

oblique section through the leaflet-sinus assembly shows this remarkable relationship, (figure 4). This section reveals that the sinus and leaflet form a circle when the valve is in a closed position. Furthermore, it is angulated to a degree as to allow pressure transduction along the entire surface of this unit. This suggests that the shape of the leaflet-sinus assembly is important in determining how stresses are developed within the valve. It is also this relationship that allows the valves to close without pulling upon the aortic valve as has been suggested. Finally, this relationship of the sinuses and valve allow for the efficient flow of blood in the coronary ostia.

The aortic root has been described to expand during ventricular contraction. The dilatation of this structure by the law of Laplace reduces tension which in turn reduces resistance to flow. It is this phenomenon that also allows for complete opening of the aortic valve. Interestingly when the cusps open there is maintained a circular dimension that is at least the same as before contraction. Moreover, it has been studied to be even larger than the original orifice. (Medical Engineering & Physics 19(8):696-710, 1997). In more detail, this behavior allows the valve to have reduced circumferential stress and a reduced Reynold's shear stress number. This is the number used to evaluate the amount of stress in a confined fluid system. In a similar manner, the inner lining of the cusp of the valve, the lamina ventricularis extends into the ventricular myocardium. There is a confluence of fibers at the base called the fibrous coronet which is a distinct separation between the elastic fibers above and the myocardium below. However, this structure is not static. In contrast it is a very dynamic structure which bends and molds to the forces which are exerted from the ventricular myocardium (Cardiovascular Research, 22, 7, 1988) (Journal of Biomechanics 33(6):653-658, 2000 June). In a similar fashion as the aortic root this structure allow the valvular apparatus to open with the least amount of strain.

The coronary arteries arise within or above the sinus of Valsalva. The blood flow of the heart occurs mostly when the ventricle relaxes. At this time the cusps of the aortic valve are closed, and as mentioned, the diastolic forces of the blood against the valve are dispersed along the valve and adjacent sinus. The opening or ostia of the coronary arteries when located near the apex and middle of the sinuses allows for the most laminar flow characteristics. This in turn promotes the greatest amount of flow with the least amount of resistance. In disease states where these relationships are lost, it has been proposed that this could lead to increase stress at the coronary ostia. (The Aortic Valve CRC press).

These integral relationships not only pertain to the gross anatomy of the valvular apparatus, but also the microanatomy shows the integral nature of these structures. The amount of elastin is in a higher concentration as shown by staining methods (American Journal of Pathology 445 (7): 1931). This allows a greater amount of dilatation of the structures in this area. Further, scanning electron micrographs have shown the unique arrangement of collagen in the valves which permit the unique reversal of curvature which is vital in the function of the valve (figure 6) (Anatomic Embryology 172(61): 1985). The fibers are unusually small and arranged in sheets with unique distances between each strand. In theory this would give a greater amount of tensile strength while allowing continued flexibility. As always, nature has selected the most efficient machinery, and we have only to discover the reasons why.

→ Predictable
Probability
of laminar
flow

→ The relationship varies, but is fairly consistent

II. Aortic Valve Dynamics and Physics

The aortic valve is better understood in a dynamic state given it is not a static structure. To fully understand this structure it is integral to understand the opening and closing of the valve, the motion of the various parts, the design of the valve in vitro and the hydrodynamics of the valve. The valve's ultimate function is to allow fluid transfer from the ventricle to the systemic circulation. In order to do this efficiently it minimizes shear stress, resistance to flow and tensile forces.

The opening and closing of the aortic valve depends upon differential pressures, flow velocity characteristics and, as mentioned earlier, the unique anatomic relationship between the valves and the sinuses of Valsalva. One of the most comprehensive study^{studies} encompassed a model developed by Bellhouse, et al. In this model, the flow of fluid through the aortic valve was studied by injecting dye within the flow of fluid. Some of the pertinent observations found within this model were as follows: 1) The valve opens rapidly, and as the leaflets move into the sinuses, vortices form between the leaflet and the sinus walls; 2) The flow enters the sinus at the sinus ridge, curls back along the sinus wall and leaflet and then back into the main stream; 3) During the end of systole the vortical motion created during contraction forces the valves back toward a closed position. These observations are important to show that absolute pressure differences created between the aorta and ventricle are not the source of initial closure of the aortic valves. In fact, it would be detrimental to valve stress if these forces dictated closure of the aortic valve. For example, if two objects are a greater distance apart and a set amount of force is applied to each, the greater distance would produce greater velocity and the momentum at impact would be greater. Therefore, if the leaflets are closed or near closure as contraction is coming to an end then the force used for coaptation would be less. Less force per cycle equates to greater longevity of the valve. In conclusion, the cusps and the relationship of closure for prosthetic valves must incorporate passive closure during systole which would logically lengthen the lifespan of any such device.

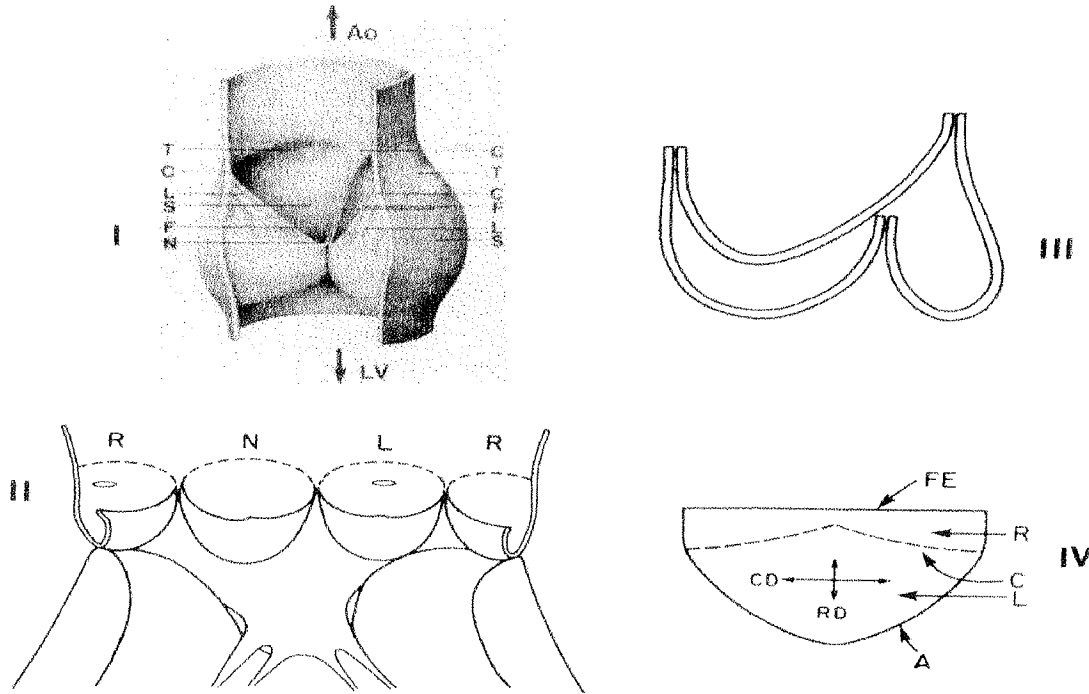
To expand these concepts, we must explore the theory of laminar flow as it relates to aortic valve function. Laminar flow is predicted by Reynold's number, which incorporates the laws as described by Pouiselle and Bernoulli. In general, the lower the Reynold's number the more likely that flow will be laminar. The equation that describes the Reynold's number in the aorta is as follows:

$$Ua/v = \text{Reynold's number}$$

That is, U which equals the velocity of blood and (a) which represents the radius of the aortic valve is inversely related to the viscosity of blood. As the velocity increases or the viscosity decreases, the tendency towards turbulent flow also increases. Moreover, the behavior of the system is also predicted by the rate of acceleration or deceleration which is described by the Strouhal number. In explanation, in a system where viscosity, velocity and radius vary slightly, the rate of acceleration or deceleration predicts laminar versus non-laminar flow. When looked at in perspective, it is easy to see the relevance. Only a small pressure difference is required to open the native aortic valve. Maintaining a small pressure difference minimizes acceleration to flow. Thus, laminar flow is more likely. The deceleration phase is naturally a gradual process; however, as stated above it is the relationship between the sinuses and the cusps which allows this deceleration to

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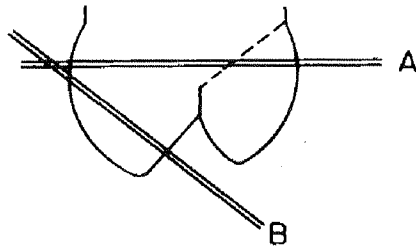
occur without an abrupt pressure drop. When laminar flow is produced, the resistance to flow, wall stress, shear stress and circumferential stress is reduced. This reduction decreases cardiac work and increases the longevity of the valvular apparatus. Ultimately a design to replace a diseased aortic valve must incorporate many if not all of these relationships.



III. Adult Aortic Stenosis

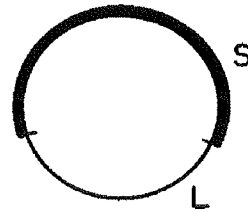
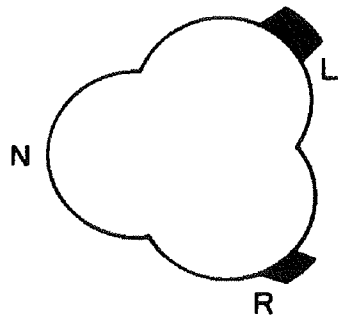
Aortic stenosis is a condition where there is a restriction to the ejection of blood from the left ventricle to the systemic circulation at the aortic valve level. If the aortic valve cusps do not open, or there is failure of the valvular apparatus, ~~then~~ a pressure gradient develops. In order to overcome this pressure difference, the left ventricle begins to hypertrophy. Over a period of time this produces pressure overload on the left ventricle. Clinically, this produces dramatic symptoms, and in the most severe form it is fatal unless treated.

The incidence of aortic stenosis varies considerably. In epidemiologic studies the incidence is between 2 to 4% of the general population. In the early 20th century the most common etiology of aortic stenosis was rheumatic fever. This streptococcal infection produces inflammatory changes in the aortic valve. Interestingly, these changes affect the coaptation surface to a greater degree than the other structures of the aortic valve. Affecting the coaptation points, results in fusion of cusps. This fusion results in a restriction to the opening of the cusps. A pressure difference develops as well as non-laminar flow. Once this cycle develops, ~~then~~ the valve has increased deterioration and calcification. Unfortunately, post infectious aortic stenosis can result in rapid progression to severe aortic stenosis. Of the total cases of aortic stenosis in the 1940's, reportedly 52% were the result of rheumatic fever. Currently, less than 9% of the cases of aortic stenosis are postinflammatory.



(A)

(B)



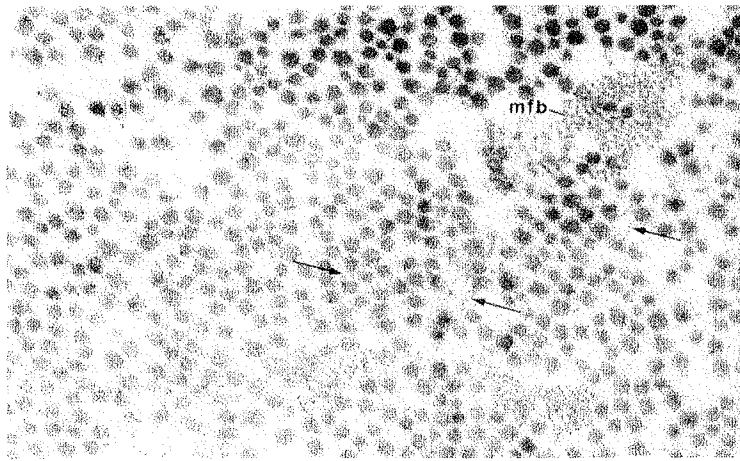
? put most common first

~~What is the most common cause of aortic stenosis?~~

The second most common cause of aortic stenosis is a bicuspid aortic valve. This has remained relatively constant throughout the decades. It accounts for 33 to 40% of the total cases of aortic stenosis. This condition affects most parameters of aortic function. Inherently, it loses the anatomic relationship between the sinuses and the valve cusp. Further, the opening and closing characteristics of the valve are altered, which in turn alters the acceleration and deceleration to flow. As a result, non-laminar flow characteristics are developed. Because of the altered anatomy, a bicuspid aortic valve cannot easily reverse curvature. Due to this limitation, the bicuspid aortic valve has increased stress at the base. It is at this point where morphologic changes first appear. However, this valve is usually survived into adulthood.

Currently, the most common cause of aortic stenosis is degenerative aortic stenosis. By the 7th decade, the normal aortic valve can undergo degenerative changes. The characteristics which define these changes are increased calcium deposition along the ~~the~~ body of the cusps. ~~Predominantly the calcification is located at the bases of the cusp and on the aortic side. When enough calcium is deposited as to restrict flow, then there will be a variable amount of fusion along the coaptation surface.~~ The incidence of aortic stenosis reaches as high as 12% in octogenarians. This population accounts for 51% of the current cases of aortic stenosis. The factors which promote aortic stenosis in

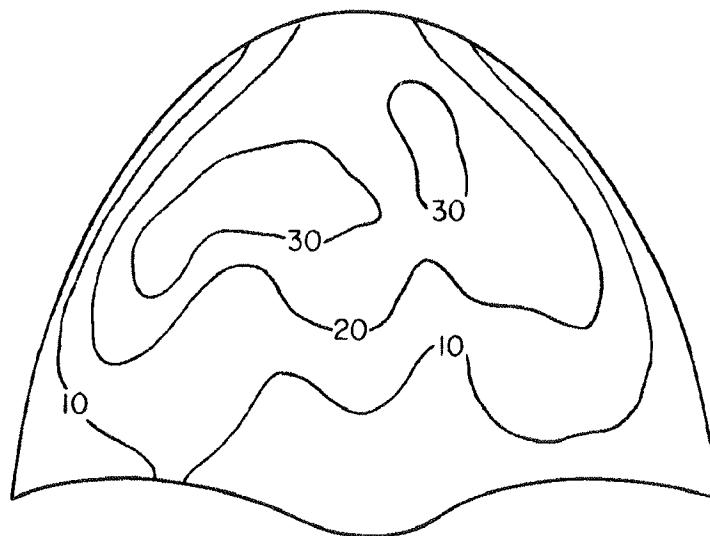
the calcification is predominantly



a normal valve are the same as those which affect atherosclerosis. (nejm 1996). Thus, degenerative aortic stenosis has become the most prevalent etiology.

Clinically, symptomatic aortic stenosis has not only disabling symptoms, but also a high mortality. Currently aortic stenosis is graded upon the calculated aortic valve area (**figure 7**). As represented in the table, severe aortic stenosis occurs when the valve area is less than 1.0cm^2 (AVA index of $<0.6\text{cm}^2/\text{m}^2$). The most frequent symptom is angina pectoris occurring in up to 70%. This is followed by syncope or presyncope. Once aortic stenosis becomes symptomatic, the 2 year mortality can be as high as 50% (**Braunwal 1973**). The 10 year survival is a dismal 10%. In conclusion, aortic stenosis is a condition that can produce severe life-limiting symptoms and ultimately is fatal.

IV. Aortic regurgitation



Aortic Regurgitation is a condition where there is backflow of blood from the aorta to the left ventricle. This regurgitation results in a decreased effective cardiac output. In turn, longstanding aortic regurgitation results in an increased amount of volume work on the left ventricle. In time, the left ventricle begins to dilate. Contrary to aortic stenosis, this condition can be well tolerated for many years. However, once the left ventricle begins to dilate and lose its contractility, it becomes rapidly symptomatic. The most common symptoms result from heart failure. Etiologically, aortic regurgitation and stenosis are very similar.

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