Steady Flow Visualization in a Rigid Model of the Aortic Bifurcation: Application to Atherosclerosis

QASEM M. RAMADAN*, O. HAMID and K.O. LIM

School of Physics, Universiti Sains Malaysia, 11800 Pulau Pinang, Malaysia

(*Author for correspondence, e-mail: ph043782@ntu.edu.sg)

Abstract. Hemodynamics have long been implicated in atherogenesis. The studies reported here seek to explain the mechanisms for the formation of atherosclerotic plaque in an aortic bifurcation. Flow studies were made in a model constructed from plexiglass to represent an aortic bifurcation. Under steady flow conditions at inflow Reynolds numbers of 80–1250, the streamline flow patterns and the boundary layer separation zones were investigated in relation to the location of atherosclerotic plaques clinically found at regions in the human aortic bifurcation. The streamline flows were visualized by a slow injection of dye over the cross section of the tube entrance and along the tube walls. The studies revealed a complex flow field where secondary flows, induced by the centrifugal and viscous forces, cause the fluid to move towards the inner walls of the aortic bifurcation. The effect was more clearly seen with increasing Reynolds number. Boundary layer separation zones were observed to occur at the outer corners of the branching. The nature of the separation zone formed was found to be dependent on Reynolds number. The residence time of fluid particles within such a separation zone was estimated by measuring the washout time of a bolus of dye injected at strategic locations along the tube walls. The residence time was found to decrease exponentially with increasing Reynolds number. These observations provide strong support for the role of flow separation in the accumulation of LDL and platelet aggregation within the aortic bifurcation.

Key words: Aortic bifurcation, atherosclerosis, steady flow, separation zone, secondary flow, residence time

1. Introduction

Atherosclerosis develops at the outer corners of bifurcations. Model studies and animal studies suggest that hemodynamic factors are involved [3, 10, 20]. Many theories for the origin and the development of atherosclerosis have been postulated and among the more prominent hypotheses are those related to wall shear stress. Early studies of Fry [14] suggested that areas of artificially-induced shear stress were favorable for atherosclerotic processes. Also other authors pointed to the fact that transport of blood constituents e.g. proteins, and platelets, into the arterial walls increase with increasing shear stress [7, 21, 29]. Later, several authors have pointed out that the high shear stress achieved by Fry's experiments are not likely to occur in vivo in man [6, 39]. Caro et al. [6] hypothesized that atherogenic substances accumulate in areas with low shear stress because the efflux of substances

Figure 1. Schematic diagram of the aortic bifurcation model with model terminology. $A_t = A_1 = A_2$.

is inhibited at those sites. They assumed that mass transport from the blood to the arterial vessel occurred by means of mass diffusion which increased at low local shear stress. Fox and Hugh [12] postulated that regions of flow separation at arterial branch and along curved segments caused zones of stasis to form. The blood stream stagnates locally and allows platelets and fibrin to form a mesh at the wall in which lipid particles become trapped and eventually coalesce to form atheromatous plaques.

A new trend in cardiovascular research centres around what is called vascular gene expression. The results of recent experiments [17, 33, 37, 44, 45], confirm that endothelial cells can sense and respond distinctly to different shear stresses at the level of gene expression.

A bifurcation can be considered as two superimposed curved tubes bending in opposite directions. In a curved tube, the secondary flow tends to push the flow in the curving plane towards the outer wall, resulting in a relatively high shear rate on the outer wall [19, 36], and the opposite is expected to be true in a bifurcation. The secondary flow induces a higher shear rate along the inner wall of a bifurcation. The outer wall of the curved tube can be considered as the inner wall of a bifurcation (Figure 1).

Flows at both aortic and carotid bifurcations have previously been investigated by several authors [3, 10, 22, 25, 31, 35]. These studies have demonstrated several important features of the flow such as strong secondary flow in the branches, separation zones in the branches with lower mean velocity, both in steady and pulsatile flows and higher shear stress at the apex in comparison to the outer corners of the branches. Among Y-shaped bifurcations in the human arterial system, only the

Figure 2. Schematic diagram of the flow system.

aortic bifurcation is relatively symmetric in geometry with respect to the trunk axis [20]. In this study the results of steady flow conditions in a bifurcation model are presented and discussed under three main headings: Streamline flow patterns, separation zone formation, and residence time.

2. Materials and Methods

2.1. CONSTRUCTION OF THE TUBE MODEL

The model under study is a symmetrical bifurcation of constant diameter (a parent tube and two branches). It represents the aortic bifurcation i.e. where the aorta bifurcates into two common iliac arteries. The inner radius of the parent tube, as well as, the two branches is 16 mm. An area ratio (total out flow area to total inflow area) of 2.00 resulted (Figure 1).

The tube was machined out of two halves of Plexiglass which were then polished, so as to make flow within the tube visible, and cemented together at the plane of symmetry of the tube. Carefully smoothening and polishing of the inlet surfaces were also carried out to ensure laminar flow at the tube entrance.

2.2. EXPERIMENTAL SETUP

The test section was incorporated into a mock-circulatory system providing steady flow. The schematic diagram of the system is shown in Figure 2. Water as working fluid was pumped from a reservoir R to a constant head tank T_1 placed at a height

that provides a static pressure close to the mean blood pressure at the aortic bifurcation. T_1 consists of two vertical adjacent parts, where water was pumped into the first part which when full the water then drained with laminar flow into the second part. In this way the flow will be free from any disturbance that may result from the pump. Any over flow from the second part of T_1 feeds back to R. A bypass tubing with a valve V_2 regulates the pump flow rate. The second part of T_1 is connected by means of silicone tubing to a settling chamber 'S' of dimensions $38 \times 32 \times 11$ cm. 'S' has a multiple orifice plate and a wire screen to reduce velocity variations and to damp out any eddies that may be present when water flowed from T_1 . The flow to the 'S' entrance was controlled by a valve V_1 which was placed upstream from 'S', so that the flow rate could be varied. The presence of 'S' thus helped to ensure laminar flow into the test section, and that the velocity profile of the flow entering the test section is practically uniform as 'S' is much larger than the cross section of the tube. From the settling chamber, water then flows into the test section via a bell-mouth piece attached to the straight entry section of the tube. To ensure a fully developed laminar flow in the test section water was introduced to the test section via a 120 cm long straight tube with the same inner diameter as that of the test tube (Figure 2). El Masry et al. [10] and Bharadvaj et al. [3] used an entrance length of 15–20 the vessel diameters to get a fully developed flow in the bifurcations.

Water after leaving the test section next flows into two constant outlet tanks T_2 and T_3 via two 70 cm long straight pipes of the same inner diameter as the test section outlets. Water level is kept constant in T_2 and T_3 and any excess was drained into collecting vessels to obtain the flow rate measurements. The flows from T_2 and T_3 could be diverted using valves V_3 and V_4 into the sink so that the flowing water can be changed periodically.

2.3. FLOW VISUALIZATION

The circulating fluid was water and filaments of Methylene blue dye was used for flow visualization. The concentration of the Methylene blue was 2.5 g/liter water. The dye has an adequate visibility and natural buoyancy and does not diffuse readily across streamlines (Scarton et al., 1977). The dye was held in a small reservoir with multiple outlets and each of these outlets was connected via small flexible tubings to injection sites along the test section walls. Dye filaments were also introduced into the test section through the bell-mouth entrance by the use of a thin dye pipe of inner diameter 0.5 mm whose location over the cross section of the bell-mouth could be varied (Figure 2). The dye was introduced into the set-up in such a way that it gently oozed out from the holes at the tube walls and from the dye pipe at the bell-mouth entrance. This was achieved by carefully adjusting the height of the dye reservoir. Since dye was used in the visualization of the flow, water in the reservoir R had to be changed periodically.

The flow patterns were carefully observed and photographically recorded and perspective drawings of the flow patterns were made based on them. The photo-

graphs were taken using a Minolta camera SRT101 with MD zoom 22–70 mm 1:3.5–4.8. Precautions were taken to avoid unwanted reflections by the placement of light absorbing paper behind the test section. A direct back lighting was used to provide a clear image of the dye streamline. The camera was fixed on a tripod and Fuji-400 films were used.

2.4. RESIDENCE TIME MEASUREMENT

In order to measure the particle (dye) residence time within the separation zones, a dye-dilution technique was used. A bolus of dye (Mythelene blue) was injected at the separation point and the time taken for the dye particles to stay within the separation zone until washed out was measured. The dye particles enter and leave the separation zone after a period of time; this we call the residence time. A known and constant quantity of Mythelene blue is always injected into the separation zone (at the separation point). The concentration of the dye was again 2.5 g/liter. The relation between the Mythelene blue dye solution concentration versus absorbance was determined using a UVIS Shimadzu spectrophotometer at a wavelength of 880 nm. This relation can be evaluated by the Beer-Lambert law. The relative change in the light transmission is proportional to the dye concentration within the separation zone assuming that the dye concentration is small enough (2.5 g/liter) as reported in our previous study [34]. More details are reported in Nitzan et al. (1998).

The measurement system consists of an Infrared Light Emitting Diode (LED) SFH-484-2 5 mm and an integrated photodiode TPL 10530 DAW both attached to the two lateral surfaces of the test section where the separation zones occur. The distance between the LED and the photodiode is the same during the measurements for all the Reynolds number studied. This arrangement measures the concentration variations of the dye within the separation zone. The light from the LED was modulated at a frequency of 1 kHz and the detected transmitted light was filtered through a narrow band pass filter to avoid background light. The signal was then demodulated (Figure 3) in order to obtain the dilution curve. When a bolus of dye was injected at the separation point under the condition of flow separation, the dye concentration modulates the light transmission and the resulting signal was recorded continuously by a Gilson-multichannel biophysical recorder thus generating the dilution curve, until the dye was completely washed out.

The following are the assumptions and precautions used in the above measurements:

1. In order to measure the residence time it is necessary that flow be constant during the period of measurement and the system must exhibit stability.
2. The indicator be injected into the system suddenly as a bolus and it was washed out gradually with respect to time.
3. The chart recorder velocity was fixed throughout all measurements.
4. The bolus volume was kept small and constant with respect to the water flow (0.5 ml).

Figure 3. Schematic diagram of the residence time measurement system, LED: Light Emitting Diode.

5. The location of the photodetector and LED was fixed throughout the measurements process at all Re numbers studied.

The model is similar to the aortic bifurcation, but the scale is approximately three times the normal. The bifurcation angle is 75° (Figure 1). The bifurcation region is the main region under study, where the fluid bifurcates into the two branches. This region contains the following geometrical parameters:

- **Flow divider:** The inner walls of the bifurcation tube. (Figure 1).
- **The outer corners:** the parts of the bifurcation region where the parent tube changes the direction through the two branches, or the points which join the parent tube walls with the outer walls of the branches.
- **The apex:** the point where the inner walls intersect.
- **The saddle region:** the part in the bifurcation region located in front of the apex where the flow direction reverses after impinging the apex (Figure 1).

According to Whitmore [46], the Reynolds number of the blood flow in the human arterial system in large arteries (down stream of the descending aorta) varies from 110 to 850. Stein et al. [41] measured blood velocity in the descending aorta proximal to the aortic bifurcation and obtained a peak Re ranging from 400 to 1000.

The present experiments were carried out for upstream Reynolds numbers in the range of 80–1250.

3. Results and Discussion

3.1. STREAMLINE FLOW PATTERNS

In the following it was assumed that the bifurcation is placed with its plane horizontal, so that there would be symmetry of flow about the horizontal (xy) plane. The upper half of the bifurcation corresponds to that part of the model that is above the plane of symmetry and the flow in the parent tube is from left to right. The fluid flow in the tube is a fully developed laminar flow as it comes from a long entrance tube (120 cm). The streamline flow patterns are presented at a common parent tube Reynolds numbers of 115, 412 and 680. To show the flow patterns at different parts of the vessel, the flows in the two branches were made equal and dye was injected at different locations over the tube cross section. More photographs of interest for different Reynolds number are shown in Figure 7. All figures and photographs show a top view of the test tube.

Figure 4 shows the streamline flow patterns at $Re = 115$. Filaments 1 and 2 injected towards the right lateral wall (Figure 4a) tend to flow away from the outer wall of the branch towards the inner wall. Streamlines 4 and 5 flow with similar paths but they skewed towards the left branch since the injection was close to the left lateral wall. Filament 3 injected at the center of the parent tube cross section (Figure 4a), strikes the apex and splits into two parts. Filaments 6, 7 and 8 injected at sites above the plane of symmetry xy are shown in Figure 4b. Filament 6 injected at the upper right of the cross section, tries to flow towards the left branch but it changes direction and turns back to the right branch with a helical motion that is closer to the inner wall. Filament 7 injected over the center point strikes the apex, then splits. The behavior of filament 7 is similar to that of filament 3 but the latter strikes the apex more strongly. Filament 8 flows with a pathway similar to that of filament 4 and it broadens after leaving the flow divider region. On the other side of the symmetrical plane xy , are filaments 9, 10 and 11 as shown in Figure 4c. These filaments have flow behavior similar to that of filaments 6, 7 and 8.

The streamline flow patterns at $Re = 412$ are shown in Figure 5. A group of streamlines emanating from the central plane xy (plane of symmetry) at the entrance, as shown in Figure 5a are labeled 1, 2, 3, 4 and 5 and the flow is parallel to the parent trunk walls. The filaments were injected at roughly selected sites and not necessarily in symmetrical locations about the center. As the filaments reach the flow divider area, their behavior become different. Filament 1 was injected at the plane xy (plane of symmetry) close to the right lateral wall as shown in Figure 5a. As the filament reaches the branch mouth, it starts to flow with a 3-dimensional helical motion forming an open recirculating vortex, displaying a separation zone. The flows enter and leave the separation zone after being trapped for a certain time (residence time). After leaving the separation zone, the filament flows towards the

Figure 4. Streamline flow patterns in an aortic bifurcation (top view). Numbers indicate the locations of injection over the cross section of the tube entrance. xy is the plane of symmetry, $Re = 115$. (a) The filaments 1, 2, 3, 4 and 5 are injected at the plane of symmetry. (b) the filaments 6, 7 and 8 are injected towards the upper wall of the model, and in (c) the filaments 9, 10 and 11 are injected towards the lower wall of the model.

Figure 5. Streamline flow patterns in an aortic bifurcation (top view). Numbers indicate the locations of injection over the cross section of the tube entrance. xy is the plane of symmetry, $Re = 412$. (a) The filaments 1, 2, 3, 4 and 5 are injected at the plane of symmetry. (b) The filaments 6, 7, 8 and 9 are injected towards the upper wall of the model, and (c) the filaments 10, 11 and 12 are injected towards the lower wall of the model.

inner wall then out again along the outer wall with a twisting motion that leads to some broadening. Filament 2 tends to flow away from the outer wall of the branch towards the inner wall. Filament 4 flows with a pathway similar to that of 2 but the second one skews towards the left branch since the injection was close to the left lateral wall. In the case of filament 3 which was injected at the center of the parent tube cross section, it continues to flow along the central line of the parent tube until it strikes the apex. The velocity of the fluid at the central line is high compared to other parts of the lumen. The flow symmetry around the central line leads to straight streamlines without any skewing. After the filament strikes the apex, it splits into two broadened bands, with each flowing for a certain distance along and adjacent to the inner wall before spreading towards the outer wall. Filament 5 was injected at the xy plane close to the left lateral wall. It starts to twist counterclockwise, after leaving the bifurcation angle, and this leads the filament to spread into a band which then flows away from the outer wall to follow the branch central line. Filaments 6, 7, 8 and 9 injected at sites above the plane of symmetry xy are shown in Figure 5b. Filament 6 exhibited a helical motion after leaving the outer corner area to fill the region adjacent to the outer wall with a 3-dimensional reverse and helical flow. Filaments 7, 8, and 9 deflect towards the inner walls of the test tube as they reach the bifurcation region with filament 9 showing a clear helical motion. Filament 10, injected towards the lower right side wall (Figure 5c) showed marked changes in the streamline pattern. First, it flows with a flow path similar to that of 6. After that, a part of the dye reverses backwards and moves towards the flow divider region to follow the outer wall of the left branch with a helical motion. Filaments 11 and 12 (Figure 5c) flow with pathways similar to those of 7 and 8.

As Re is increased to 680, additional characteristics, were observed, as seen in Figure 6. A major feature of this flow is the formation of disturbances that start at the outer corners. These disturbances continue within the proximal part of the branches, especially for filaments that were injected closer to the walls of the parent tube as shown in Figure 6a. The filament 3 which was injected at the center of the cross section of the tube entrance splits into two bands further upstream from the apex. The resulting bands flow towards, and later follow, the outer walls. The filaments 6, 7 and 8 were injected towards the top of the cross section. They flowed helically starting from the saddle region moving first towards the inner walls near the apex, before starting to twist and spread out into a band in the region adjacent to the inner wall. The complementary group of filaments labeled 9,10 and 11, flow with a similar motion with filament 11 showing trapped helical motion along the outer wall of the right branch. The filaments, in general, come closer to the apex and the inner walls than those at low and moderate flow rates at the same locations. This can be attributed to their higher velocities.

Most of the filaments, for all Re numbers, that originate near the lateral walls of the parent trunk flowed into the side branches. This reflects a tendency for the branches to accept preferentially the slower streamline flow (with low momentum) near the wall of the parent trunk. These streamlines diverted most easily from those

Figure 6. Streamline flow patterns in an aortic bifurcation (top view). Numbers indicate the locations of injection over the cross section of the tube entrance. xy is the plane of symmetry, $Re = 680$. (a) The filaments 1, 2, 3, 4 and 5 are injected at the plane of symmetry. (b) The filaments 6, 7 and 8 are injected towards the upper wall of the model, and (c) the filaments 9, 10 and 11 are injected at different locations.

Figure 7. Streamline flow visualization in an aortic bifurcation model (top view). The circle on the left represents the cross section of the tube entrance, and the dots indicate the location of injection. Water flow is from left to right.

Figure 7. Continued.

at the central core of the trunk. None of the stream filaments that were initially adjacent to the wall reach the apex region, but the filaments with the highest momentum in the central core impinged on the apex then flowed around the axis of the branches.

The apex zone is filled quickly from the core flow and then cleared rapidly as the axial filament deflected into the branches. Helical patterns may form in the branches from these deflected filaments. Several studies have characterized the region of the apex as a high shear rate area [10, 13, 25, 31, 32].

The dye in the saddle region, which is located in front of the apex, is swept continuously when the filament impinged the apex. The saddle shape of dye resulted

Figure 8. Axial velocity distribution of flows in the plane of the bifurcation. The circle at the end of each branch represents the two counter-rotating vortices formed down stream of the flow divider due to the flow around a bend (branch bending).

from the interface between the dyed trunk fluid and the non-dyed fluid swept from the apex.

The sudden increase in the total cross-sectional area as the tube bifurcates into two branches will result in a rise in static pressure at the outer corners [3]. This causes a redistribution of the axial velocity in the xy plane shifting the streamline peak towards the apex and producing a decreased velocity along the outer walls of the bifurcation. Thus, the fluid approaching the outer corners encounter an adverse pressure gradient that depends on the upstream Re and flow division. This causes the fluid to decelerate and possibly to retrograde.

The streamlines located near the tube walls are affected by the stronger secondary flow. They skewed towards the branch before they reach the apex. The velocity of the fluid elements in this part of the tube is less than that of the central core. Therefore, they diverted easily towards the branch.

The helical flow within each of the two branches that is characterized by the slow motion from the inner wall towards the outer wall will result in two counter-rotating vortices downstream of the flow divider. Figure 8 shows the velocity profile skewed towards the inner walls, which are therefore exposed to a high shear stress, while the outer walls are exposed to a low shear stress as reported by many authors

[22, 25, 40]. The two circles illustrate the cross sections visualized at the distal part of each branch with two counter-rotating vortices caused by the secondary flows.

Langille and Adamson [18] compared the orientation of endothelial cells near arterial branch sites in casts of rabbit with flow streamlines near the arterial wall in glass models and found that endothelial cells are oriented in the direction of the blood flow. The streamlines presented in our current study show strong similarity with the streamlines in their models.

Many visualization techniques have been used to investigate flows through bifurcation models. Such techniques include hydrogen bubbles [3], filaments dye injection [2, 10], bulk dye injection [3] and microspheres [11]. These studies tried to show the velocity profile, the secondary flow and the disturbed flow within the vessel, but did not present the flow patterns at different parts of the model. In the present study, many filaments of dye were injected at the entrance as well as along the tube walls, thus revealing the flow patterns at different parts of the model and the disturbed flow near the walls. This study therefore provided a more detail description of the flow field and locations of disturbance in the aortic bifurcation.

3.2. SEPARATION ZONE FORMATION

To visualize the regions of disturbed flow and separation zones, dye was injected into the tube entrance and at several small holes (of 0.5 mm diameter) located around the flow bifurcation region (Figures 9). The separation zone visualization was made for symmetrical flow i.e. $Q_R = Q_L$.

The filaments injected through the tube entrance nearest to the wall in the parent tube seems to flow around an obstacle at the lateral corner. When the dye was injected into holes 1 and 4 of Figure 9a, at a $Re = 412$, it showed the formation of complex 3-dimensional vortices downstream of the lateral corners. The streamline emanating from the separation zone tends to flow towards the inner wall of the branch and with a twisting motion it flows into the central core flow of the branch.

When the dye was injected into holes 2 and 5 of Figure 9b, it simply pooled within the region at the branch mouth adjacent to the outer wall indicating a virtual static zone there. This zone starts at the separation point, as illustrated in Figures 9 and 10, and extends to different sites downstream of the branch. The size of these separation zones, but not the location, was found to be dependent on Re . Sometimes a wide band of slowly reversed fluid was seen beneath the separated boundary-layer stream line. This band was fed by streamlines turned back from the core a short distance downstream from the apex.

The flow within these regions of separation is not exactly a reverse flow but the fluid elements in these regions move with a 3-dimensional helical (disturbed) manner and are washed downstream along helical trajectories. A given particle may experience a reversal of axial velocity during its transit within the separation zone, but due to the tangential velocity component the particle path becomes helical.

(a)

(b)

Figure 9. (a) injections from the holes 1 and 4 show two separation zones at the lateral corners of the bifurcation. (b) Injection from the holes 2 and 5 very close to the separation points shows the dye pooled at the lateral corners. *Se* is the separation point.

Figure 10. Separation zones visualization in an aortic bifurcation model.

Some dye drained from the first zone to the second one so that they become linked. This may be attributed to the low momentum of the boundary-layer fluid and the relatively high adverse pressure gradient downstream may cause the reversing fluid to cross the flow divider region and reach the second separation zone in the other branch.

Many studies reported that the locations of these separation zones are regions of low shear stress [3, 12, 31, 47] or oscillatory shear stress [8, 27].

3.2.1. *The Mechanism of Separation Zone Formation in a Bifurcation*

When the fluid passes from a region of small cross section (the parent tube) into a region of larger cross section (the tube branches), and to maintain flow continuity, the average velocity must decrease in the direction of flow. As Bernoulli's equation suggests, the lost of kinetic energy, is partly converted to pressure energy. Therefore at this location the pressure downstream will be higher and an adverse pressure gradient will occur [23]. The fluid in the outer wall boundary layer has a lower momentum and this momentum is not sufficient to drive the fluid from a low pressure to a high pressure region. So, the fluid may rapidly be brought to rest at the separation point and its flow will be reversed beyond this point.

3.2.2. *Effect of Re*

As the flow rate or Re increased in a branch, the greater momentum of the fluid in that branch appears to enable it to negotiate the adverse pressure gradient more easily. At the region distal to the outer corner the adverse pressure gradient will increase [3] resulting in the formation of a larger separation zone. Figure 10 shows the increase of separation zone size with increasing Re . The flow within these separation zones gets more disturbed and becomes turbulent as Reynolds number increases.

3.3. RESIDENCE TIME

The dye washout profile (dilution signal) from the separation zone was recorded as described in [34]. The residence time of a bolus of dye injected into the separation

Figure 11. Dye-dilution signal of a separation zone in a bifurcation obtained by the chart recorder at $Re = 202$.

Figure 12. Residence time in the separation zone in the right branch vs Reynolds number.

Figure 13. Residence time in the separation zone in the left branch vs Reynolds number.

zone was evaluated starting from the end of dye injection. This procedure was done for both of the separation zones formed in the two branches. Figure 11 shows a sample of the dilution signal obtained at $Re = 202$. It has a sharp rising slope and long down slope. The total period of the measured signal T and the residence time T_{res} for both of the separation zones were recorded. The data were obtained by taking the mean value of several measurements for each Re . The trend lines shown in Figures 12 and 13 indicate that the residence time decreases exponentially with increasing Re .

4. Implication of Disturbed Flow and Separation Zones in Atherogenesis

Our observations indicate that geometry plays the key role in determining the nature of flow patterns and consequently wall shear stress patterns in the arterial system. As such, these investigations can be employed to obtain a better understanding of the environment in which atherosclerosis develops. The streamlines presented here showed that the flow is complex and the branch fluid is influenced by a strong 3-dimensional secondary flow. These streamline patterns show the enhanced chance of formation of separation zones and disturbed flow.

The locations of separation zones found in the bifurcation model in our study are very similar to those found in pathological and in vivo studies. Comprehensive reviews of more recent histopathological studies relevant to the connection between atherogenesis and fluid mechanics are given by Lou and Yang (20).

Cholesterol exists in blood in the form of lipoproteins, mostly as a major constituent of low density lipoproteins (LDL) [46]. The concentration of LDL in plasma is an important factor in the pathogenesis of atherosclerosis [9]. The movement of

Figure 14. Flow path of blood constituents (LDL particles) at separation zones. The reverse flow occurred between the separation point (**Se**) and the reattachment point (**R**) because of an adverse pressure gradient. The radial component of the velocity at the reattachment point is maximum e.g. the particles moving at right angles towards the vessel wall may lead to a deposition (infiltration) of these particles within the intima.

LDL particles along the vessel wall is very important in determining the interaction between these particles and the vessel wall.

The importance of the near wall velocity of flowing blood in the delivery of cholesterol into the blood vessels is more readily apparent when one considers the movements of individual cholesterol particle flowing along a permeable vessel wall at the microscopic level. Because of the fact that every cholesterol particle has a certain finite size, their longitudinal velocity component will not be zero even when they are in contact with the endothelium. Thus, their movement over the endothelium will be largely affected by the fluid velocity in the vicinity of the endothelium.

Mass transfer phenomena in the arterial system is largely affected by the flow patterns. It has been shown that the flow is disturbed and separated at the bifurcation (Figures 9 and 10). From our results we can predict that the separation zones are susceptible to high LDL accumulation and the development of atherosclerosis. As such, the concentration of atherogenic particles, in particular LDL, should be significantly elevated in separation zones [9], with a local maxima located at the reattachment point where wall shear rate is zero, the radial velocity is maximum and the longitudinal velocity minimum (Figure 14). This situation alters the endothelial permeability and may lead to the denudation of the endothelium that represents a barrier to lipoprotein substances. The elevated surface concentration of atherogenic substances is believed to result in an increase in LDL infiltration into the vessel wall. Because of the difference in pressure between the reattachment point and the separation point, the LDL particles that accumulate at the reattachment point may diffuse or migrate towards the separation point where the pressure is lower. Disturbed flow and LDL accumulation within the separation zone may also facilitate the deposition of platelets as advocated by Gear [15]. Platelets that are activated may stimulate cell proliferation by secreting growth factors (PDGF)

and thus induce intimal thickening [36]. These processes can then lead to the growth of atherosclerotic plaques and with time the narrowing of the arterial lumen.

Though the condition of steady flow is not met in the circulation where flow is pulsatile, flow in blood vessels can be treated as having a steady component on which pulsations are superimposed. Besides the present study, the influence of flow rate on the particle (LDL) residence time has not been investigated. We have shown that an increase in flow rate (Re) leads to an exponential decrease in the residence time as shown in Figures 12 and 13. In general, residence time is a function of Re although the flow in the separation zone is complex.

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