THE MICROCIRCULATION AND THE LYMPHATIC SYSTEM

- The most purposeful function of the circulation occurs in the microcirculation: the transport of nutrients to the tissues and removal of cellular excreta

STRUCTURE OF THE MICROCIRCULATION AND CAPILLARY SYSTEM:

- In general, each nutrient artery entering an organ branches 6-8 times prior to forming arterioles (internal diameter 20 micrometres), then further branching 2-5 times to become capillaries (5-9 micrometers)
- Blood from the arteriole passes through a series of metarterioles (terminal arterioles) before entering the capillary
- After leaving the metarteriole, blood enters the capillaries, some of which are large and called preferential channels, whereas others are small and are true capillaries
- Then enters venules
- Arteriolar walls are highly muscular, changing diameter several fold
- At the point where each true capillary originates from a metarteriole, a smooth muscle fibre usually encircles the capillary, called the PRECAPILLARY SPHINCTER
    - Metarterioles and precapillary sphincters are in close contact with the tissues that they serve
        - Great impact on local conditions and resultant changes in blood supply by DIRECT EFFECTS

- STRUCTURE OF THE CAPILLARY WALL:
    - Wall is composed of a unicellular layer of endothelial cells and is surrounded by a basement membrane on the outside
    - **Total thickness capillary wall is only 0.5 micrometers**
    - "PORES":
        - There are only two minute passageways connecting the interior of the capillary with the exterior
            - **INTERCELLULAR CLEFT (slit pores):**
                - Lies between adjacent endothelial cells
                - Fluid can percolate freely through the cleft
                - Does not allow albumin through
                - Only at the edges of cells, thus only represent 1/1000 of the total surface area of the capillary
                - Still sustain rapid diffusion of water and soluble ions
            - **PLASMALEMMAL VESICLES:**
                - Form at one surface of the cell by imbibing small packets of plasma or extracellular fluid
                - Not important

        - Special types of pores occur in certain organ capillaries
            - **Brain:**
                - Tight junctions between cells that only allow small molecules (O_2, CO_2 and H_2O to pass)
            - **Liver**:
                - **Large clefts** that allow even plasma proteins to pass into the liver tissues
            - **Kidney**:
                - Glomerular tufts contain numerous **fenestrae**, so that tremendous amounts of very small molecular and ionic substances can filter through **(esp if <4nm and neutral/cationic)**

VASOMOTION: FLOW OF BLOOD IN THE CAPILLARIES:

- Blood does not flow continuously through capillaries, it **flows intermittently**
    - Called **VASOMOTION**
    - Intermittent contraction of the metarterioles and precapillary sphincters
- REGULATION OF VASOMOTION:
    - The most important factor is CONCENTRATION OF OXYGEN IN THE TISSUES
    - When oxygen usage is great so that tissue oxygen decreases, intermittent flow occurs more often and the duration of each period of flow lasts longer
- AVERAGE FUNCTION OF THE CAPILLARY SYSTEM:
    - Even though flow is intermittent, so many capillaries are present that their overall function becomes averaged (average rate of flow, capillary pressure and transfer of substances)

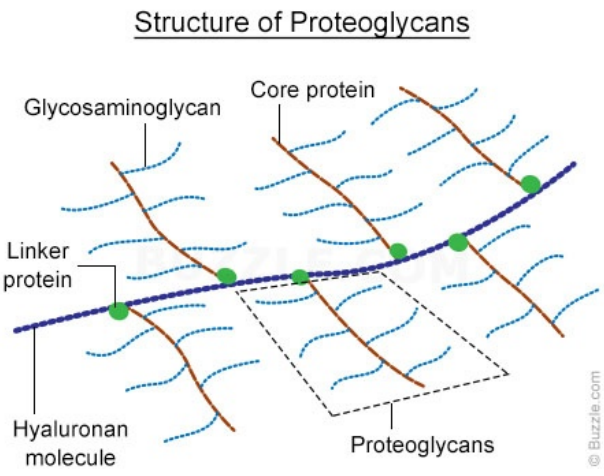
EXCHANGE OF NUTRIENTS BETWEEN THE BLOOD AND INTERSTITIAL FLUID:

- **DIFFUSION** THROUGH THE CAPILLARY MEMBRANE:
    - Diffusion is by far the most important mechanism of transfer
    - LIPID SOLUBLE SUBSTANCES:
        - Can diffuse directly through the cell membranes of the capillary endothelium, without having to go through pores
        - E.g. O_2 and CO_2
        - Rates of transport better than for lipid insoluble substances due to far greater surface area available for diffusion
    - WATER-SOLUBLE, NON-LIPID SOLUBLE:
        - Diffuse through intercellular pores in the capillary membrane
        - E.g. Water molecules, sodium, chloride and glucose

        - Velocity of thermal molecule motion is so great that it makes up for decreased surface area available
- EFFECT OF MOLECULAR SIZE ON PASSAGE:
    - Width of the channel is 6-7 nanometers
    - Diameters of plasma proteins are slightly greater than the width of the pores
    - This determines the permeability or otherwise of water-soluble substances
- HOWEVER:
    - Capillaries in different tissues have extreme differences in their permeability
- CONCENTRATION DIFFERENCE:
    - The "net" rate of diffusion of a substance through any membrane is proportional to the concentration difference between the two sides of the membrane
        - E.g. oxygen in capillary blood has greater concentration than in the interstitial fluid, facilitating transport
        - Converse applies for CO2

THE INTERSTITIUM AND INTERSTITIAL FLUID:

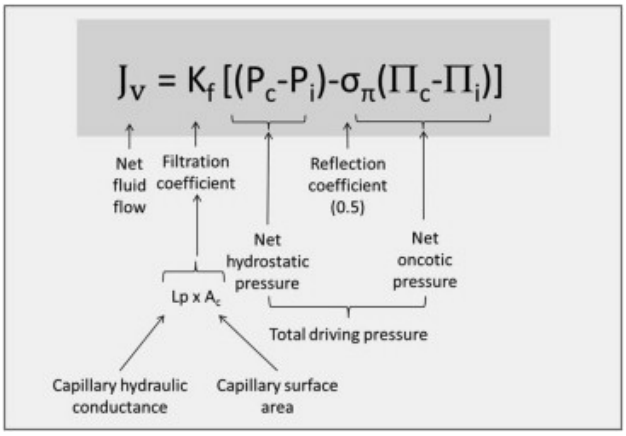
- About one sixth of the body consists of spaces between cells, which collectively are called the interstitium and the fluid is called the interstitial fluid
- Two major types of structures in the interstitium:
    - **COLLAGEN** FIBRE BUNDLES
        - Extremely strong and provide most of the tensile strength
    - **PROTEOGLYCAN** FILAMENTS:
        - 98% **hyaluronic acid**



- "GEL" IN THE INTERSTITIUM:
    - Derived by filtration and diffusion from the capillaries
    - Same components of plasma except for **much lower plasma protein concentration**
    - **Fluid trapped in spaces among the proteoglycan** -> forming a gel
        - Fluid diffuses rather than flows
            - Allows rapid transport of water, electrolytes, nutrients and excreta
- FREE FLUID IN THE INTERSTITIUM:
    - Free of proteoglycan, thus fluid can flow freely
    - Free fluid expands dramatically in patients who have developed oedema

FORCES THAT DETERMINE FLUID MOVEMENT THROUGH CAPILLARY MEMBRANE:

- CAPILLARY PRESSURE:
    - Functional capillary pressure about 17mmHg
    - Tends to force fluid outward through the capillary membrane
- INTERSTITIAL FLUID PRESSURE:
    - Forces fluid inward when positive and out when negative
    - Usually values are positive in tightly encased tissues (cranial vault around the brain, fibrous capsule around the kidney, sheaths around muscles, sclera around eye)
        - Usually these pressures are still less than the pressure exerted by these capsules on the outside of these tissues
    - Usually values are negative in loose subcutaneous tissue, thereby holding these tissues together
    - LYMPHATIC SYSTEM ACTS AS A SCAVENGER:
        - Removes excess fluid, protein molecules, debris and other matter
        - **Lymphatic capillaries propel fluid forward, creating NEGATIVE INTERSTITIAL FLUID PRESSURE**



- PLASMA COLLOID OSMOTIC PRESSURE (ONCOTIC PRESSURE):
    - Proteins are the only significant dissolved constituents that do not readily penetrate the pores of the capillary membrane
        - It is the dissolved proteins in the plasma and interstitial fluid that are responsible for the osmotic pressure on the two sides of the capillary membrane
    - **Normal value for human plasma is about 28mmHg**
        - 19mmHg contributed by dissolved **protein** and 9mmHg contributed by **cations** held in the plasma by the proteins **(DONNAN effect)**
    - Osmotic pressure is determine by the number of molecules dissolved in a fluid rather than by the mass of these molecules, hence albumin having greater impact than fibrinogen or globulins.
        - **Albumin accounts for 80% of the total colloid osmotic pressure**

- INTERSTITIAL FLUID COLLOID OSMOTIC PRESSURE
    - Average protein concentration of the interstitial fluid is usually about 40% of that in plasma
    - Pressure equates to about 8mmHg in normal adults

- Net outward force at the arterial end is about 13mmHg
- Net inward force at the venous end is 7mmHg
    - Remember that **venous capillaries are more numerous and more permeable than the arterial capillaries**, so that less pressure is required to cause the inward movement of fluid
    - **90% is reabsorbed by venous system, remainder by lymphatics**

- **Compared to interstitium… capillary blood has**
    - **Higher hydrostatic pressure**
    - **Higher oncotic pressure**
- **Net efflux of fluid at arteriole end (13mmHg outwards)**
- **Net influx of fluid at venous end (7mmHg inwards)**
- **But the venous side of the capillaries are more permeable, so most fluid is reabsorbed (90%)**
- **10% goes to lymphatics.**

- **ABNORMAL IMBALANCES OF FORCES AT CAPILLARY MEMBRANE:**
    - If the mean capillary pressure rises above 17mmHg, the net force tending to cause filtration increases

TABLE 31–12 Causes of increased interstitial fluid volume and edema.

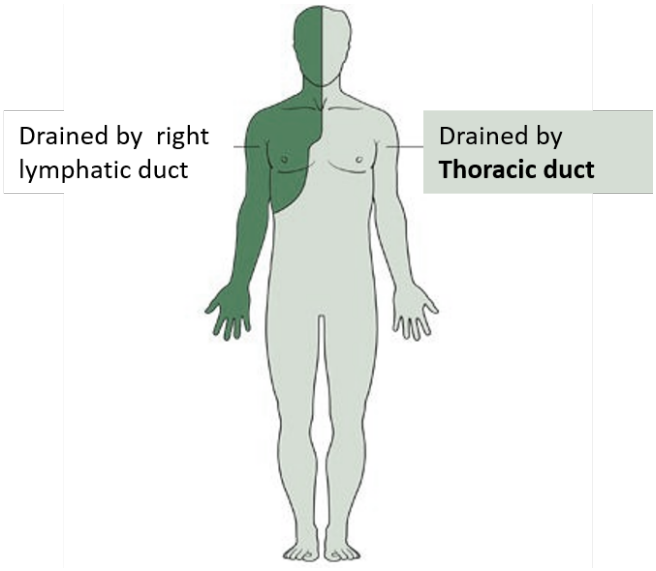
Increased filtration pressure
Venular constriction
Increased venous pressure (heart failure, incompetent valves, venous obstruction, increased total ECF volume, effect of gravity, etc)
Decreased osmotic pressure gradient across capillary
Decreased plasma protein level
Accumulation of osmotically active substances in interstitial space
Increased capillary permeability
Substance P
Histamine and related substances
Kinins, etc
Inadequate lymph flow

I.e. oedema determined by Starlings equation:

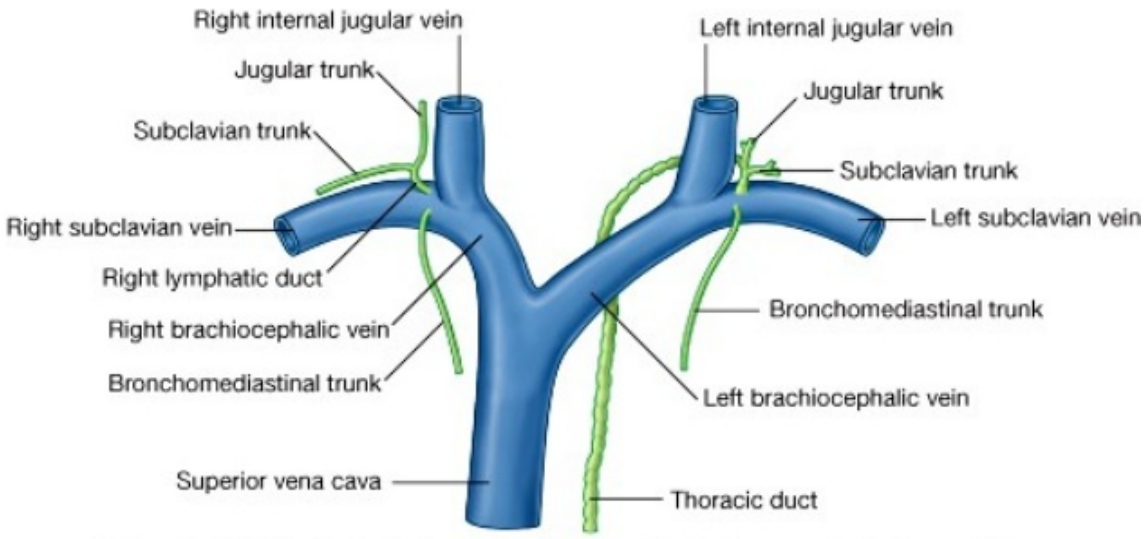
- **Changes in net hydrostatic pressure**
- **Changes in net oncotic pressure**
- **Changes in filtration coefficient (vessel permeability)**

LYMPHATIC SYSTEM:

- Represents an accessory route by which fluid can flow from the interstitial spaces into the blood
- Lymphatics can carry proteins and large particulate matter away from the tissue spaces
- LYMPH CHANNELS:
    - Almost all tissues of the body have lymph channels
    - **TISSUES WITHOUT WELL FORMED LYMPHATICS**:
        - Superficial portions of the skin
        - CNS
        - Endomysium of muscles
        - Bones
        - Even these areas have interstitial channels called "pre-lymphatics"
    - Essentially all lymph from the lower part of the body eventually flows up the thoracic duct and empties into the venous system at the juncture of the left IJV and subclavian vein (where it forms the brachiocephalic vein)
    - Lymph from the left side of the head, the left arm and parts of the chest also enter the thoracic duct
    - Lymph from the right side of the neck and head, right arm and parts of the right thorax enter the right lymph duct which then empties into the venous system at the juncture of the right subclavian vein and IJV



Termination



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- TERMINAL LYMPHATIC CAPILLARIES:
  - **About 10% of the fluid filtered enters the lymphatic capillaries and returns to the blood through the lymphatic system**
  - Normally 2-3 litres/day
  - Highly important as high molecular weight substances, such as proteins cannot be absorbed from the tissues in any other way
    - Passage is facilitated by special structure of terminal lymphatic capillaries:
      - Endothelial cells attach by anchoring filaments to the surrounding connective tissue, allowing free edge to flap inwards, but forms valve function preventing back flow
- FORMATION OF LYMPH:
  - Derived from interstitial fluid that flows into the lymphatics
  - **About 2/3 derived from liver and intestines**
  - Usual protein concentration of 3-5g/dL.
- Lymphatics also one of the major routes of **absorption of nutrients**
  - **Especially fats**
- RATE OF LYMPH FLOW:
  - Effect of interstitial fluid pressure on lymph flow:

        - Very little flow if interstitial fluid pressures are more negative than-6mmHg
        - Increases rapidly though
    - Any factor that increases interstitial fluid pressure also increases lymph flow:
        - Elevated capillary pressure
        - Decreased plasma oncotic pressure
        - Increased interstitial oncotic pressure
        - Increased permeability of capillaries
    - NOTE:
        - **If interstitial fluid pressure increases more than +1-2mmHg, then lymphatic flow DOES NOT increase at still higher pressures**
        - **I.e. lymphatic outflow from interstitium quickly reaches a maximum.**
    - LYMPHATIC PUMP:
        - **Valves exist in all lymph channels**
        - Lymphatic vessels **pump in response to stretch**
        - Each segment between successive valves acts as separate automatic pump
        - **Lymphatic capillary endothelial cells are contractile, containing actinomysin filaments**
        - FURTHERMORE:
            - Pumping is also caused by intermittent compression of the lymphatics by:
                - Contraction of surrounding skeletal muscles
                - Movement of parts of the body
                - Pulsation of arteries adjacent to lymphatics
                - Compression of the tissues by objects outside body
- FEEDBACK LOOP OF LYMPHATIC FLOW:
    - Leaked proteins tend to accumulate in the interstitial fluid and this in turn increases the colloid osmotic pressure of the interstitial fluids
    - Increasing interstitial oncotic pressure shifts the balance of forces in favour of filtration into the interstitium, thus increasing fluid volume and interstitial fluid pressure
    - Increasing interstitial fluid pressure greatly increases the rate of lymph flow, which in turn carries away excess interstitial fluid volume and excess protein