Changes of Boundary Layer Flow in Model Systems: IMPLICATIONS FOR INITIATION OF ENDOTHELIAL INJURY

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Experimentally induced damage to very small areas of the vascular wall in rabbits may be followed by rapid development of arterio-atherosclerotic lesions at the site of injury. Localized mechanical forces of sufficient intensity to initiate such injuries may be generated by events in the boundary layer of blood flow in certain instances. One of these is a local contour change in the wall of the vessel, for example a sudden change of diameter. Another is that of branching of the vessel. At the locations where these changes occur, there is a local increase in turbulence. As a consequence the viscous shearing stresses in the boundary layer may become large enough to cause injuries of the vessel wall. Some mention has been made of boundary layer events and arterial thickenings, but the boundary layer theory of fluids has not been extensively investigated in connection with arterio-atherosclerogenesis. It is the purpose of the present paper to indicate how boundary layer events can initiate damage to vessel walls in model systems and to suggest possible ways in which human arteriopathy may develop as a consequence.

Methods

Cylindrical glass and plastic tubes, 0.5 to 0.75 inches internal diameter were coated on the inner surface with wax, collodion, silicon or synthetic resins. The coatings were either dyed with acid dyes or dusted with carbon to facilitate visualization. An axial segment of the tube, approximately 1 cm in length was drawn out by heat prior to coating, producing a reduction in diameter of about 50%. Tap water, heated to 37°C, was caused to flow through the tubes. The average velocity of flow was adjusted to Reynolds numbers in excess of 4000, the Reynolds number being defined as $Re = \frac{\rho V D}{\mu}$, where $\rho$ is the density, $V$ the average velocity, $\mu$ the viscosity of the fluid and $D$ the diameter of the tube. The fluid entered the tubes under turbulent conditions and remained turbulent throughout. The downstream end of the constriction is a location where boundary layer separation is to be expected as will be noted below. This region, where the diameter undergoes a rather sharp change, produces flow into a divergent channel. The backflow characterizing inipient boundary layer separation was indeed observed in the small air bubbles carried along in the fluid, which in the region near the walls of the tube moved in a direction opposite to that of the main stream. The fluid was allowed to run through the tubes for several hours. Visual and photographic observations were made of the coated surface. It was estimated that these surface coatings varied from 0.05 mm to 0.5 mm in thickness. After drying, all coatings were difficult to remove by mechanical means.

The experiments were repeated using Y-shaped glass tubes. The straight portion measured several feet in length, with an internal diameter of 0.75 inch; the limbs were each 18 inches long with internal diameters designed to give a total cross-sectional area equal to that of the main portion of the tube and set at an angle of 45°C.

Results

Observations were made every fifteen minutes for a period of one to five hours. Within the first thirty minutes of flow, the lining of the inlet portion of the tube began to peel away and continued to do so for several hours until it was completely removed for a distance of approximately 12 cm.

The time interval between onset of experiment and beginning of peeling varied with the velocity of the fluid and the nature of the coating.

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BOUNDARY LAYER FLOW AND ENDOTHELIAL INJURY

FIGURE 1
Upper: Constricted tube, coated with Permount and dusted with carbon before connection to water tap. Lower: Same tube two hours after water at 37°C had passed through. Velocity adjusted to give Reynolds number of approximately 4200. Internal diameter of nonconstricted portion = 0.75 inch. Arrow shows direction of flow.

CONSTRUCTED TUBE
Depending on the fluid velocity and on the material used on the inner surface, small blisters began to appear in the lining of the downstream side of the constriction either within 30 minutes or after several hours. As the flow continued these small blisters coalesced and clear areas began to appear circumferentially just "beyond" the constriction in the direction of flow, figure 1. This clear zone developed circumferentially around the tube in a symmetric fashion and indicated the removal of the lining at the wall. With time, the removal of this lining was propagated backward into the region of the constriction, against the direction of flow, but never reached the upstream side of the reduced diameter, figure 2.

Fifteen such experiments were run under identical conditions of Reynolds number, tube diameter, temperature of fluid, etc., and always resulted in the same preferential removal of the applied coat, other portions of the tube remaining intact except for the occasional appearance of small blisters, randomly formed. Decreasing the fluid velocity resulted in a longer time interval for the development of maximal shearing away of the surface. However, below a certain fluid velocity (Reynolds number much below 4000), the effect was not observed even after several hours had elapsed. Conversely, increasing the velocity of the fluid shortened the time interval required for maximal effect. Increasing the fluid temperature resulted in a shortening of the time required for removal of the coating. In some cases, such as when paraffin was used for the coating, the effect was noted within a few minutes. However, in all circumstances, the shearing action was consistently preferential, being confined to the inlet and divergent-channel portions of the tube. When plastic, (Tygon) was substituted for glass, the same results were obtained.

BRANCHED TUBE
Similar results were observed in the branched tube. After a suitable time interval had elapsed, small blisters began to appear in the region of the junction. These were first observed close to the bifurcation, along the inner surface, just downstream of the point of division and gradually tapered off. Coalescence gradually occurred and breaks and desquamation of the lining occurred at the junction itself and along the inner surface of the limbs. At no time were either the small blisters or sheared-off areas observed on the outer surfaces of the tubes, figure 3.

The experiments were not aimed at establishing a strict quantitative relationship between the various parameters of flow, but were intended to show a consistent qualitative
FIGURE 3
Branched tube as described in text, two hours after flow begun with same flow conditions as in figure 1. Internal diameter of straight portion of tube = 0.75 inch. Arrow shows direction of flow.

FIGURE 4
Flow through branched tube. Each branch corresponds to half an inlet as the flow divides. Average velocity gradients much steeper on inner surfaces where viscous stresses are greatest. Arrows indicate relative magnitudes of mass velocity of fluid across tube diameter.

effect of the shearing stresses which were preferentially greater at certain locations than at others as a result of the special conditions of flow brought about by changing the shape of the tube at certain points.

Discussion
The results may be discussed in terms of boundary layer theory.3-8 As is well known, the velocity profile changes from a parabola in streamline flow to a more and more flattened profile as the degree of turbulence, i.e., the Reynolds number, of the fluid is increased (cf. ref. 5; fig. 7-1, p. 147). In the experiments under discussion, water was used. In the case of blood, the velocity profile deviates from that of water because of lack of homogeneity.9-10 However, as the degree of turbulence increases these differences in velocity profiles tend to decrease. As a consequence of the flattening of the average velocity profile the transverse, i.e., radial for the case of flow in a tube, velocity gradients become steeper in that region of the fluid which is adjacent to the vessel walls. This region is known as the boundary layer in contrast to the midstream region of the fluid, also known as core. In a turbulent fluid the shearing stresses of importance in the core region are those due to turbulence. These shearing stresses are proportional to quadratic products of the turbulent velocity components, and they may be quite large for flows with high Reynolds number. Because the fluid velocity is small in the boundary layer region and drops to zero as the wall is approached, the boundary layer acts as a buffer, shielding the vessel walls from the turbulent shearing stresses prevalent in the core. However, the viscous shearing stresses in a fluid, being proportional to the fluid viscosity and the velocity gradients, may be quite large in the boundary layer region. As pointed out above, the higher the degree of turbulence of a streaming fluid the steeper the transverse velocity gradients in the boundary layer and hence the larger the viscous shearing stresses to which the vessel wall is exposed. It is important to appreciate the two kinds of shearing stresses which can occur in a turbulent fluid and the separate regions in which they act. The turbulent shearing stresses of the core are relatively unimportant in producing injury to the walls.

Any local disturbance tending to increase the degree of turbulence of the fluid and to further flatten the velocity profile will also cause the velocity gradients and hence the viscous shearing stresses on the walls to be increased. Such local disturbances in the velocity profile occur, for example, at the inlet of tubes, at branch points, and also at the
downstream end of local constrictions. At a branch point the velocity profile characteristic for flow in a tube is destroyed and it will not be re-established for some distance downstream from the point of bifurcation (fig. 4). Therefore the transverse average velocity gradients and hence the viscous shearing stresses will be excessively large at the inner banks of the tubes in the downstream region near a branch point, and preferential damage to the tube lining is to be expected there (fig. 3). A similar phenomenon occurs at the downstream end of a constriction, where the turbulence is locally increased and the velocity profile flattened due to boundary layer separation. Hence the viscous shearing stresses and the damage to the walls are also relatively increased in this region (figs. 1 and 2).

The significance for the pathology of the circulatory system of the above physical considerations lies in the fact that they suggest a means for initiating or perpetuating arterial injury in a manner which would favor the development of arterio-atherosclerosis. Since, even microscopically small disruptions of the endothelial surface are capable of giving rise to large fibro-elastic or atherosclerotic plaques, it is apparent that the boundary layer plays an important part in buffering against, or inducing such injuries. Changes in the contour of arteries, such as local vasoconstriction or vasodilatation, flow into branches, etc., by altering the average velocity profile, create high viscous shearing stresses; these stresses coupled with stress fracture-points which are probably frequent in arteries, tend to induce small discontinuities in the endothelial surface. Vasoconstriction as a means of promoting arterial injury has been investigated elsewhere. Of added importance is the inhibiting effect on arterial repair of hyperlipemic serum, lending itself to enhancement of plaque formation. The manner in which these events may be translated into pathophysiological effects on the cellular level in terms of arterio-atherogenesis has been reported elsewhere.

Consideration of the viscous stresses of the boundary layer and their augmentation under certain conditions may aid in the explanation of some common observations associated with arterio-atherosclerosis. Among these are the greater frequency of lesions at certain locations in preference to others, involvement of arteries (where average velocities are higher) rather than veins, the more common occurrence in states of hyperlipemia, and the much more usual finding in man rather than in other mammalian species. In view of more pronounced vasomotor activity in man, it seems likely that local contour changes of vessels are more common in man than in animals and hence contribute to greater visous stress damage of vessel wall lining. Boundary layer phenomena as a contribution to the pathogenesis of arterio-atherosclerosis have previously received little attention, although when considered in connection with inducing vascular injury they merit consideration as a means of producing arterial disease.

Summary

A model system using fluid driven through glass and plastic tubes coated with resin, demonstrated augmentation of the viscous shearing stresses at the inner surface of the wall when variations in shape were introduced into the tube and at branch points. The hydrodynamic basis of these increased stresses is presented from the point of view of boundary layer theory, and the relevance for initiation of arterio-atherosclerosis is discussed.

References

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