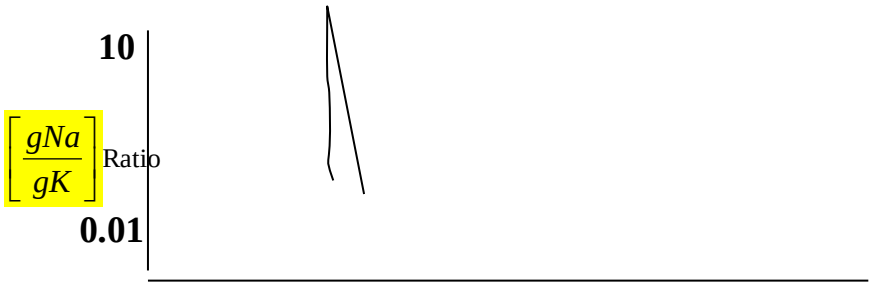
The three situations where Na channels are availabe (g_{Na}) are:
Low g_{Na} (closed but ready to open) ↔ high gNa (open and active) →closed inactive (low g_{Na}) → Low g_{Na} (closed but not ready to open) ↔ Low g_{Na} (closed but ready to open).
Using voltage clamp we can move from **closed active** to **closed inactive**. From closed inactive we never can go to open and active.

At -55 mV the fast Na^+ channels are inactive, while the slow Na^+ channels can become active.
SRAP:
Phase (4):
- Is less negative (-65 mV).
- There is slow depolarization wave duo to Na^+ entry and later on this phase Ca^{++} enters too. Both I_f and I_{Ca}^{++} are opposed by I_K^+.
- I_f is different from I_{Na}^+. It is activated when MP is less than -50 mV, but it shuts down when MP reaches -50 mV. It is not blocked by tetradotoxin TTX.
- At the end of this stage, when RMP reaches -55 mV I_{si} gets activated. It carries Ca^{++} and Na^+ (mainly Ca^{++}). It leads to upstroke. If $[Ca^{++}]_o$ is decreased then both the amplitude and the slope are decreased.
Norepinephrine: ↑ I_f & ↑ I_{Ca}^{++} →↑ slope. It makes RMP less -ve and thus reaching threshold faster.
Threshold is 15-30 mV upward (-65 mV means -35 to -50 mV)
Acetylcholine → ↑ g_K^+ & ↓ I_f & ↓ I_{Ca}^{++}. It makes RMP more -ve but not enough to activate fast Na channels.



In skeletal muscle cells, gk increases (not decreases) during depolarization phase. In cardiac gk shuts down and gx increases.

At RMP $\left[\frac{gNa}{gK}\right]$=0.01. Upon stimulation, and when reaching threshold, allowing Na+ channels to open, gNa increases 500-5000-fold and $\left[\frac{gNa}{gK}\right]$ = 10 in skeletal muscle cells, even though, gK also increases 10-20 times.



IONIC BASES of SRAP

Phase (O):

- The amplitude of AP is 75 vs 120 mV in FRAP.
- The extent of AP is only +10 mV vs +30 mV in FRAP.
- the slope "dV/dt" is smaller than FRAP. Fast Na^+ channels are not activated in SA.
- **is mainly due to I_{Ca} and not to I_{Na}.**
  - I_K also starts to act at this phase.

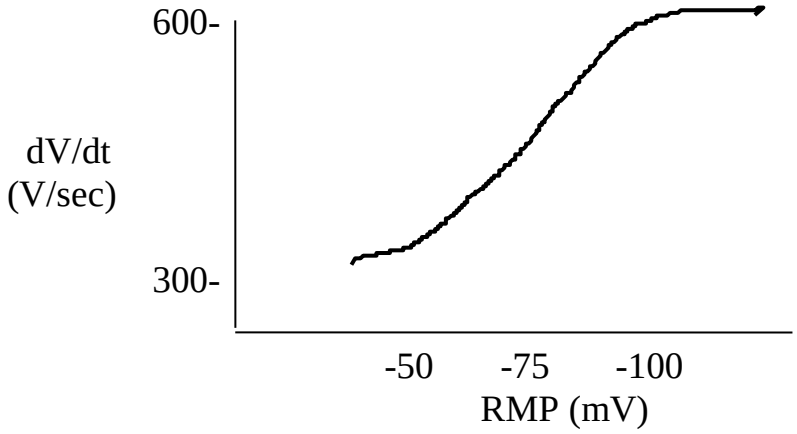
Phase (2):

- Is duo to I_{Ca}^{++} (mainly Ca^{++} and to less extent Na) which is opposed by I_K.
- Its duration is shorter than that in FRAP because I_{K+} turns on fast and I_{Ca++} turns off fast too.

CONDUCTION IN CARDIAC MUSCLE

The slope and the amplitude of depolarization depend on the amount of currents and the time needed for this current to reach maximum. Large current in short period of time causes the neighboring area to depolarize faster. Both things depend on RMP. The more -ve the more the I_{Na}, the more the amplitude the faster the conduction. dV/dt increases with increasing negativity of the RMP.

If [K]o is ↑ → RMP becomes less -ve → ↓ $\mathbf{g}_{Na}$ and thus shifting AP type from FRAP towards SRAP → ↓ conduction.
If H.R increases then AP duration decreases because of the increase in I_K, and the shorter duration of phase (2).



NATURAL EXCITATION OF THE HEART:

Intrinsic Automaticity: The ability to initiate its own beat.
Intrinsic Rhythmicity: The regulatory of such pacemaking activity.

ATRIO-VENTRICULR (AV) CONDUCTION AND THE AV DELAY:

Retrograde conduction through AV node cannot occur, otherwise serious abnormalities develop. Forward conduction is OK, but not backward. In rare circumstances, an abnormal muscle bridge can penetrate the fibrous ring, and therefore, backward conduction may occur leading to serious arrhythmias.

The delay in general is due to 1. Small cell size, 2. More -ve RMP, 3. and less gap junctions.

From SA to left atrium through interatrial bundle. From SA to right atrium through three internodal pathways (0.03 sec delay) (anterior, posterior, and midle)→ transitional fibers (0.04 sec delay) → AV node (0.05 sec delay) → penetrating portion of the AV bundle, where the bundle penetrate the atrio-ventricular fibrous tissue (0.04 sec delay) → Equals 0.16 sec

LECTURE (3)
MICROCIRCULATION (capillary exchange)
*Chapter 14 and 16 (***161-170, and 181-194***)*

Lecture Topics

- Capillaries and Nutrient Exchange.
- Capillary Filtration (Starlings' forces).
- Diffusion of Solute and Water, Osmosis.
- The microcirculation and vascomotion.
- The role of lymphatic vessels.

Objectives:

After completing these two lectures, students should be able:

1. Explain the factors involved in regulation capillary blood flow.
2. Explain the mechanisms that may increase or decrease lymph flow.
3. Define and explain the occurrence of edema.
4. Explain the relationship between blood pressure, plasma protein concentration, and tissue factors in regulating interstitial fluid volume (Starling Forces).

The cardiovascular system provides blood flow to the tissue capillaries. These lectures describe factors that alter capillary blood flow, the mechanisms that contribute to these alterations, and their consequences. It also discusses Starling's Law of the capillaries and how alterations in the Starling forces can contribute to the formation of edema fluid in peripheral tissues and to lung and to tissue dehydration.

STRUCTURE: Single layer of endothelial cells with a coat called basement membrane. The cells show intercellular clefts, intercellular gaps, and intercellular fenestrations.

Idealized capillary: filtration occurs at the arterial end and absorption at the venous end. Glomerular capillary in the Kidney show only filtration across their entire length. Gastrointestinal capillaries show only absorption. Also if precapillary sphincter contract, this specific capillary will exhibit absorption only.

STARLING EQUILEBRIUM:
Pc: capillary hydrostatic pressure= 17.3, Pt = -3, Πc= 28, and Πt=8 mm Hg.

Net outflow force is 0.3 mm Hg. This extra amount is return by lymph. This 0.3 mm Hg causes a filtration of 2 ml/min in the entire body, or 6.67 ml/min.mm Hg/entire body (filtration coef.) which is also equal 0.01 ml/min.mm Hg/100 gm of tissue. This number is so small in the brain and muscle, moderate in subcutaneous tissue, large in intestine, and extreme in liver and kidney.

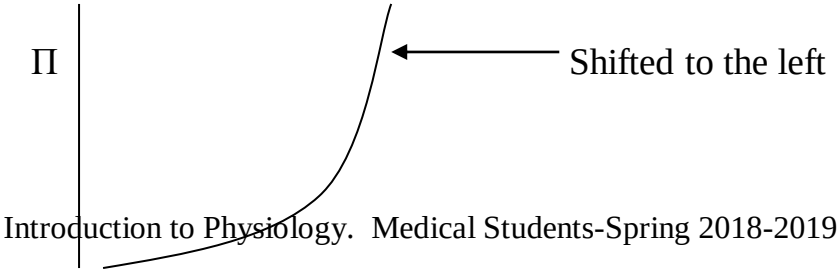
STARLING FORCES:
$F = K [(Pc-Pt) – (\Pi c-\Pi t)]$
At the arterial End these values are:
$F = K [30-(-3)] – (28-8) = K (+13)$ mm Hg
At the Venous End
$F' = K' [10-(-3)] – (28-8) = K(-7)$ mm Hg
At the venous end we have less driving forces but more permeability (more pores K'>K).
Π Osmotic pressure:
$\Pi = \sigma RT\Delta C$
Πc (*c for capillary*):

75-80% duo to albumin 4.5 gm/dl (22mm Hg)

20-25% duo to globulin 2.5 gm/dl (6mm Hg)

Albumin MW is around 70 K and the globulin MW is around 140 K. This means that one gram of albumin contain the same number of molecules as in 2 grams of globulin.
Albumin leaves and re-enter the capillaries under the control of thyroid hormone.
Πt (t for tissue): (8 mm Hg)
Interstitial protein is 40% of that of plasma (the concentration in gm/dl: muscles 1.5, subcutaneous 2 intestine 4, and liver 6).

Its relationship with albumin is not linear… higher albumin → higher Π than expected. If albumin concentration is 8% → Π = 35 mmHg. If albumin concentration dropped to 4% → Π = 10 mmHg (not 17.5). Therefore, edema becomes worse than expected as hypoalbuminemia progresses. For albumin alone cause Π = 22 mm Hg wee need albumin concentration higher that what we really have.

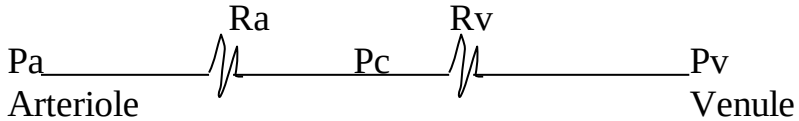


[Albumin]

Capillary Hydrostatic Pressure "Pc":

By direct measurement it shows a decreasing profile 35 at the arterial end, midcapillary 25, and at venous end 15 mm Hg. It averages 20-30 mm Hg, but varies between

1. Organ activity: hepatic sinusoid 6-7 mm Hg
2. Gravity: pulmonary 7 mm Hg
3. Location: kidney 60-70 mm Hg



$$Pc = \left(\frac{\left\langle \left[\frac{Rv}{Ra} \right] * Pa + Pv \right\rangle}{1 + \left[Rv / Ra \right]} \right)$$

Rv/Ra = 1/5

Pc = (1/6) Pa + (5/6)Pv = 16.7% Pa + 83.3% Pv

Note that an increment in Pv has more impact on Pc than Pa does. Pc reflects the P in the draining veins rather than the P in the feeding arteries.

In standing individual → ↑ Pv → ↑ Pc → contraction of precapillary sphincter → closure of some capillaries → ↓ K → works as a protective mechanism against edema.

LYMPH

The Lymphatic (A Scavenger System = الكناس):

A closed-end of highly permeable capillary → larger lymphatic vessels which empty into Lt & Rt subclavian veins. All lymph vessels have valves few mm apart all the way until they empty into systemic circulation.

Its function is extremely important. It cleans proteins, viruses, bacteria etc. If we do not remove interstitial proteins for just 24 hours we will dye. Almost all tissue have lymph with few exception.

10-15% of the fluid filtered return back by lymphatics (2-3 L/day). The flow through the thorax duct is 100 ml/hr and in the Rt lymphatic duct is 20ml/hr. The more the interstitial fluid pressure, the more the lymphatic flow (Fig. 16-11) until it reaches plateau because of the imposing forces on lymph flow. During exercise lymph flow increases 20-30 times.

Factors affecting lymphatic return are the same as for venous return

- Lymphatic vessel wall work as a pump.
- Protein concentration in lymph is the same as interstitial.

EDEMA

- Indicate something being a miss. It interferes with the proper oxygenation of cells, predisposes to infection, cosmetically unpleasant …etc.
- It is accumulation of fluids between cells or inside cavities (pleural effusion, ascites).
- Either localized or generalized.
- Generalized edema means disturbance in ECF regulation.
- Most of the interstitial fluid is in gel form. Small % is in a free fluid form. The later increases in edema (pitting edema). Edema over the legs which is pitting (i.e. leaves a little pit when the fluid is pressed out, which resolves over a few seconds).
- If the cell swell, then the edema is nonpitting, or when fluids are clotted with fibrinogen and thus cannot move freely.

Safety Margin for edema formation

1. 3 mmHg for the negativity of the interstitium, the negative pressure in the interstitium makes is less compliant to accept fluids. Even if interstitial pressure is lowered to -13 mmHg, the tissue duo to proteoglycan microscopic fibers would not allow water to enter between their spaces.
2. 7 mmHg duo to lymphatic drainage
3. 3. 7 mmHg duo to washout proteins from the interstitium through the lymphatic vessels.

All sum to 17 mmHg. If you consider the net filtration pressure across the capillary is 0.3 mmHg, then raising the pressure to 17 mmHg, as if you increase it 55 times. This means lymph flow can increase 50 times normal to take care of the extra fluids filtered.

Etiology: Local Factors & Systemic Factors.
HINTS

Arterioles	Resistance vessels which regulate flow
Capillaries	Exchange vessel
Venules	Exchange and collecting vessel

Main function of the circulatory system is exchange between blood and tissue. 85% of the filtered amount is reabsorbed though the capillaries and 15% through lymphatics.

16ml/min (20 liter/day) is filtered … (this is less than 0.5% of Q). Only 14 ml/min is absorbed. The remaining 2 ml/min is NET filtration and are returned by lymph. Normally only 1/3 of capillaries are open at a given tissue at a given time.

The capillary flow is intermittent because of the rhythmical contraction of metarteriols and precapillary sphincters. However, the hydrostatic pressure in the capillary is not pulsatile because of damping of the pressure pulse. The flow is intermittent but not pulsatile … pulsatile means cyclic change during systole and diastole.

The cells of our body have ICF of 40% and are bathed in ISF of 20% of our body wt. The bathing medium is not enough to keep cell survival for appreciable time. Thus, ISF (ECF) is not a good reservoir and will not keep homeostasis. We need to refresh ISF with new nutrients and continuously remove the waste products exactly as we do in cell culture. This can be achieved by plasma. Therefore, it is important to understand how plasma flow to the tissues is regulated.

Ejection of blood from the heart to the arterial system permits a volume containing nutrients and oxygen to flow to the periphery. In an adult, this is equal to 5 L/min at rest. This volume is distributed to different tissues. Each organ or tissue will receive according to its needs (heart, muscles, brain etc) or according to its function (reconditioner organ such as kidney, liver, lungs, skin….etc). There are factors that impede this flow and others that facilitate it. These two lectures explain these factors and how they influence the arterial or driving pressure as blood flow towards the tissue. Actually, it is the Resistance within that organ which determines its blood flow. If it is increased, blood flow will be shifted to other organs. If it is decreased, that tissue will take most of the Q (such as the muscles during exercise).

- Functional parts of circulation**: arteries → linking system (metarteriols, preferential channels and true capillaries) → veins**
- Blood is distributed as the following:

64% in veins 9% in lungs 13 % in arteries
7% in capillaries 5% in the heart

Resistance to blood flow:
Flow is directly proportional to driving force (ΔP) and inversely proportional to resistance to blood flow (R)……..Q = (ΔP/R)

Balance of Forces (Starling pressures) Involved in Glomerular Ultrafiltration

	Rat	Dog
Mean Arterial Pressure (mmHg)	110	100
Glomerular Capillary Hydrostatic Pressure (mmHg)	45	60
Bowman's Space Hydrostatic Pressure (mmHg)	10	20
Capillary Colloid Osmotic Pressure (mmHg)	28	30

Difference between pulmonary capillary & that of systemic:

	Pulmonary capillary	Systemic capillary
Pc	7-10 mm Hg	17.3 mm Hg
Πc	28 mmHg	28 mmHg
Pi	- 5 mmHg	-3 mmHg
Πi	**14 mmHg***	8 mmHg
Outward Forces	**29 mmHg**	**28.3 mmHg**
Inward Forces	**28 mmHg**	**28 mmHg**
Net force	**1 mmHg Filtration**	**0.3 mmHg Filtration**

***** Πi**: Pulmonary capillaries are leaky to proteins, so the colloid osmotic P in ISF is 14 mm Hg. In systemic is only 7 mm Hg.** No body made a direct measurement, however, by measuring the protein content of lymph coming from the lung scientists predicted this much value. This is the reason behind the controversy in regard to Πi.

Hence, outward forces of 29 mmHg while the inward forces are only equal to Πc=28 mmHg which makes 1 mmHg in favor of filtration. The lymphatic can take care of this small outward fluid keeping the lung dry.

The filtrate will be pumped by the highly effective lymphatic drainage. Actually, if, duo to H.F. the pulmonary capillary P reaches 23 (in dogs) or 28 (human) P (21 mm Hg above normal) pulmonary edema would not develop. (21 mm Hg is a safety factor). That is true in case of acute state, however, in chronic conditions (< 2 WKS) the lung become even more resistant to pulmonary edema and a capillary P of 40-45 develop without significant pulmonary edema (safety factor 40 in chronic while 21 in acute).