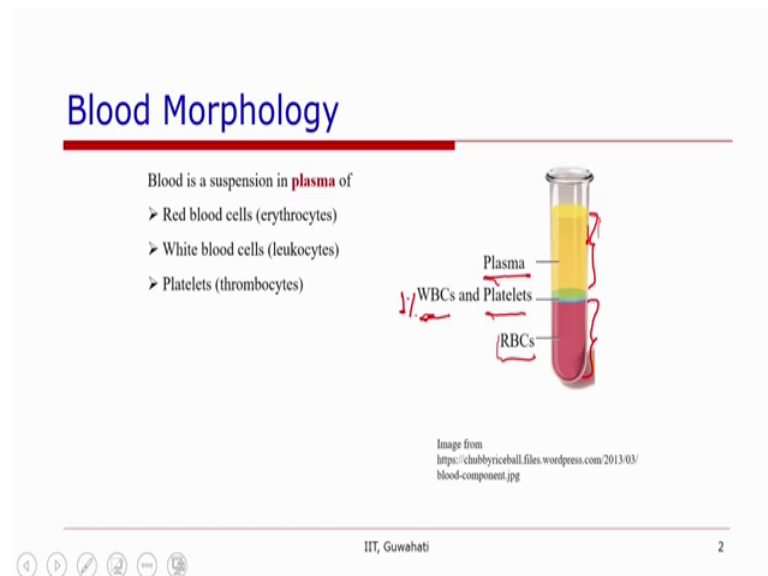


Cardiovascular Fluid Mechanics
Dr. Raghvendra Gupta
Department of Chemical Engineering
Indian Institute of Technology Guwahati

Lecture – 05
Blood Morphology

In the last lecture we looked at the Rheology fundamentals. We looked at what is rheology and what are different models that can be used to explain the non Newtonian behaviour of complex fluids. We also saw that when there are particles suspended in a simple fluid, the suspension of particles in a simple fluid behaves as a complex fluid. So, as we know that blood is a suspension of different flexible particles in a simple fluid, we need to understand first the different components and their mechanical properties in the blood or its then mechanical property. So, in this lecture we are going to look at the different components of blood and their properties.

(Refer Slide Time: 01:40)



So, as you can see in this image if we separate the different parts of blood, it has a clear fluid called plasma and in this plasma there are 3 different types of particles called white blood cells, red blood cells and platelets which are suspended in the blood. They are also known as red blood cells are known as erythrocytes white blood cells are known as leucocytes and platelets, they are helpful in the process of they are one of the major

factor in the process of thrombocytes or clot formation, so they are also known as thrombocytes.

You can see from here that plasma constitute about 55 percent of blood and red blood cells they constitute about 40 to 45 percent of the blood, and white blood cells and platelets they constitute about 1 percent of the blood volume, so let us look at these component one by one plasma.

(Refer Slide Time: 02:58)

Plasma

- An incompressible, Newtonian fluid
 - Viscosity 1.1-1.6 cP
 - Generally taken as 1.2 cP at 37°C
 - Density 1030 kg/m³
- Contains
 - Plasma proteins
 - Blood clotting factors
 - Sugars
 - Lipids
 - Vitamins
 - Hormones
 - Enzymes
 - Antibodies

IIT, Guwahati 3

Plasma is an incompressible Newtonian liquid which has a viscosity of about 1.1 to 1.6 centipoises. The viscosity of blood is dependent on a number of factors on the age of the human, the weather, the geographical conditions, the race the pathos physiological condition, it can also vary with the day and time of the day.

So, it is a very variable property, so there is it is not possible to have or give one value of viscosity and there is one range. Nominally for calculation purposes; it is generally taken as 1.2 centipoises at 37 degree centigrade which is body temperature. It is not known what is the, a how the viscosity of plasma blood behaves with temperature.

So, it is generally it is generally studied all the rheological measurements are generally performed at body temperature which is about 37 degree centigrade. The density of plasma is about 1030 kg per meter cube which is same as that of water and plasma apart from water it contains different kind of molecules, protein, plasma proteins, blood

different blood clotting factor from blood clotting factor 1 2 3 4 and so on and sugars lipids vitamins hormones enzymes antibodies ok.

(Refer Slide Time: 04:52)

Plasma

- Plasma contains 3 major types of proteins:
 - Albumin:
 - A small molecule
 - Provides colloidal osmotic pressure in plasma
 - Globulin:
 - A relatively symmetric molecule
 - Involved in transport of lipids and antibody reactions
 - Fibrinogen:
 - A large, asymmetric molecule
 - Plays major role in coagulation of blood

IIT, Guwahati 4

So, among the proteins plasma contains 3 major type of proteins, albumin which is a small molecule and it provides the colloidal osmotic pressure in the plasma, the another protein which is present in plasma is globulin and it is a relatively symmetric molecule and it is mainly involved in the transport of lipids as well as in the antibody reactions. The third protein is known as fibrinogen, it is a large asymmetric molecule and it plays a major role in the coagulation of blood or thrombosis process. All of these also effect the viscosity of plasma to a extent; the second major component of blood is red blood cells and they constitute more than ninety 9 percent of particulate matter.

(Refer Slide Time: 05:47)

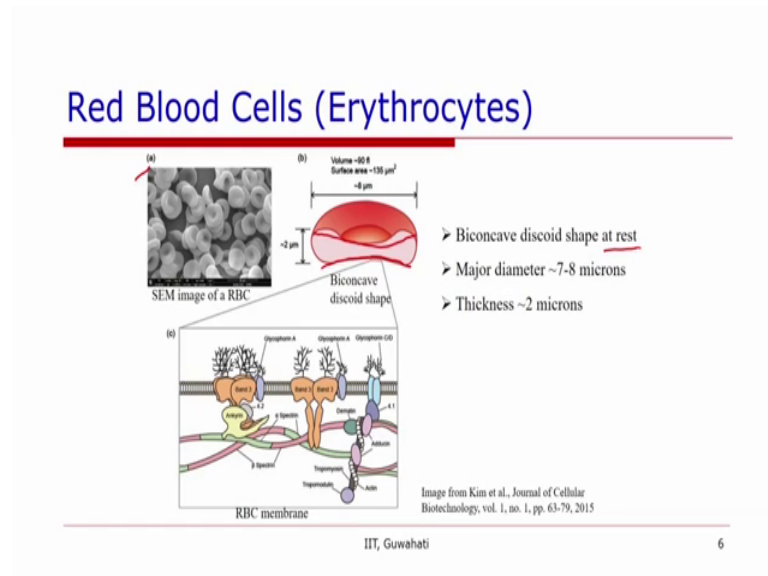
Red Blood Cells (Erythrocytes)

- Constitute more than 99% particulate matter in blood
- 40-45% of the blood by volume
- Proportion of blood that is RBC is called Hematocrit (Hct)
- $Hct = \frac{\text{Volume of RBCs}}{\text{Volume of blood}} \times 100$
- Hct = 40 in men and 38 in women
- 5.2×10^6 per mm^3 in men; 4.7×10^6 per mm^3 in women
- Dominate rheological behaviour
- Density 1080 kg/m^3

Particulate matter means particles. So about 99 percent of the particles which are present in the blood are red blood cells or erythrocytes; the volume fraction of red blood cells in the blood is about 40 to 45 percent and because it is an important factor pathologically. So, this has been given a specific name, a the volume fraction of red blood cell in the blood is known as hematocrit, which is percentage volume fraction of red blood cells in the blood. The Hct or hematocrit in man is about 40 and about 38 in women on an average.

The number of red blood cells per millimetre cube is about 5.2 million in man and about 4.6 or 4.7 in per millimetre 4.7 million per millimetre cube in women; again these numbers are only indicative. So, because the red blood cell constitute the major suspended particles in plasma. So, they determine or they are the main factor determining the rheological behaviour of the blood. The density of red blood cells is not very different from plasma it is about $1080 \text{ kg per meter cube}$, whereas that of plasma is about $1030 \text{ kg per meter cube}$.

(Refer Slide Time: 07:47)



So, on this image what you see here in part a is a SEM image of RBC and you might notice there that the shape of an RBC is a disc shape, which is biconcave concave on both sides and the diameter of this disc is about 7 to 8 micron and 2 micron is the thickness of the disc. So, the red blood cells are disc shape particles, they are not spherical in shape and this shape is at rest, so they can deform from this shape under the flow conditions.

(Refer Slide Time: 08:37)

RBC: Shape

- Function: Transport haemoglobin which in turn carries oxygen.
- Mass transfer: High surface area per unit volume desired
- Volume of RBC is about 90 μm³
- Cell surface area of 140 μm²
- Compare the surface area with that of the sphere of same volume.
- RBC has the ability to change shape without changing its volume or surface area

$$V = \frac{4}{3} \pi R^3$$

$$R = \left(\frac{3V}{4\pi} \right)^{1/3} = 2.78 \mu\text{m}$$

$$S_{\text{sph}} = 4\pi R^2 = 97 \mu\text{m}^2$$

IIT, Guwahati 7

As we know that red blood cells they have haemoglobin in it, and the function of haemoglobin is to carry oxygen to different parts of the blood. So, it should have very good rate of mass transfer and mass transfer is dependent on the surface area; the higher the surface area the higher the rate of mass transfer. So, red blood cell should have higher surface area per unit volume it is desired.

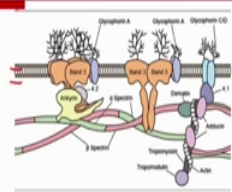
The volume of RBC is about 90 micron cube and the cell surface area is about 140 micron square. So, the minimum surface area for a given volume is that of a sphere let us compare this number with that of a sphere. So, for a sphere the volume is $\frac{4}{3} \pi R^3$ and R will be $\sqrt[3]{\frac{3V}{4\pi}}$. So, if we substitute it here we will get the radius to be about 2.78 microns; now we calculate the surface area of a sphere of this volume that is equal to $4\pi R^2$ we will get about 97 micron square.

So, the surface area of discoid shape is about 1.5 times of a sphere of the same volume, and because of this property RBC have the ability to change their shapes without actually changing the surface area or the volume. So, they can take infinite number of shapes, different shapes without having extra stress on the membrane surface.

(Refer Slide Time: 11:04)

Red Blood Cells (Erythrocytes)

- RBC membrane:
 - A viscoelastic solid
 - Thickness of 80 nm
 - Phospholipid bilayer
 - Purely viscous
 - Almost no contribution to elastic behaviour
- Membrane Cytoskeleton
 - A network of proteins (Spectrin etc.) lying just beneath the cell membrane
 - Responsible for maintenance of the biconcave discoid shape



The diagram illustrates the structure of the red blood cell membrane. It shows a phospholipid bilayer with various proteins embedded within it. Some proteins are integral, spanning the membrane, while others are peripheral, attached to the surface. Below the membrane, a network of proteins (the cytoskeleton) is shown, which is responsible for maintaining the biconcave discoid shape of the cell. Labels include Glycophorin A, Glycophorin B, Glycophorin C, Ankyrin, Spectrin, Band 3, and Band 4.1.

IIT, Guwahati
8

The membrane of the RBC it is a viscoelastic solid and it is made up of phospholipids bilayer. Bilayer means 2 layers; so 2 layers of lipids here and this layer is purely viscous it does not contribute the RBC as we said earlier that it is a viscoelastic solid, but this lipid bilayer does not contribute towards the elastic behaviour, elastic behaviour comes

from membrane cytoskeleton, which is a network of proteins; just below the lipid bilayer and this is responsible for the biconcave shape.

It gives the shape whatever shape the RBC have, it is responsible for the shape biconcave discoid shape, it is responsible for the shape of the RBC and the thickness of this membrane is about 80 nanometre.

(Refer Slide Time: 12:03)

Red Blood Cells (Erythrocytes)

- Filled with saturated haemoglobin solution (32% by wt.)
- Haemoglobin viscosity: $0.006 \text{ Pa s (6 cP)} = 5 \times (1.2 \text{ cP})$
- Man contains about 15 gm of haemoglobin per 100 ml of cell (and women 14)
- Each gram of Hb is capable of combining with 1.34 ml oxygen.
- How much oxygen can be carried with Hb per 100 ml of blood?

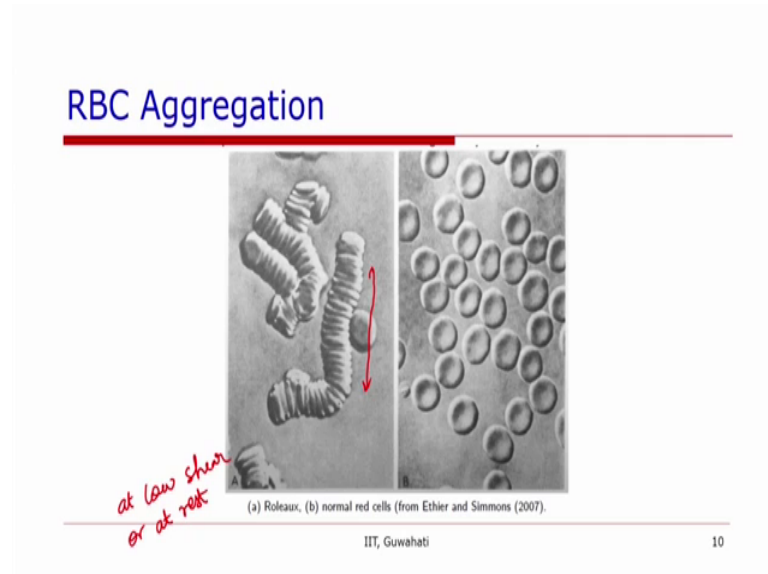
$$= \left(15 \frac{\text{gm Hb}}{100 \text{ ml blood}} \right) \left(\frac{1.34 \text{ ml O}_2}{1 \text{ gm Hb}} \right) = 15 \times 1.34 = 20 \text{ ml O}_2 / 100 \text{ ml blood}$$

IIT, Guwahati 9

Inside the red blood cells, it is filled with a liquid solution which is saturated haemoglobin solution which is about 32 percent by weight, and the viscosity of this haemoglobin is about 6 centipoises which is about 5 times, if you compare this with the plasma viscosity. So, this is about 5 times of the viscosity of the plasma; the quantity or the of haemoglobin in man is about 15 gram per 100 ml of cell and in women is about on an average 14 gram of haemoglobin.

So, as we said earlier that the function of haemoglobin is to carry oxygen and 1 gram of haemoglobin has the capacity to carry about 1.34 ml of oxygen. So, let us work out some numbers and find out how much oxygen can be carried by 100 ml of blood. So, if we want to calculate that, we know that 100 ml of blood has 15 gram haemoglobin per 100 ml of blood and 1.34 ml oxygen can be carried by 1 gram of haemoglobin. So, that will turn out to be 15 into 1.34 which is about 20 ml oxygen that can be carried by 100 ml of blood. So, 100 ml of blood in the normal human being can carry about 20 millilitre of oxygen.

(Refer Slide Time: 14:12)



The another property of red blood cells which is rheologically very important is called Roleaux, it is the property of the red blood cells to combine and make stack like that of coins and this happens at low shear stress. So, what you see here on the left hand side is at low shear or even at rest. So, they form a network of red blood cells at low value of shears whereas, at high shears the RBC are separated from each other and these this process and we just takes are known as Rouleaux.

(Refer Slide Time: 15:12)

Red Blood Cells: Dynamic States

- In simple shear flow RBC present a variety of dynamic states such as tank-treading, swinging, unsteady tumbling and chaotic motion.
- Tank-treading in a shear flow.
 - the wall rotates about itself like the belt of a tank.
 - Different points on the belt take turn on being at the front, top, bottom and back.


IIT, Guwahati 11

The RBC they can take any shape under the dynamic conditions when the blood is flowing, and they can tumble slip can have a chaotic motion can rolls swing, and tank tread. So, one of the motions that is important is tank treading, which is which means that the wall of the RBC moves itself. So it rotate itself like the belt of a tank and different points on the RBC they take turn this point which of the membrane which was here after some time it comes here and then it moves to the another point. So, basically the points on the membrane they rotate themselves, so like belt in a treading tank.


(Refer Slide Time: 16:02)

White Blood Cells (Leukocytes)

- Largest in number after RBCs
- constitute less than 1% of total volume of blood cells
 - have little influence on the bulk rheological properties in large arteries
- Spherical in shape with mean diameter of about 7-22 μm
- May play an important role during flow in capillaries
- Surface area is not smooth
- Much less deformable than RBCs
- have a viscoelastic interior



d ~ 10 μm



IIT, Guwahati

12

The next important constituent of blood is white blood cells, their volume is very small compared to RBC they constitute about 1 percent of the total blood volume and because of their very small volume as compared with red blood cell, they have very little influence on the rheological properties in large arteries, where the size of the channel or size of the artery is very large compared with the size of cells.

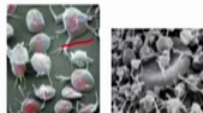
The RBC they are spherical in shape and their diameter is about 7 to 22 microns, there are 3 different kind of r b white blood cells and they can have different sizes. In smaller channel where the size of the channel is about the size of the capillary, size of the channel is about the size of the cell; that means this capillary size is about 10 micron; in these capillaries the rheological behaviour is determined by each blood cell that is passing through the channel.

So, they may play or they can play an important role in determining the flow resistance in small capillaries. The surface area as you can see is not smooth and they are much less deformable than red blood cells. So, they are almost rigid it is not very much known then about the rigidity, what has been seen that if a RBC and a white blood cell, they collide the particle that deforms is red blood cell. So, it is clear that their deformability is much less than that of RBC and they have viscoelastic interior.

(Refer Slide Time: 18:19)

Platelets

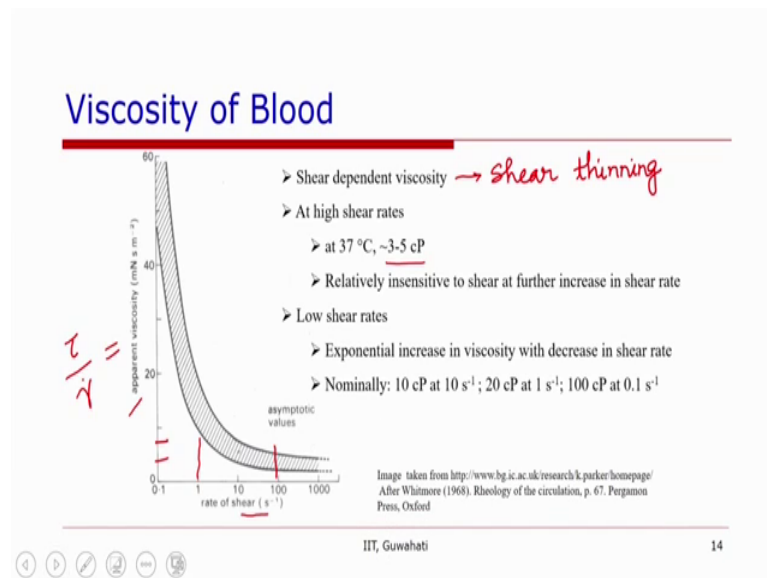
- Volume concentration of 0.3%
- Round or oval discoid shape
- Maximum dimension $\sim 2 \mu\text{m}$
- When brought in contact with adenosine diphosphate (ADP), they aggregate and a thrombus can be formed



IIT, Guwahati 13

The third important particle that is suspended in blood is platelet their volume is about 0.3 percent of the total blood volume, and they have a round or oval discoid shape as you can see here. The size of the platelets is about 2 microns, and when they are brought into contact with ADP they have a tendency to aggregate and form the thrombus. So, they have a very important role to play in the blood clot formation. So, even though in the normal flow of blood platelets do not play an important role in determining the rheological behaviour; however, in understanding the blood clot formation process for different regions for example, for haemophilia or for thrombosis it is important to understand the flow and margination of platelets.

(Refer Slide Time: 19:32)



So have a look at the mechanical properties shape and size, numbers of the volume fraction of different particles that are present in the blood, let us look at the rheological behaviour of the blood. So, in this graph what has been plotted is the viscosity or apparent viscosity of blood as a function of shear rate. So, apparent viscosity is nothing, but shear stress divided by the strain rate or shear rate and this has been plotted with respect to rate of shear.

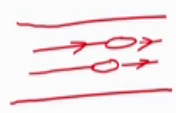
So, you might notice here that this is not constant; the viscosity of the blood is not constant with change in the rate of shear. So, the viscosity is shear dependent and you can also notice that as the shear rate increases the viscosity decreases. So, this behaviour if you remember from the previous lecture this behaviour is known as shear thinning behaviour. With the increase in the viscosity, with the increase in the shear rate the viscosity of blood is decreasing, that is shear thinning behaviour.

Now, if you notice at high shear rates which is above 100 per second, the viscosity of blood is almost independent of the shear rate. So, at 37 centigrade this value is between 3 to 5 centipoises, further there is no effect of shear at these high values; however, at low shear rates which is below 100 per second, the viscosity increased drastically with decrease in the rate of shear and there is very steep increase after shear rate of 1 per second; let us try to understand why does this happen.

(Refer Slide Time: 22:07)

RBC and Blood Viscosity

- At high shear rates:
 - RBCs orient with the flow streamlines and behave like droplets
- At low shear rates
 - RBCs tend to aggregate (Rouleaux)
 - Aggregation determines the viscosity at low shear rates



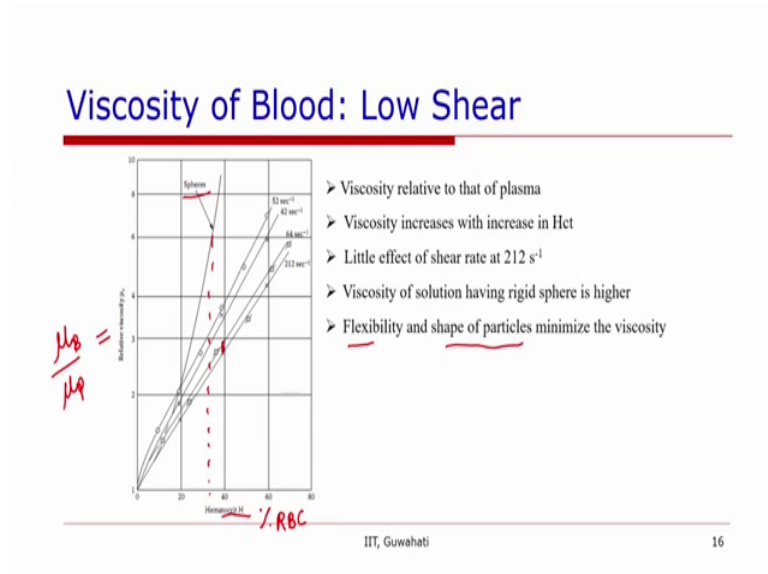
IIT, Guwahati 15

At high shear rate as we know that the blood is suspended with the red blood cells, which are flexible disc shape particles; at high shear rates what happens? RBC they orient themselves at high shear rates, the RBC they orient themselves with respect to the flow. So, the larger dimension of the RBC that is aligned with the flow and the resistance to the flow is minimum, so the viscosity is lower and further increase in shear rate does not affect the alignment of the RBC. So, that is the reason that the viscosity is lower because, when they are aligned with the flow; they offers the minimum resistance to the flow plus with the increase in shear rate there is no further change in the alignment.

However at low shear rates what happens? That the RBC tend to aggregate. So, at very small shear rate or at rest RBC they have formed a network of red blood cells or they have aggregated and with the increase in rate of shear, the network start breaking up and at a particular value of shear stress, the blood shear stress the blood starts flowing and that is where that value will be known as the yield stress.

And after the network is broken the particles or the RBC they start to orient themselves with the flow. So, that orientation is happening until about 100 per second of shear rate. So, that is why the viscosity of the blood is changing or decreasing with the increase in shear rate up to 100 per second. So, the aggregation of the RBC that determines the viscosity of the low shear rate or that is the major factor that controls the rheological behaviour at low shear rates.

(Refer Slide Time: 24:40)

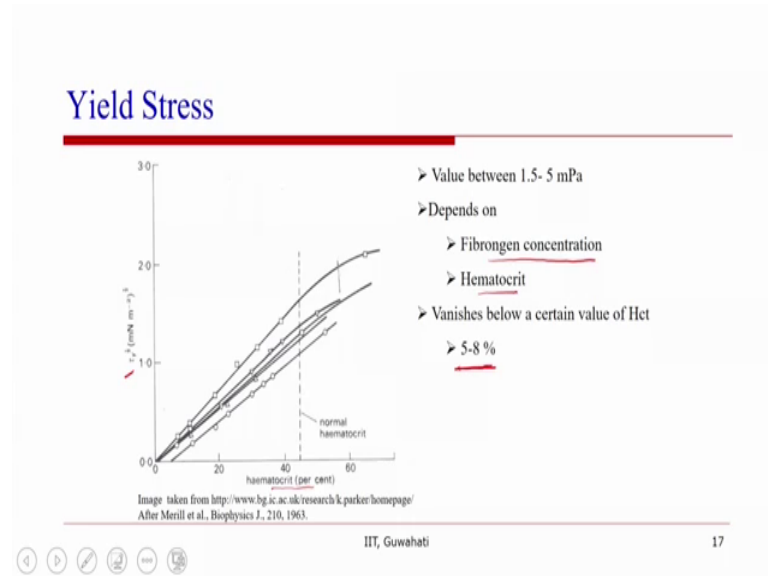


So let us look at the effect of volume fraction of red blood cells on the viscosity; what you see here on the x axis is hematocrit which is volume fraction of RBC and on the y axis is μ_{blood} or the apparent viscosity of blood normalised by the viscosity of the plasma. So, that is why it is called relative viscosity that is viscosity with respect to the viscosity of the plasma.

So, as you can see from here the viscosity of the blood increases with respect to the or with increase in volume fraction of red blood cells or with increase in hematocrit, the viscosity of the blood increases. At one particular hematocrit value with the increase in shear rate the viscosity decreases, however there is not much effect of the shear rate from 44 to 212. In the same graph, another line has been plotted which is the viscosity of a solution which contains rigid spheres and you can see that for the same volume fraction. The viscosity of a solution which contains rigid spheres is significantly higher about twice then that of blood which has flexible and disc shape particles.

So, these clearly suggest that the flexibility and shape of particles that is responsible for minimising the viscosity of the blood.

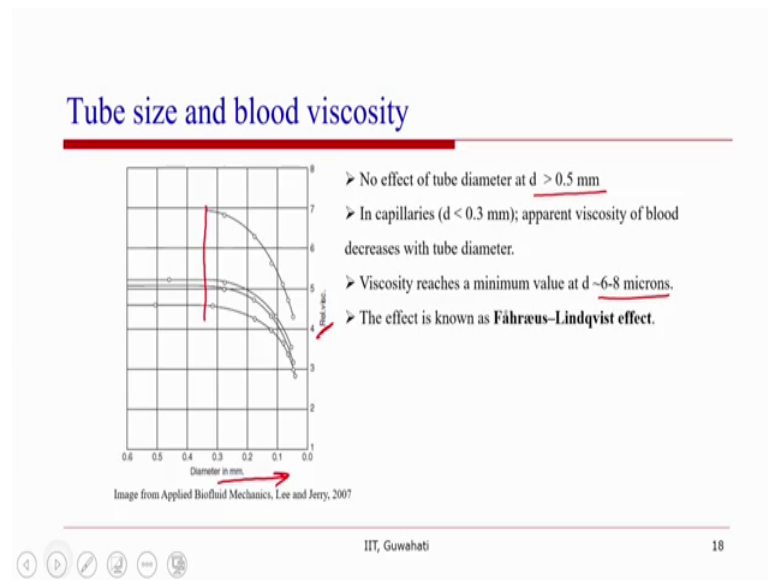
(Refer Slide Time: 26:41)



Now, as I said earlier that the hematocrit or the percentage of RBC is also responsible for the yield stress behaviour of the blood and it has been shown that it depends on experiments are shown that; it depends on the concentration of fibrinogen as well as concentration of hematocrit, if there is no fibrinogen then actually the yield stress disappears and the rouleaux formation is also not seen if there is no fibrinogen present in the blood.

On this graph the yield stress to the power 1 by 3 or 1 third power of yield stress is plotted with respect to the volume fraction of red blood cells and it is seen that the value of yield stress increases with increase in the hematocrit value or the volume fraction of RBC; that is below a certain RBC volume fraction the yield stress is 0. So, that value can be between 5 to 8 percent or has been seen in experiments to be between 5 to 8 percent below which there is no yield stress behaviour observed of the blood ok.

(Refer Slide Time: 28:08)

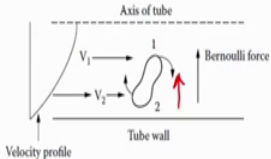


Another important effect which is seen in the rheology of blood is the effect of the size of the channel. So, as you can see from this graph that the relative viscosity again the viscosity of blood with respect to the viscosity of the plasma, it decreases with decrease in diameter and this behaviour is observed only below certain channel diameter. So, it is seen that there is no effect of the channel diameter for up to 0.5 mm; channels for the channels having diameter 500 micron or 0.5 mm or more there is no effect of channel diameter.

However, for small diameter capillaries specially less than 300 micron or 0.3 mm, the viscosity of the blood decreases with the channel diameter and it happens so, until the diameter of the channel approaches towards the size of the capillary, which has same diameter as that of the red blood cells about 6 to 8 microns and this effect is known as fahraeus Lindquist effect.

(Refer Slide Time: 29:42)

Tube size and blood viscosity



The diagram illustrates the velocity profile of blood flow in a tube. The horizontal axis represents the 'Axis of tube' and the vertical axis represents the 'Tube wall'. A parabolic velocity profile is shown, with velocity V_1 at the center and V_2 near the wall. A red arrow labeled 'Bernoulli force' points from the wall towards the center. A red squiggly line represents a red blood cell (RBC) moving towards the center. To the right, a red squiggly line is labeled 'cell free' and another red squiggly line is labeled 'core'.

Image from The Human Circulation, Chandran and Yoganathan, 2007

- Spinning RBCs tend to move towards the centre.
- Cell-free or plasma skimming layer exists near the wall.
- In small diameter channels, cell free layer comparable to core region

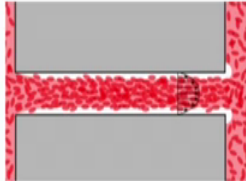
IIT, Guwahati 19

Why does that happen? This is explained or this has been explained in the literature that when the red blood cells flow in a channel, because of the velocity profile or the velocity gradients they spin and then spinning RBC they have a lift force that push them away from the wall. So, the RBC always has a tendency to move towards the core of the channel and in this core. So, the red blood cells move in the centre of the channel or core of the channel and the layer near the wall is only plasma it is called cell free or plasma skimming layer, as we have seen that the viscosity of the plasma is about one-third of that of the blood, and the flow resistance in a channel is determined by the viscosity of the fluid which is near the wall.

So, we can see this in this manner that near the in the court there are RBC and this is cell free layer and this is core. So, this small diameter channels because the thickness of the cell free layer is almost constant, in this small diameter channel this becomes the cell free layer becomes a significant part of the core region or sorry is a significant part of the channel cross section and it helps in minimising the flow resistance or the viscosity or apparent viscosity of the blood.

(Refer Slide Time: 31:48)

Fåhræus effect



➤ In capillaries ($d < 0.5$ mm); RBC concentration decreases with decrease in diameter.

➤ One of the causes of Fåhræus-Lindqvist effect.

Image from https://en.wikipedia.org/wiki/Fåhræus-Lindqvist_effect

IIT, Guwahati 20

This effect is known as Fåhræus effect, that in a small diameter capillaries RBC concentration is decreased with decrease in diameter and RBC there is a cell free layer near the wall, this effect is known as Fåhræus effect and this can explain or this is one of the causes that can explain Fåhræus Lindqvist effect, that is decrease of the blood viscosity in small diameter channels.

(Refer Slide Time: 32:21)

Summary

- Plasma and RBC determine rheological behaviour of blood
- Newtonian fluid at high shear rate
- Shear thinning behaviour at low shear rate → Aggregation of RBC
- Viscosity decreases with decrease in capillary diameter (at $d < 300 \mu$)

Shape & flexibility of RBC

May 18, 2017 IIT, Guwahati 21

So, in summary what we have studied in this lecture is, that the viscosity of plasma the components of plasma the mechanical properties and concentration of red blood cells

which is also known as hematocrit, they are major determinant of the rheological behaviour of blood.

The blood behaves as a Newtonian fluid at high shear rates at low shear rates a shear thinning behaviour is observed and 2 major factors are responsible for it, 1 is aggregation of RBC, the another factor is shape and flexibility of RBC and then the viscosity decreases with decrease in capillary diameter. So, this diameter is the channel diameter is between about 10 to 300 microns, then the viscosity decreases with decrease in capillary diameter.