Cellular Biophysics
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Hagen - Poiseuille equation

We have so far spoken about mobility and viscosity with respect to an object. Now, I want to switch a little bit to just fluids themselves. And in this respect, we are going to review a law that is referred to as Hagen-Poiseuille equation.

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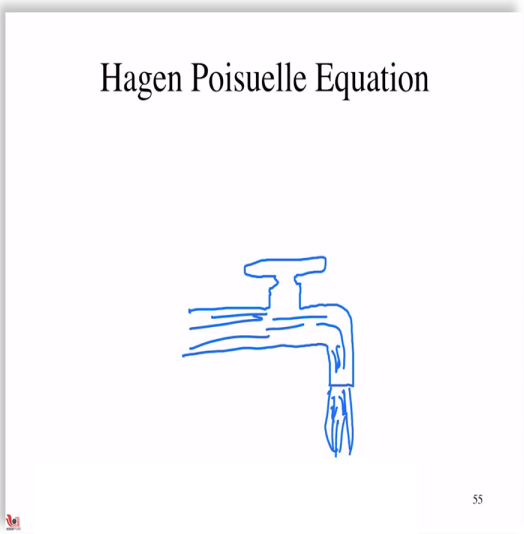

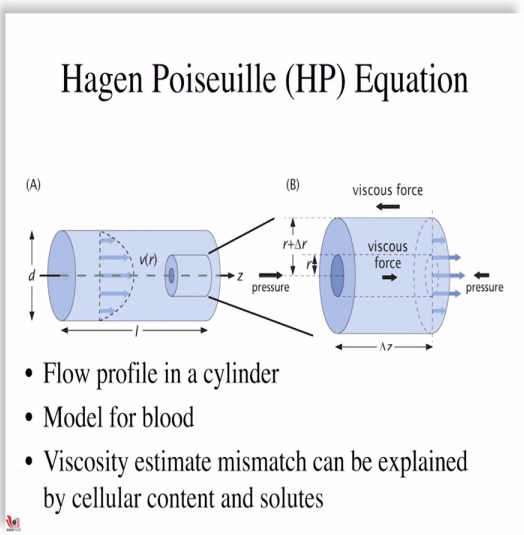

Now, the relevance of this equation is with regard to the fact that when fluids are in a pipe they have a certain flow property and you are all familiar with tap water I hope you all have access to what we usually think of in terms of flow is this picture where the velocity of flow is not uniform in the pipe. In other words, it is uniform along the L axis the part here along the length, but along radius or the diameter it shows a characteristic trend, which you can see with these arrows of increasing lengths in the case of this arrow it is small, long, longer still small, smaller and dissipating.

These are also called no slip conditions, which means that the velocity of flow of a fluid flowing through a pipe at the boundaries that is to say at the wall of the pipe is zero. And as you go to the center as far away from the pipe wall as possible, v of r that is velocity as a function of radial position reaches its maximum. If you now consider a sub part of this pipe or parcel we may say a segment of it concentric with the pipe itself, but of a smaller diameter, we can understand that we can make infinitesimally smaller and smaller and smaller cylinders within the cylinders as you mean pipe as a simple cylindrical geometry.

Knowing the radius of the inner cylinder and the difference to the radius of the concentric and larger cylinder, we can demonstrate that the viscous forces at the boundary between the two cylinders act to create drag as we go outwards there is more and more drag and at an extreme view, the outermost cylinder meaning the one in contact with the pipe boundary is at zero. The arrows here indicate that there is a pressure which is different from the two ends.

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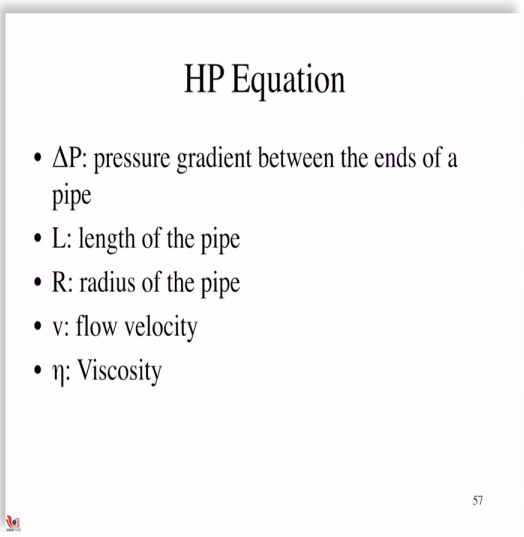

This results in us having a pressure gradient a drop in pressure across the length of the pipe. In fact, you will be surprised to know that this is a good model for flow of blood in our blood vessels and this is where what is otherwise considered a very engineering problem. I spoke about tabs at the beginning becomes a very biological problem. In fact, it turns out that given the flow velocities of blood in blood vessels, the viscosity that it appears to suggest may be higher than the viscosity of serum. If you recall our earlier section on centrifugation serum is the non cellular part of blood. The difference in viscosities can be explained by the presence of cellular content as well as solutes.

Now, further Hagen Poiseuille equation, we need to take into consideration a few symbols, for example, the pressure gradient between the ends of the pipe as I mentioned earlier, which is Δp, the length of the pipe L, the radius of the pipe R, flow velocity and viscosity.

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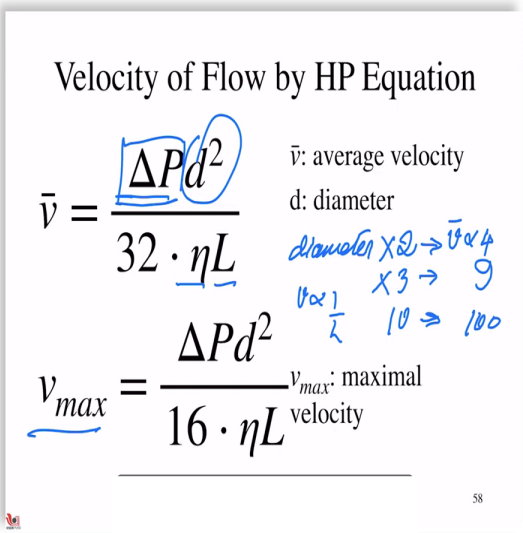

I am not going to derive the equation for the flow velocity, because these are roughly 100 year old results and you are welcome to look up classical physics textbooks that help you derive it suffice to say they are based on solving for velocity as a function of radial position giving you a spatial profile of velocity, which if integrated over the diameter gives you the average velocity, which is what is noted here. So, the average velocity is equal to Δp that is the pressure difference, pressure drop times the square of the diameter of the pipe up on 32 η L, let us just take a look at this equation and ask what does it mean.

And what I mean by what does it mean is that supposing we increase the diameter of the pipe by a factor of 2 it implies that the average velocity increases by a factor of 4, if we increase it by a factor of 3 by a factor of 9, 10, by a factor of 100 I hope you notice this is due to the quadratic nature or we call it the squared dependence of velocity on diameter. Incidentally, when we do such a thing, we assume that all other parameters are constant length is constant η is constant and more importantly the pressure drop is constant.

If we increase the diameter, you have to make some effort to keep the pressure drop constant, anyone who has used a hose pipe to water plants or been in a farm you know this intuitively, at the same time, an increase in the length only results in an inverse proportionality to flow velocity all other parameters being constant.

This suggests that if we are thinking in terms of biological principles of physical regulation of blood flow, then in a capillary for example, it could be considered to be more advantageous to simply increase or decrease the diameter of the blood vessel to get a very big change of quadratic change in the velocity average the quadratic dependence on diameter is consistent between average velocity and maximal velocity, which is But sometimes we are not interested in velocity because remember velocity is meters per second in units its length per time in dimensions. But in flows and volumes, how much volume flows.

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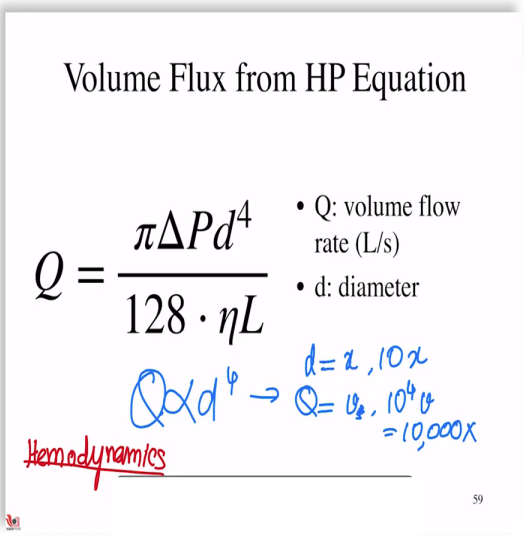

So, to do that, we need to do some arithmetic and derive the expression which I have just presented here for the volumetric flow rate of volume flux that comes out of the HP equation or the Hagen Poiseuille equation. Here, interesting enough, the volume flow rate now scales not quadratically but by the power of 4 with the diameter suggesting that if the diameter goes from some x to 10x the volumetric flow rate goes from V1, V2, to 10^4 V1, that means a tenfold change in diameter results in a 10,000 fold change in the volumetric flow rate this is quite dramatic. Often this question is framed in the question about what is the purpose of modifying flow rate in terms of the physiology of what is being trying to be achieved by the body.

Is the body trying to put more volume of blood in a certain part because it is getting cold? Or is there a need to supply more white blood cells? Is there a need to get them faster there? Is there a need to carry away carbon dioxide from a certain region of the tissue? Should it be optimizing

volume? Should it be optimizing length? All these questions are part of a discipline referred to broadly as hemodynamics. And if you want to learn more, I recommend you read more about it.

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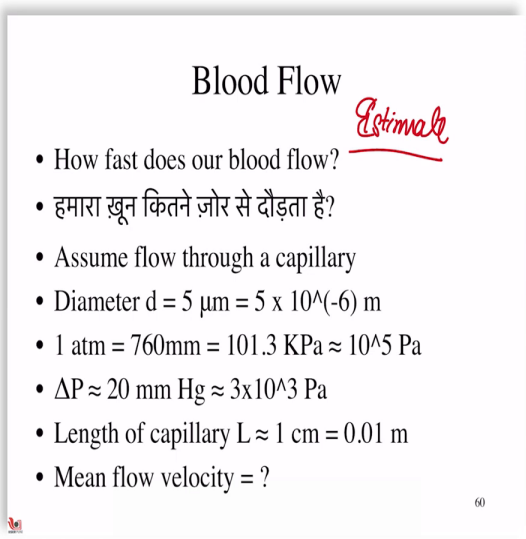

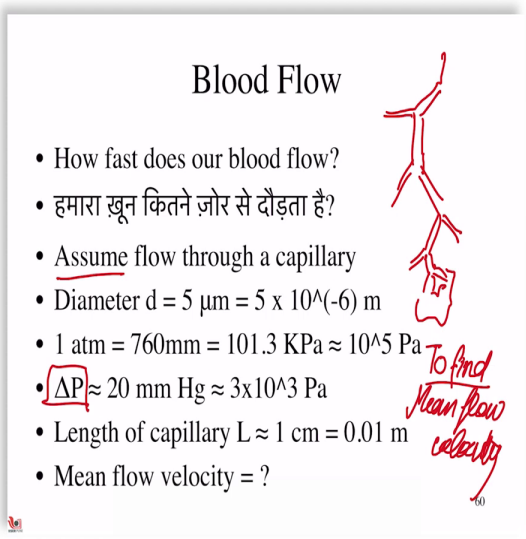

So, given that we know that blood can flow at a certain rate, can we get an estimate? Or in Hindi one would say “Khun kitna zor se daudta hai”, how fast does your blood flow? We are all so used to assuming that people whose blood flow is very fast are very hot headed and tempered. Again, these are anecdotes I do not want to say more about them.

But from a physiological perspective, and biological perspective, we do want to quantify this and we ask how do we get at this number? So, we need to make some assumptions in order to get a general value otherwise, we will not reach any answer. So, we assume that the flow is through a capillary.

As you recall, capillaries are the smallest vessels to which blood vessels branch and they encounter cells and organs and tissue material to which they are delivering oxygen and nutrients or taking away carbon dioxide and waste. These are also some kind of terminal blood vessels and they have an approximate diameter of 5 micrometers that is 5×10^{-6} meters.

In order to calculate rate of flow or velocity of flow, we will aim to calculate the average flow rate or flow velocity of blood, in order to complete this calculation, we need a few more details we need ΔP which means we need to know the difference between two ends of a blood vessel. Now, usually the medical methodology of measuring blood pressure again many of you have been to clinician you know that they use a Mercury readout in terms of column height of mercury.

And the pressure of the atmosphere used in Barometers is 760 millimeters that corresponds to one atmospheric pressure at sea level, 760 millimeters corresponds to 10^5 Pascal that is 101.3 kilo Pascal, but human blood pressure typically is in the range of 20 milli molar mercury height that means, it is approximately 30 times smaller than atmospheric pressure. So, if we take 10^5 or 1 or 1.3 kilo Pascal and divided by 30 we should end up with about 3 kilo Pascal which is 3 into 10^3 Pascal.

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Velocity of Flow by HP Equation

$$\bar{v} = \frac{\Delta P d^2}{32 \cdot \eta L}$$

$\bar{v}$: average velocity

d: diameter

$$v_{max} = \frac{\Delta P d^2}{16 \cdot \eta L}$$

v_{max}: maximal velocity

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Blood Flow

$\frac{\Delta P d^2}{32 \eta L} = \frac{3 \times 10^3 \text{ Pa} \times (1/100)^2}{}$

- How fast does our blood flow?
- हमारा ख़ून कितने ज़ोर से दौड़ता है?
- Assume flow through a capillary
- Diameter d = 5 μm = 5 x 10^(-6) m
- 1 atm = 760mm = 101.3 KPa ≈ 10^5 Pa
- ΔP ≈ 20 mm Hg ≈ 3x10^3 Pa
- Length of capillary L ≈ 1 cm = 0.01 m
- Mean flow velocity = ?

To find Mean flow velocity

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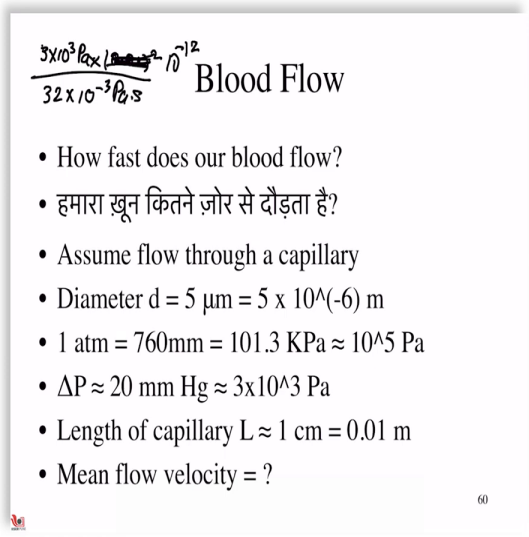

The length of the capillary which we also need for this calculation is approximately 1 centimeter. So, to calculate the mean velocity mean for velocity we only need to substitute into this since length is we said 1centimeter that is 0.01 meter 100^{th} of a meter, ΔP was 3000 Pascal and the denominators the constant 32 we can write 3 x 10^3 Pascal into 1 by 100 squared meters square 3 x 10^3 Pascal into 0.01 squared upon 32 into 10^3 Pascal second into N which is 1 centimeter or 5 microns 10^{-6} m, 10^{-12} you can do the calculation yourself and we will discuss the answer in class when it happens you should get an answer that is comparable at least conceptually with the answer found in experiment.

So, of course, you should ask the question now, what is the value found in experiment and in fact how does one measure blood flow velocity experimentally? So, I will answer the first question and for those interested I will encourage you to go back and look in textbooks of Bioengineering and hemodynamic talks about the method of measurement of blood flow velocity in capillaries. So, the experimentally measured rate is 0.05 centimeter per second we want to find out what is it given these numbers.

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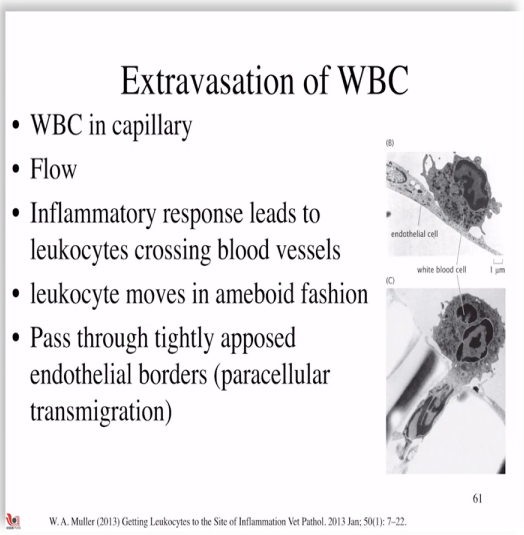

Now, if it is 0.05 centimeters per second, which is 0.5 millimeters per second, which is 500 microns per second, we want to know whether this has any effect on any physiological process. So, the physiological process we will concentrate on is referred to as extravasation. And I refer you to a paper in veterinary pathology called getting leukocytes to the site of inflammation. As it turns out, that while the blood is flowing along with the red blood cells and white blood cells. Now, as suspended particles are also flowing, they are moving and so long as there is active pressure and flow the particles the cells keep moving with the flow.

They are incapable of resisting the flow but during inflammatory response, leukocytes, white blood cells are required to cross blood vessels, they move in an amoeboid fashion like amoeba and pass through the endothelial borders in something called paracellular trans migration, it is a big word but what it implies is that the endothelial border, I mean, think about it like this, that the blood vessels have to be made of cells that make tight junctions between them, the walls of the blood vessels, because otherwise the blood will leak.

So obviously, for the process of blood flow to be intact, blood vessel junctions have to be tight to the cells, but at the same time when leukocytes need to respond to inflammatory activity, and signaling, the blood vessels need to also allow the WBCs leukocytes to pass through the borders. This is called para cellular trans migration.

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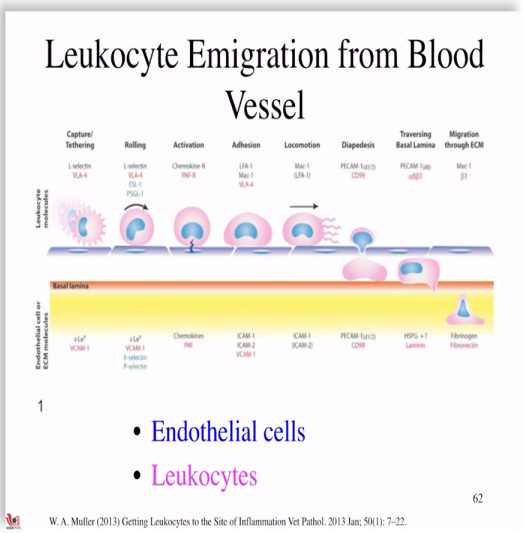

The first step in this process is the capture and tethering of leukocytes on the endothelial cells. So, the molecules involved in this capture process are selectins, and there is a lot of biophysics. That has been done on the specific nature of selectin mechanics and their role in mediating leukocyte emigration from blood vessels.

Once the leukocyte is captured or tethered, it does what is called ruling motility. It kind of rolls around the surface. The activation of chemo coins ending with adhesion and amoeboid locomotion are followed by diapedesis. They the cells then traverse the basal lamina which is an outer layer of the blood vessels. So I mentioned the endothelial cells, but there is a little bit more to the blood vessels and just endothelial cells and then eventually migrate through the extracellular matrix in a manner driven by fibronectin.

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So, leukocyte migration is unusual in many respects, because these cells can be passive particles that go with the flow or they can also migrate upstream against the flow and they are able to resist the drag force of blood flow. The intraluminal crawling, this is that we refer to over here as locomotion after adhesion is mediated by a subset of leukocyte integrands, integrands as you know, are molecules that allow for cell adhesion.

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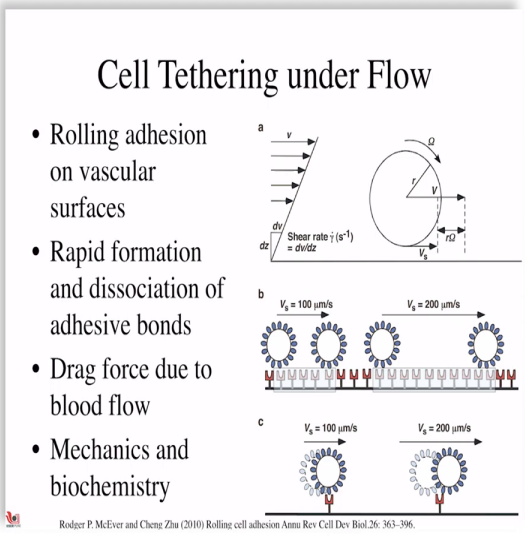

Now, you know, in a simple consideration that is described by Roger McEver and Cheng Zhu. The ruling cell adhesion of leukocytes happens while there is a shear rate being imposed on the fluid. So, if we treat a leukocyte for a moment as a ball or a circle, rolling in two dimensions on a line, which is the boundary of the blood vessel, then we get a ruling angular frequency Ω, a linear translational velocity v. And a surface velocity vs, the shear rate is

$$\dot{\gamma} = \frac{dv}{dz}$$

dv is the change in velocity, dz is the incrementing height from the blood vessels. So, you could say along the radius of the blood vessels, but going from outside to inside this time, I mean from the wall to the inside. The process by which leukocyte rolling motility occurs involves range of velocities that are interspersed between hundreds of microns per second to 200 hundreds of microns per second. And potentially this is due to the binding. These selectins that bind to leukocyte cell surface markers have a peculiar nature in terms of their binding that is referred to as a catch on slip bond.

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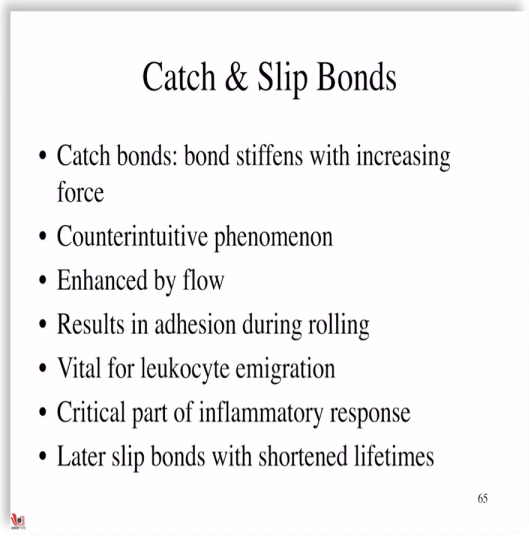

Catch bonds are those whose affinity increases within reinforce, in other words, the bonds difference with increasing force, it is a very unusual thing to think about think about it. If you are trying to remove a bandage from a wound, and as you pull at it, if that bandage becomes tighter bound, this will be very difficult, it will be harder to remove it. It is counterintuitive in that sense.

So, in the case of the selectin leukocyte bond formation, the force that is acting to detach it is the flow as it appears in measurements, this binding force is enhanced by flow. It in fact is a major cause for reliable adhesion and emigration of leukocytes. And it is vital for leukocyte migration to positions where the inflammatory response is triggered. It also happens that the catch bond is accompanied by a slip bond, where force reduces the lifetime this is something that we are more familiar with. This combination of stick and slip is thought to result in reliable leukocyte extravasation.

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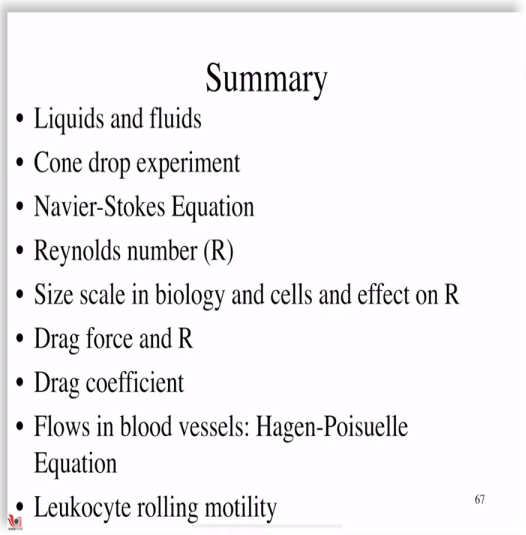

So, with this I end this segment and to summarize, we talked a bit about liquids and fluids and the distinction between gases and liquids. We revisited the cone Drop Experiment in terms of how to make the cone and how to quantify this measure. It is not called Reynolds number when he discovered it as a measure of the qualitative nature of the flow arising out of drag force. We then spoke about the dimension this constant called the drag coefficient which is dependent on the shape of the object. And finally, we spoke about the Hagen-Poisuielle equation applied to flows in blood vessels and leukocyte rolling motility as a feature of the response of the cells to inflammation. That is it for now.