International Journal of Mathematical Archive-4(7), 2013, 221-233
Available online through www.ijma.info ISSN 2229 – 5046

USING MATHEMATICAL RELATIONS TO DEDUCE THE RATE OF CLOT DISSOLUTION IN THE HUMAN CIRCULATORY SYSTEM

Sampson T. Appiah

University of Mines and Technology, Department of Mathematics, Tarkwa, Ghana

(Received on: 07-06-13; Revised & Accepted on: 03-07-13)

ABSTRACT

In this work, we made the hypothesis that the velocity of blood in the human circulatory system has an effect on the dissolution of cylindrical non – occlusive blood clots. The dissolution of clot is not only dependent on the biochemical setting but also on the power dissipated along the clot by the blood. Our prediction is that the rate of thrombolysis is faster when blood flow velocity is turbulent than when blood flow velocity is laminar through an axially directed channel along the clot. Our aim is to study the effect of each of the blood flow velocities on the rate of non – occlusive blood clot lysis and to derive a mathematical model for the process of thrombolysis in each case. The observed data fitted well to the model and confirmed the expected increase in the dissolution rate when blood flow transitioned to turbulent from laminar flow regime.

Keywords*: Non- occlusive, thrombolysis, laminar flow, turbulent flow, blood clots.*

INTRODUCTION

The free flow of blood in the human circulatory system is essential for sustaining human life. Any disorder with the human blood circulatory system such as *intra corpus* blood clotting can pose healthy complications. Some of which can lead to stroke (ischemic), heart attack and damage of cell or organs due to lack of provision of oxygen and blood nutrients. These complications can be life threatening.

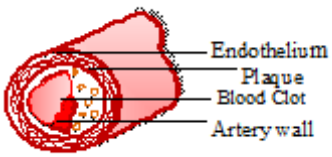

Fig.1: *Blood Clot Formed in the artery*

Thrombolytic therapy is used in the treatment of ischemic stroke (Zoppo, 1999), pulmonary embolism (Meschia *et al*, 2002), acute and subacute arterial thrombosis (Kandarpa, 1999) and in some cases, myocardial infarction (Pislaru and Van de Werf, 1999). According to Blinc and Francis (1996), the properties of the thrombolytic agent, the structure of the thrombus and the characteristics of molecular transport into the thrombus determine the success of thrombolysis. They continued that, occlusive clots are initially reanalyzed by slowly penetrating channels that follow the path of the thrombolytic agent, but are almost never completely dissolved when blood flow is re-established. The residual clot impedes normal blood flow and rethrombosis can re – occur. In disparity with the fairly well described interactions of the biophysical environment and the thrombolytic processes in occlusive clots (Anand and Diamond, 1996), (Anand *et al*., 1997), (Diamond and Anand, 1993), not much is known about the influence of fast axially directed blood flow on thrombolysis on non – occlusive clots.

Sakharov and Rijken (2000) and Tratar*et al*., (2004) asserted that high velocity of blood plasma enhances the dissolution of blood clots under favorable biochemical conditions. Wootton *et al.* (2002) developed a model of thrombolysis of mural clots that took into consideration changing concentrations of the major components of the fibrinolytic system by accounting for plasminogen adsorption to fibrin, plasminogen activation by rt – PA, fibrin degradation by plasmin and plasmin consumption by α_2 antiplasmin. Playdell *et al*. (2002) developed a similar model for thrombolysis or canalized clots.

Corresponding author: Adetunde, I.A.

In addition to the rate of biochemical degradation of the clot, mechanical forces of "tangentially" flowing blood play a role in determining the rate of dissolution on non – occlusive blood clots. (Serša *et al*, 2006).

When blood flow changes from laminar to the high velocities of turbulent flow, the viscosity of the blood emanate forces that may considerably speed up clot dissolution by eroding the clot surface.

CONCEPTUAL FRAMEWORK

We considered a cylindrical blood vessel which is narrowed in one segment by a non-occlusive blood clot. Continuous flow through the vessel is provided by a constant pressure source Δq. The vessel consists of two sections.The first with a lengthl_1 and a cross sectional area S_1 represents the normal part of the vessel and the second-with a lengthl_2 and a cross sectional area S_2 (where$S_1 \geq S_2$) – represents the channel along the non-occlusive clot through which the blood is flowing.

We shall consider three different regimes with regards to the nature of the flow in each of the two vessel sections. In the first section the pressure is low; flow is slow and laminar in both sections. In the second section, the pressure is somehow higher so that flow is still relatively slow and laminar in the non-obstructed part of the vessel but is already fast and turbulent in the narrowed section. The third regime occurs when pressure is very high so that flow is rapid and turbulent in both sections.

The model is formulated based on the following simplifying assumptions:

- the clot behaves as a rigid no-slip solid interface;
- no entrance or exit length hydrodynamic effects, so the flow profile is constant along the flow channel;
- the flow is non-pulsatile and is generated by a constant pressure drop,
- the concentrations of the components of the fibrinolytic system and the associated rate of biochemical fibrinolysis are constant along the channel.

(a)

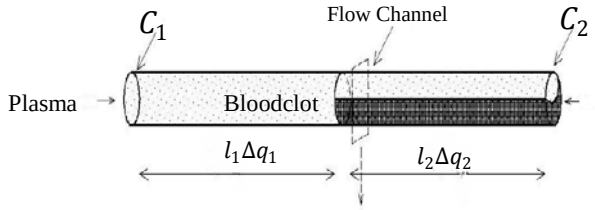

Fig 2a: Cylindrical blood vessel which is narrowed in one segment by blood clot.

(b)

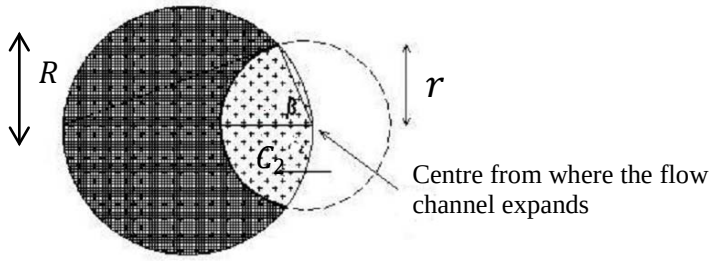

Fig. 2b: The clotted vessel

Fig.2 An unobstructed blood vessel of cross-sectional area of C_1 and length l_1 and a section of the vessel of length l_2 that is partially closed by a clot with a flow channel of cross- sectional area C_2. Δq_1andΔq_2 are the respective pressure drops int the first and second sections.

The clotted vessel (b) is filled with the clot (dark grey) everywhere except in a flow channel (light grey) next to the vessel's wall.

2.0 MATHEMATICAL FORMULATION

2.1 Laminar – laminar flow

Laminar flow through a vessel is the major reason for the pressure drop Δq across the vessel is viscosity of the blood. From the Poiseuille's law, this drop is proportional to the average blood velocity *v*, to the vessel's length *l* and is proportional to the cross – sectional are *C* of the vessel (Serša, *et al*, 2006):

© 2013, IJMA. All Rights Reserved

$$\Delta q = 8\pi \frac{vl}{c} \tag{1}$$

The two vessels of different diameter are joined in series to the same pressure source Δq and so the pressure is distributed between them. The first vessel with the average velocityv_1, length l_1 and cross – sectional areaC_1, has a pressure drop of Δq_1 and likewise, the second vessel with the parameters v_2, l_2, C_2 has a pressure drop Δq_2. From Eq. (1) it follows that

$$\Delta q = 8\pi \left(\frac{v_1 l_1}{C_1} + \frac{v_2 l_2}{C_2}\right) \tag{2}$$

Furthermore, the conservation of volume flow $v_1 C_1 = v_1 C_2$ as blood is incompressible at normal pressures. Combining this condition with Eq. (2), the expression for the average velocity through the second vessel segment as a function of the ratio between the cross – sectional areas of the two vessel segments $x \equiv \frac{C_1}{C_2}$ is obtained as (Serša, *et al,* 2006):

$$v_2(x) = v_L \frac{1}{x + \frac{1}{Dx}} \tag{3}$$

The parameter $v_L = \Delta q C_1/(8\pi l_1)$ and $D = l_1/l_2$ is the average blood velocity in the first vessel alone and the ratio between the lengths of the first and the second vessel segment, respectively.

Equation (3) has two intersecting limits. The first is when the clot almost completely blocks the vessel so that $x \approx 0$. In this limit, the average velocity through the clot region is proportional to the open area of the vessel. Thus

$$v_2(x) = v_L \frac{1}{0 + \frac{1}{Dx}}$$

$$v_2(x) = v_L Dx.$$

This corresponds with the situation when the pressure drop in the normal vessel region is negligible.

In the second limit, where$x \approx 1$, the cross – section of the narrowed segment is very similar to the cross – section of the normal vessel segment. Assuming that the length of the narrowed segment is much shorter than that of the normal vessel ($D \gg 1$), it follows that $v_2 = v_L$, which means that the clot no longer represents an obstacle for blood flow and the average velocity in the region with the small, non – occlusive clot is identical to the average velocity in the normal vessel

2.2 Laminar – turbulent flow

In this model, flow is laminar in the normal vessel segment and turbulent in the narrowed vessel segment. In the turbulent flow regime the pressure drop per unit length is proportional to the average velocity squared and inversely proportional to the square root of the vessel's cross – sectional area. (Serša, *et al,* 2006)

$$\Delta q = f\rho \frac{lv^2}{\sqrt{C}} \tag{4}$$

Turbulent flow is influenced mainly by the density of the fluid ρ, rather than the viscosity. In equation (4) $f$is a frictional coefficient which was experimentally determined to be approximately equal to 0.011 for most round tubes (Dryden *et al,* 1965). Also the total pressure drop has two contributions: a pressure drop of Δq_1 in the first vessel segment with parameters v_1, l_1, C_1 where flow is laminar, and a pressure drop of Δq_2 in the second vessel segment with parameters v_2, l_2, C_2 where flow is turbulent:

$$\Delta q = 8\pi \frac{l_1 v_1}{C_1} + f\rho \frac{l_2 v_2^2}{\sqrt{C_2}} \tag{5}$$

The equation for the average velocity in the narrowed vessel segment follows from the conservation of volume flow that
$v_1 C_1 = v_1 C_2$ (Serša, *et al,* 2006):

$$v_2(x) = v_{LT} Dx^{3/2} \left(\sqrt{1 + \frac{G}{Dx^{5/2}}} - 1\right) \tag{6}$$

© 2013, IJMA. All Rights Reserved

Where x and the constant D have the same meaning as for the case of laminar – laminar flow and the newly introduced coefficients corresponds to $v_{LT} = 4\pi/(f\rho\sqrt{C_1})$, and $G = \frac{f\Delta q\rho C_1^{3/2}}{16\pi^2 l_1}$.

2.3 *Turbulent – turbulent flow*

Under this system, the flow is turbulent in both vessel sections. This condition is met at very high velocities. Again, the pressure drop in both vessels is the sum of the partial pressure drops in the individual vessels. According to Eq. (4) this is equal to

$$\Delta q = f\rho\left(\frac{l_1 v_1^2}{\sqrt{C_1}} + \frac{l_2 v_2^2}{\sqrt{C_2}}\right) \tag{7}$$

If the volume flow is conserved in both segments, it can be extracted that the narrow segment as a function of the ratio between the cross – sectional areas of the two vessel segment: (Serša, *et al.,* 2006)

$$v_2 = v_T \frac{1}{\sqrt{x^2 + \frac{1}{K\sqrt{x}}}} \tag{8}$$

Here $v_T = \sqrt{(\Delta q\sqrt{C_1})/(f\rho l_1)}$ correspond to the blood velocity when the clot is totally dissolved ($x = 1$). However, this is true when the length of the clot is significantly shorter than the length of the remaining vessel ($D \gg 1$).

2.4 Reynolds Number (Re)

Reynolds number (Re) is dimensionless parameter that relates inertia forces to viscous force. We shall use Re to determine which of velocities of the three regimes of blood flow under consideration clot dissolution occurs.

$$Re = \frac{\rho d v}{\eta} = \frac{\rho d_\infty \sqrt{x} v_2(x)}{\eta} \tag{9}$$

Here d and d_∞ are the obstructed and normal (after complete clot dissolution) diameters of the vessel, respectively, v is the average blood flow velocity in the vessel, ρ is blood density and η is its viscosity. It is experimentally determined that for steady flow in pipes with perfectly smooth surfaces, flow is most likely turbulent when Re is more than 4000 and laminar when it is less than 2000. Schiller (1922) added that this is just an approximate value. The laminar flow regime may also persist at Re much higher than 2000 when the vessel walls are very smooth and may turn into fully developed turbulent flow also at Re much lower than 3000 if the walls were rough. Transitions to turbulent flow also occur at lower Re for pulsatile flow instenotic (an abnormally constricted canal) geometries (Ghalichi et al., 1998). For example, turbulence can occur with flow de – acceleration during diastole even at Re < 1000 (Nichols and O'Rourke, 2005). Bugelski*et al,* (1989) discussed that based on electron micrographs of recanalization channels through blood clots, it is clear that non – occlusive blood clots have rough walls and since flow along non – occlusive clots is also pulsatile, the onset of turbulence is expected at Re lower than 2000.

During clot dissolution the average blood velocity and the channel's diameter changes together with Re. Re is not largest at beginning or at the end of thrombolysis, but at some time between, when the product of the channel diameter and the blood velocity is the largest. For the laminar – laminar model this occurs at $x = 1/\sqrt{D}$ and for the laminar – turbulent model at$x = (9G/16)^{\frac{2}{5}}$. (Serša, *et al.,* 2006) Re increases as velocity increases and decreases as viscosity increases. Therefore, high velocities and low blood viscosity (as occurs with anaemia due to reduced haematocrit) are more likely to cause turbulence. An increase in diameter without a change in velocity also increases Re and the likelihood of turbulence; however, the velocity in vessels ordinarily decreases disproportionately as diameter increases. (Appiah*et al.,* 2011) Appiah*et al.,* (2011) continued that the reason for this is that flow (F) equals the product of mean velocity (V) times cross – sectional area (A), and area is proportionate to radius squared; therefore, the velocity at constant flow is inversely related to radius (or diameter) squared. For example, if radius (or diameter) is doubled, the velocity decreases to one – fourth its normal value, and Re decreases by one – half. Turbulence generates sound waves that can be heard with a stethoscope. Because higher velocities enhance turbulence, mummers intensify as flow increases. Elevated cardiac outputs, even across anatomically normal aortic valves can cause physiological murmurs because of turbulence. This sometimes occurs in pregnant women who have elevated cardiac output and who have elevated cardiac output and who may also have anaemia, which decreases blood viscosity. Both factors increase the Reynolds number and increase the likelihood of turbulence (Klabunde, PhD, 2007).

© 2013, IJMA. All Rights Reserved

METHOD OF SOLUTION

2.5 Rate of clot dissolution

Suppose that a pharmacological concentration of a thrombolytic agent is added to the blood that flows in the two-segment vessel. The non – occlusive clot begins to dissolve and the non – obstructed channel along the clot expands radially as thin layers of the clot are gradually removed by the flowing blood. Suppose that the blood flow channel is aligned to the vessel's circle with a radius R and the channel's circle with a radius r (as illustrated in Figure 1b). Consequently, r is in the range between 0 and 2R. In the transverse view, the contact between the flowing blood and the clot is an arc with a length sthat can be calculated as:

$$s = 2r\ \cos^{-1}\left(\frac{r}{2R}\right) = \frac{dC_2}{dr}. \tag{10}$$

C_2denotes the cross – sectional area of the flow channel, which is calculated by integrating the arc length (Eq. 10) in the range from 0 and r

$$C_2(r) = \int_0^r 2r'\ Cos^{-1}\left(\frac{r'}{2R}\right)dr'$$

$$\therefore C_2(r) = \int_0^{\frac{r}{2R}} (4\,Rt\ Cos^{-1}t\,)\ 2R\ dt$$

$$= 8R^2 \int_0^{\frac{r}{2R}} t\ Cos^{-1}t\ dt \tag{i}$$

$$\int t\,Cos^{-1}t\,dt = \frac{t^2}{2}Cos^{-1}t + \frac{1}{2}\int \frac{t^2}{\sqrt{1-t^2}} \tag{ii}$$

$$= \frac{1}{2}Sin^{-1}t - \frac{t}{2}\sqrt{1-t^2} \tag{iii}$$

$Puting\ (iii)\ into\ (ii)$:

$$\int t\ Cos^{-1}t\ = \frac{t^2}{2}Cos^{-1}t + \frac{1}{4}Sin^{-1}t - \frac{t}{4}\sqrt{1-t^2} \tag{iv}$$

$substitution\ \ (iv)\ becomes$

$$\int t\cos^{-1}t\,dt = \frac{t^2}{2}\cos^{-1}\frac{1}{4}\left(\frac{\pi}{2} - \cos^{-1}t\right) - \frac{t}{4}\sqrt{1-t^2} \tag{v}$$

$Putting\ (v)\ into\ (i)$:

$$C_2(r) = 8R^2\left[\frac{t^2}{2}Cos^{-1}t + \frac{1}{4}\left(\frac{\pi}{2} - Cos^{-1}t\right) - \frac{t}{4}\sqrt{1-t^2}\right]_0^{\frac{r}{2R}}$$

$$= \pi R^2 + 2(r^2 - 2R^2)\,Cos^{-1}\left(\frac{r}{2R}\right) - r\sqrt{R^2 - \left(\frac{r}{2}\right)^2} \tag{11}$$

C_2 in Eq. (11) corresponds to the cross – sectional area of the channel along the clot in all the three blood flow regimes: laminar – laminar, laminar – turbulent and turbulent – turbulent; thus in equations (3), (6) and (8), whereas C_1 is equal to the cross- sectional area of the non – obstructed vessel's segment πR^2.

Now to the essence of the proposed model, namely that for every biochemical setting, the rate of non – occlusive clot dissolution is proportional to the dissipated power of the blood flowing along the clot. That is the rate of dissolution is a function of the average blood flow velocity. In other words, the higher the rate of mechanical forces on the clot's surface, the fewer plasmin-susceptible bonds in the fibrin network have to be cleaved biochemically for removing a corresponding fragment of the non – occlusive clot.

Work done by internal forces due to viscosity and turbulent velocity fluctuations cause heating of the blood in the main stream, while the same forces exerted on the clot surface are responsible for the clot degradation and can significantly accelerate clot lysis. (Seršae*tal.* 2006)

© 2013, IJMA. All Rights Reserved

The work done by the flowing blood in contact with the clot can be estimated by the energy dissipation in the thin layer close to the surface. The dissipation power density dP/dV is equal to the product of the wall shear stress τ and the wall shear rate. (Dryden *et al.* 1956)

Therefore, the workdone dW to the surface of the clot in a layer of thickness λ in time dt is given as:

$$dW = \tau\gamma\lambda s l_2 dt \quad \text{(vi)}$$

Where; sl_2 = area of the clot in contact with the flowing blood,

λ = depth of the clot to which mechanical forces are exerted.

Using the assumption made by Serša *et al.* (2006) that the wall shear stress and the wall shear rate are such as in a round tube of radius $\delta = \sqrt{S_2/\pi}$ and a parabolic velocity profile, the wall shear stress is then $\tau = \Delta q_2\, \delta/2l_2$ and the wall shear rate is $\gamma = v_2/\delta$, so that the mechanical work of the flowing blood done on the clot is

$$dW = \frac{\Delta q_2 v_2 \lambda s dt}{2} \quad \text{(vii)}$$

Equation (vii) is obtained by substitutingδ, τ and γ in equation (vi)

The mechanical work is used for clot degradation and volume dV of degraded clot is proportional to the work dW.

$$dW = csl_2 dr \quad \text{(viii)}$$

In equation $(viii)dW$ is the work done needed to expand the clot channel by dr. Here, cis a proportionality constant dependent on the to the biochemical setting. The more efficient the thrombolytic agent, the lower the value of c and the lower the mechanical work W necessary for removing a layer of the clot.

The final expression for the progressive rate of the clot dissolution front is obtained. Thus $(vii) = (viii)$;

$$\frac{\Delta p_2 v_2 s\lambda dt}{2} = csl_2 dr$$

$$\frac{dr}{dt} = \frac{\lambda v_2 \Delta q_2}{2cl_2} = \frac{\lambda \Phi \Delta q_2}{2cV_2} \quad (12)$$

Here, $\Phi = \Delta V/\Delta t = S_2 v_2$ is the blood volume flow and $V_2 = S_2 l_2$ is the volume of the clot channel. It can be seen from Eq. (12) that the rate at which a clot dissolves is proportional to the velocity of blood and to the pressure gradient along the clot.

Equation (12) can be further be considered for two cases: the first is when flow along the clot is laminar and the second is when the flow is turbulent. The pressure drop per unit length (Eq. (1)) is proportional to the square of the velocity of blood and inversely proportional to the cross – sectional area of the clot channel. Thus;

$$\frac{dr}{dt} = \frac{\Delta p_2 v_2 \lambda}{2cl_2}$$

$$\Delta p_2 = 8\pi\eta \frac{v_2 l_2}{s_2}, \text{the pressure drop for, laminar flow}$$

$$\frac{dr}{dt} = \frac{4\pi\eta v_2^2 \lambda}{s_2 c}$$

$$\frac{dr}{dt} = C_L \frac{v_2^2}{s_2}, \qquad C_L = \frac{4\pi\eta}{c} \quad (13)$$

$$\Delta p_2 = f\rho l_2 \frac{v_2^2}{\sqrt{s_2}},$$

© 2013, IJMA. All Rights Reserved

the pressure drop for turbulent flow

$$\frac{dr}{dt} = \frac{f\rho l_2 v_2^2 v_2 \lambda}{2cl_2\sqrt{S_2}}$$

$$\frac{dr}{dt} = C_T \frac{v_2^3}{\sqrt{S_2}}, \qquad C_T = \frac{f\rho\lambda}{2c} \tag{14}$$

In calculating the dynamics of clot dissolution Eq. (13) or Eq. (14) is integrated. Thus; Integrating Eq. (13):

$$\int \frac{dr}{dt} = C_L \int \frac{v_2^2}{S_2}$$

$$r = C_L \frac{v_2^2}{S_2}\, t \tag{13i}$$

Integrating Eq. (14):

$$\int \frac{dr}{dt} = \int C_T \frac{v_2^3}{\sqrt{s_2}}$$

$$r = C_T \frac{v_2^3}{\sqrt{S_2}}\, t \tag{14i}$$

The dynamics of clot dissolution is now governed by only one parameter: C_L for laminar flow and C_T for turbulent flow. In practice, a delay parameter T has been introduced into the model. The new parameter T corresponds to the time lag between injection of the thrombolytic agent into the blood and the time when the biochemical processes of fibrinolysis reach a steady state with the surface layer of the clot being partly degraded. After introducing the delay parameter T, Eqs. (13) and (14) changed to

$$\frac{dr}{dt} = \begin{cases} 0; & t < T \\ \dfrac{C_L v_2^2\big(x(r)\big)}{C_2(r)}; & t \geq T \end{cases}$$

for laminar flow, and to

$$\frac{dr}{dt} = \begin{cases} 0; & t < T \\ \dfrac{C_T v_2^3\big(x(r)\big)}{\sqrt{C_2(r)}}; & t \geq T \end{cases}$$

for turbulent flow; where $x(r) \equiv C_2(r)/S_1$. The velocity v_2 in Eq. (15) is the velocity of laminar – laminar flow as defined in Eq. (3),whereas the velocity v_2 in Eq. (16) can be either the velocity for laminar – turbulent flow (Eq. (6)) or for turbulent – turbulent flow (Eq. (8)).

Case I:

2.6 ***Rate of clot dissolution- Laminar flow***

$$r = C_L \frac{v_2^2}{S_2}\, t$$

From the above equation C_L is a constant, therefore the rate of clot dissolution is obtained by varying time t in ten different instances where $500 \leq t \leq 5500$. v_2 is calculated using the Re expression where flow ceases to be laminar when Re is beyond 2000. S_2 is calculated from (11) where R is taken to be the diameter of artery (0.3mm) and r is assumed to be $5/4$ of R (0.375mm).

© 2013, IJMA. All Rights Reserved

In calculating S_2;

$$S_2 = \pi R^2 + (r^2 - 2R^2)\, Cos^{-1}\left(\frac{r}{2R}\right) - r\sqrt{R^2 - \left(\frac{r}{2}\right)^2}$$

$$S_2 = -3.221858731$$

Since S_2 is a cross- sectional area and cannot be negative, the absolute value of S_2 is taken.Thus, $|S_2| = 3.221858731$ squared units. In calculating the velocity for the laminar flow regime using Re:

$$Re = \frac{\rho d v}{\eta}$$

Where $\eta, viscosity\ of\ blood = 3 \times 10^{-3}\ Pa\ s$

$\rho, density\ of\ blood = 1060 kg/m^3$

$d, diameter\ of\ vessel = 0.3mm$

DISUSSION OF RESULTS

Now according to Serša, *et al*, (2006), flow is more likely to turbulent when Re is more than 3000 and laminar when less than 2000. Then it can be deduced that Re is less than or equal 2000 when flow is laminar and Re is greater than or equal to 3000 when flow is greater than or equal to 3000.

So that Re = 2100 for laminar

$$v = 0.0170 m/s$$

Substituting the values of v and S_2 in r for the first instance where $t = 500$ gives,

$$r_{500} = 0.045$$

The remaining result for the rate of clot dissolution is given in the table below:

Time (s)	**Rate of dissolution (r)**	**Value (mm^2)**
1000	r_{1000}	.090
1500	r_{1500}	.135
2000	r_{2000}	.179
2500	r_{2500}	.224
3000	r_{3000}	.269
3500	r_{3500}	.314
4000	r_{4000}	.359
4500	r_{4500}	.404
5000	r_{5000}	.448
5500	r_{5500}	.493

The figure 3 shows a graph of the rate of clot dissolution against the time for the dissolution.

© 2013, IJMA. All Rights Reserved

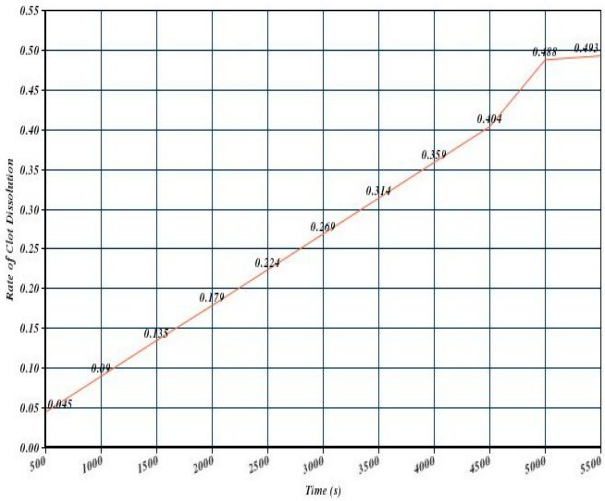

Fig. 3: *Graph of rate of clot dissolution (r) against time (s) for laminar flow.*
(Graph was drawn with software on the internet**)**

Although the lumen of the artery is almost blocked by the blood clot, the nature of blood in the laminar flow regime is unable to mount the pressure needed to aid clot dissolution. This is because an increase in pressure will simultaneously increase the mechanical forces on the surface of the clot. It can be observed from the graph that although the lysis of clot is taking place, it is at a very slow pace and at some point in time of clot lysis begins to stabilize. Thus, starting from time 5000 seconds, clot degradation begins to slow down and is expected to stop at some point beyond 6000 seconds. As it can be again observed, it would require a longer time for an appreciable area of clot to dissolve.

Case II:

2.7 ***Rate of clot dissolution- Turbulent flow***

$$r = C_T \frac{v_2^3}{\sqrt{S_2}}\, t$$

From the above equation C_T is a constant, therefore the rate of clot dissolution is obtained by varying time t in ten different instances where $500 \leq t \leq 5500$. v_2 is calculated using the Re expression where flow ceases to be turbulent when Re is beyond 3000. S_2 is the same as calculated for laminar above; where R is taken to be the diameter of artery (0.3mm) and r is assumed to be $5/4$ of R (0.375mm).

In calculating the velocity for the laminar flow regime using Re:

$Re = \frac{\rho d v}{\eta}$ Where $\eta, viscosity\ of\ blood = 3 \times 10^{-3}\ Pa$

$\rho, density\ of\ blood = 1060 kg/m^3$

$d, diameter\ of\ vessel = \ 0.3mm$

Now according to Serša, *et al*, (2006), flow is more likely to turbulent when Re is more than 3000 and laminar when less than 2000. Then it can be deduced that Re is less than or equal 2000 when flow is laminar and Re is greater than or equal to 3000 when flow is greater than or equal to 3000.

So that Re = 3100 for turbulent

$$3100 = \frac{1060 \times 0.3v}{3 \times 10^{-3}}$$

$v = 0.0292 m/s$

Then substituting the values of v and S_2 in r for the first instance where $t = 500$ gives,

$$r = \frac{v_2^2}{S_2}\, t$$

$r_{500} = 0.238$

© 2013, IJMA. All Rights Reserved

The remaining result for the rate of clot dissolution is given in the table below:

Time (s)	Rate of dissolution (r)	Value (mm^2)
1000	r_{1000}	0.475
1500	r_{1500}	0.7125
2000	r_{2000}	0.95
2500	r_{2500}	1.1875
3000	r_{3000}	1.425
3500	r_{3500}	1.6625
4000	r_{4000}	1.900
4500	r_{4500}	2.1375
5000	r_{5000}	2.375
5500	r_{5500}	2.6125

The graph below shows a graph of the rate of clot dissolution against the time for the dissolution.

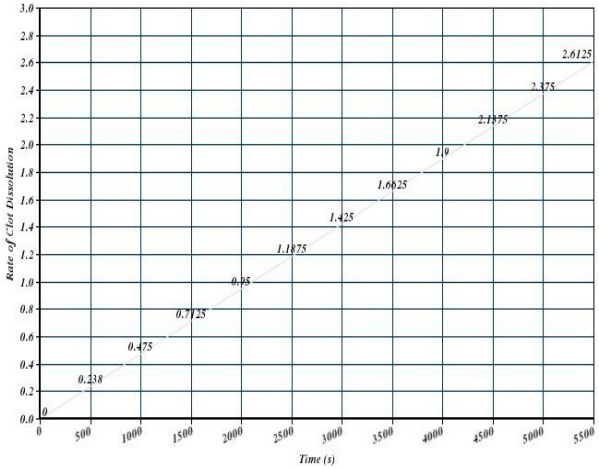

Fig. 4: *Graph of rate of clot dissolution (r) against time (s) for turbulent flow*

The nature of blood in the turbulent flow regime is able to mount the pressure needed to aid clot dissolution. This is because an increase in pressure will simultaneously increase the mechanical forces on the surface of the clot. This is evident in the turbulent flow regime, where the mechanical forces acting on the clot surface for dissolution is enough to cause an active clot lysis. It can be observed from the graph that although the lysis of clot is taking place, it is at a fast pace. It can be again observed, it would require a lesser time for an appreciable area of clot to dissolve.

The difference in the rate of clot dissolution for laminar flow and turbulent flow is shown in the graph below:

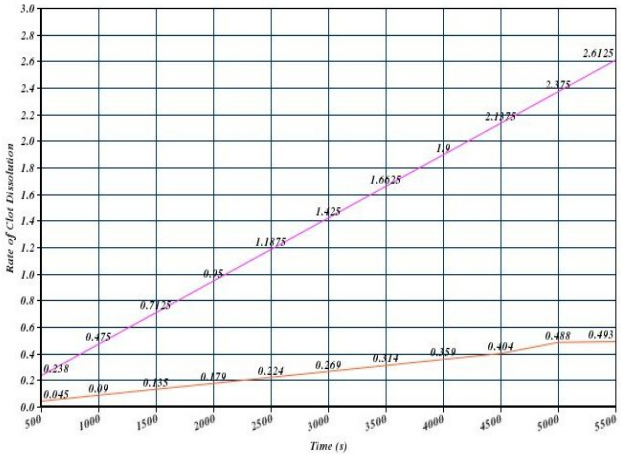

Fig. 5: *Graph of rate of clot dissolution (r) against time (s) for turbulent flow*

© 2013, IJMA. All Rights Reserved

It is evident for the graph above that at equal time interval and under the appropriate biochemical setting, clots lysis in the turbulent flow is much progressive than that in the laminar flow regime.

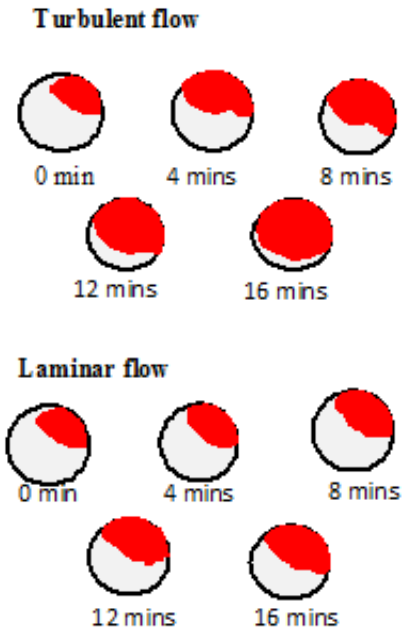

Fig. 6: *Clot dissolution in the turbulent and in the laminar velocity regime for an appropriate thrombolytic agent. Thrombolysis is taken at 2-minute intervals.*

REMARKS

After the research, it was observed that clot degradation is not achieved by only the biochemical process but also by viscous and kinematic mechanical forces of blood flowing along the clot. If the velocity of blood flow is higher, then the mechanical contribution to clot dissolution becomes larger, and vice versa. Clot dissolution depends on the velocity of the blood flow. It is therefore necessary to know whether flow along the clot is laminar or turbulent. For laminar flow, the rate of clot dissolution is proportional to the square of the average flow velocity and for turbulent flow; it is proportional to the third power of the average flow velocity.

CONCLUSION

The viscous nature and the velocity of the flowing blood in either of the flow regimes: turbulent flow or laminar flow, aids in the generation of mechanical forces for thrombolysis.

An appreciable area of clot lysis takes place when blood flow is turbulent than when blood flow was laminar.

RECOMMENDATION

In other to prevent the contracting of a deep vein thrombosis, we recommend that the following measures be adhered to:

- Exercising your body and staying active. Walking and other forms of exercise help with blood circulation and with weight loss.
- Stop smoking. Smoking increases the tendency for the blood to clot.
- Maintain a normal body weight and eat a healthy diet.
- If you are hospitalized for any medical or surgical condition,ask the doctor what he or she is planning to do to decrease yourrisks of a recurring thrombophilia and pulmonary embolisms.
- If you take long airline or auto trips, get up and walk every hour or so, and tighten the calf muscles by flexing your foot and rising on your toes 10-15 times each hour. Additionally, avoid alcohol and drink plenty of fluids.

REFERENCES

1. Appiah, S.T., Adetunde I. A., Dontwi, I. K., “A mathematical model of blood clot in the human cardiovascular system”, *International Journal of Research in Biochemistry and Biophysics 2011;* 1 (2): 9-16.

© 2013, IJMA. All Rights Reserved

2. Anand, S.and Diamond, S.L., (1996), "Computer simulation of systemic circulation and clot lysis dynamics during thrombolytic therapy that accounts for inner clot transport and reaction", *Circulation,* pp**.** 763–774.

3. Anand, S., Kudallur, V., Pitman, E.B. and Diamond, S.L., (1997), "Mechanisms by which thrombolytic therapy results in non-uniform lysis and residual thrombus after reperfusion", *Ann. Biomed. Eng.* Pp 964–974.

4. Blinc A. and Francis, C. W. (1996), "Transport processes in fibrinolysis and fibrinolytic therapy", *Thromb. Haemost.***,** pp.481–491.

5. Bugelski, P.J., Kopia,G. A., Kopaciewicz, L., Cadogan, A. S., and Morgan, D.G. (1989), "Ultra structural analysis of thrombolysis by Streptokinase and tissue -type plasminogen activator of experimental coronary arterial thrombosis, Fibrinolysis, pp. 137 – 145.

6. Diamond, S.L.andAnand, S., (1993), "Inner clot diffusion and permeation during fibrinolysis", *Biophysics. J.* pp2622–2643.

7. Ghalichi, F. X.Y., Deng, A., DeChamplain, Y. Douville, M. King and GuidonR. (1998), Low Reynolds number: turbulence modeling of blood flow in arterial stenosis, Biorheology, pp. 281 – 294.

8. Kandarpa, K., (1999), Catheter-directed thrombolysis of peripheral arterial occlusions and deep vein thrombosis", *Thromb. Haemost.* pp. 987–996.

9. Klabunde,E.R (2007), "Reynoldsnumber", *Cardiovascular Physiology Concepts textbook*, pp. 27- 28.

10. Meschia, J.F., Miller, D.A. andBrott, T.G. (2002), "Thrombolytic treatment of acute ischemic stroke", *Mayo. Clin. Proc.* **77,** pp 542–551.

11. Pislaru, S.V. and Van de Werf, F., (1999), "The current role of thrombolytic therapy in the treatment of acute myocardial infarction", *Fibrinolysis & Proteolysis*, pp 91–98.

12. Pleydell, C.P., David, T., Smye, S.W. and Berridge, D.C., (2002),"A mathematical model of post-canalization thrombolysis", *Phys.Med. Biol.* pp209–224.

13. Sakharov, D.V. andRijken, D.C., (2000), "The effect of flow on lysisis of plasma clots in a plasma environment", *Thromb. Haemost.*pp. 469–474.

14. Serša, I., Tratar, G., Mikac, U. and Blinc, A., (2006), "A mathematical model for the dissolution of non-occlusive blood clots in fast tangential blood flow", *Biorheology*44, pp. 1-16.

15. Schiller, L. (1922), "Studies of laminar and turbulent flow", *Physisk Z.*, pp. 14 – 19

16. Tratar, G., Blinc, A., Štrukelj, M., Mikac, U. and Serša, I., (2004), "Rapid tangential flow of plasma containing rt-PA promotes thrombolyis of non-occlusive whole blood clots in vitro", *Thromb. Haemost.*, pp 487–496.

17. Wootton, D., Popel, A.S. and Alevriadou, B.R., (2002),"An experimental and theoretical study of the dissolution of mural fibrin clots by tissue-type plasminogen activator", *Biotechnol. and Bioeng.* Pp405–419.

18. Zoppo, G.J. D, (1999)"Antithrombotic treatments in acute ischemic stroke", *Stochastic modeling and optimization Thromb.Haemost.*,pp**.** 938–946.

NOMENCLATURE

Δq : Continuous flow through the vessel
l_1 : Length of first sections of cylindrical
l_2 : Length of second sections of cylindrical blood vessel
S_1 : Cross sectional area of first sections of cylindrical blood vessel
S_2 : Cross sectional area of second sections of cylindrical blood vessel
v : Average blood velocity
l : Length of cylindrical blood vessel

© 2013, IJMA. All Rights Reserved

C : The cross – sectional area of the vessel
C_1 : An unobstructed blood vessel of cross-sectional area of
C_2 : Partially closed by a clot with a flow channel of cross- sectional area
Δq_1 : Pressure drops in the first sections of cylindrical blood vessel (l_1)
Δq_2 : Pressure drops in the second sections of cylindrical blood vessel is
v_1 : The first vessel with the average velocity
v_2 : The second vessel with the parameters
x : The ratio between the cross – sectional areas of the two vessel segments
ϕ : Viscosity of the blood
v_L : The average blood velocity in the first vessel alone
D : The ratio between the lengths of the first and the second vessel segment
f : Frictional coefficientis
ρ : The density of the fluid
v_{LT} : The average blood velocity in the Laminar-Turbulent section of the vessel
d : The obstructed diameters of the vessel
d_∞ : The normal diameters of the vessel
η : Viscosity Turbulent-Turbulent section of blood
r : The channel's circle with a radius
R : The vessel's circle with a radius
τ : The wall shear stress
γ : The wall shear rate
dV: Volume of degraded clot
dW: The work done needed to expand the clot channel by dr
c : Proportionality constant dependent on the to the biochemical setting
Ψ : The blood volume flow
T : Time lag between injection of the thrombolytic agent into the blood and the time when the biochemical processes of fibrinolysis reach a steady state with the surface layer of the clot being partly degraded
$\frac{dP}{dV}$: The dissipation power density
Re : Reynolds Number and optimization

Source of support: Nil, Conflict of interest: None Declared

© 2013, IJMA. All Rights Reserved