Editorial

Hypertrophic Subaortic Stenosis—A Broadened Concept

DURING the past few years physicians have encountered, with increasing frequency, patients with a form of heart disease that had previously not been recognized. A variety of names has been given to this disorder, among them being idiopathic hypertrophic subaortic stenosis, functional obstruction of the left ventricle, pseudo-aortic stenosis, muscular subaortic stenosis, obstructive cardiomyopathy, and hereditary cardiovascular dysplasia. An important observation in the first patients in whom this disease was reported was hemodynamic evidence of obstruction to left ventricular outflow, i.e., a pressure difference between the left ventricular cavity and the aorta during systole, and on the basis of this finding a number of patients were mistakenly considered to have aortic valvular or discrete subvalvular stenosis and subjected to operation. Examinations of the hearts of patients with this disorder, either at autopsy or operation, revealed diffuse hypertrophy of the left ventricle and particular prominence of the septal musculature, which was found to bulge into and attenuate the left ventricular outflow tract. Subsequent detailed analyses of the clinical and laboratory findings in these patients revealed a clinical picture that, in many instances, made it possible to establish the diagnosis prior to an anatomic examination. Most of the patients are adolescents or young adults and in some there is an impressive family history of heart murmurs, heart failure, or sudden death. Fatigue, dyspnea, manifestations of congestive heart failure, and angina pectoris are frequent presenting complaints. The findings on physical examination superficially resemble those of mitral regurgitation or ventricular septal defect, with prominence of the left ventricle, and a loud, long systolic murmur heard best along the lower left sternal border or at the apex. However, a fourth heart sound and paradoxical splitting of the second sound are frequently present. The peripheral pulse is usually sharp and bounding and unlike that which is characteristic of the discrete forms of aortic valvular or congenital subvalvular stenosis. At left heart catheterization an intraventricular pressure gradient is evident, and left heart angiocardiography reveals a small ventricular cavity, striking thickening of the left ventricular muscle, and exaggerated narrowing of the ventricular outflow tract during systole. At the National Heart Institute we have had the opportunity to carry out detailed clinical and hemodynamic studies in 27 patients with idiopathic hypertrophic subaortic stenosis. Ten patients (six males and four

From the Cardiology Branch and the Clinic of Surgery, National Heart Institute, Bethesda, Maryland.
females) have had the familial form of the disease. In two patients in this group clinical manifestations were noted shortly after birth and they are believed to have a congenital form of hypertrophic subaortic stenosis; this lesion apparently developed later in life in the other eight patients. Seventeen patients (14 males and three females) have had the nonfamilial form of hypertrophic subaortic stenosis; 14 of them are considered to have the acquired form of the disease and three the congenital form.

In this era in which so many successful operations have been developed for the relief of stenotic lesions within the cardiovascular system, it is perhaps understandable that the hemodynamic expression of the obstruction to ventricular outflow, the left intraventricular pressure gradient, has received considerable attention. As a result of the studies on our patients and from a consideration of the published experience of others, a number of features of the obstruction to left ventricular outflow that are unique to hypertrophic subaortic stenosis have emerged.

I. Variability of Obstruction during a Single Cardiac Cycle

Selective left ventricular angiography and cineangiography have consistently shown that narrowing of the outflow tract occurs during ventricular systole, while relaxation takes place during diastole. From such angiocardiographic studies it has been suggested that the obstruction results from the apposition of the hypertrophied ventricular wall and septum during ventricular systole. It is possible that careful frame-by-frame analysis of left ventricular cineangiograms will also reveal abnormalities in the sequence of contraction of the left ventricle in patients with hypertrophic subaortic stenosis.

II. Variability of the Severity of Systolic Obstruction in the Same Patient

Our attention was directed to this unique aspect of the disease by the observation that the more forceful ventricular contraction following the compensatory pause after a ventricular premature beat was associated with a larger ventriculo-arterial pressure gradient, but a smaller arterial pulse pressure than the normal beats. It was suggested that the increased force of contraction in these beats results in unusually severe narrowing of the muscular outflow tract and a decrease in the effective orifice size. The administration of a cardiac glycoside also decreased the size of the intraventricular orifice, presumably by a similar mechanism. In one patient, who did not receive digitalis, the peak systolic left ventriculo-arterial gradient was found to be 45 mm. Hg and, when remeasured several days later, it had disappeared completely, although the cardiac outputs were almost identical on both occasions (fig. 1). In two other patients, the systolic pressure gradients exceeded 75 mm. Hg when measured at left heart catheterization, but the gradient was absent when it was measured again at thoracotomy. The occurrence of such variations in the pressure gradient suggests that changes in the force of ventricular contraction, which occur as a consequence of changes in the nervous and humoral stimuli to the ventricle, may profoundly modify the size of the obstructive intraventricular orifice. The changes in the left intraventricular pressure gradient and of the orifice size, which are seen following operations for the relief of hypertrophic subaortic stenosis, should be interpreted in the light of the changes in these variables, which may occur without operation. In view of these striking variations in the severity of the obstruction to left ventricular outflow, it is of interest that Wood has proposed that the severity of right ventricular obstruction in patients with the tetralogy of Fallot may also vary from moment-to-moment and that the muscular contraction of the infundibulum, which is responsible for the cyanotic spells, may be relieved by the administration of cyclopropane.

III. Variations in the Severity of Obstruction in Different Members of One Family

Several close relatives of patients with the familial form of hypertrophic subaortic stenosis have shown many of the manifestations...
Simultaneous left ventricular (L.V.) and brachial artery (B.A.) pressure tracings recorded 4 days apart on a 19-year-old patient with idiopathic hypertrophic subaortic stenosis.

of this disease without an associated intraventricular pressure gradient. Thus they have presented with clinical, radiologic, and electrocardiographic evidence of left ventricular hypertrophy, systolic murmurs along the left sternal border, and even the characteristic appearance of the carotid arterial pulse. The clinical picture presented by these patients without a pressure gradient was almost indistinguishable from that of their relatives who had large gradients, with the possible exception that the systolic murmurs were shorter and less prominent in the former group. It is suggested that the presence or absence of the pressure gradient is dependent on the precise localization and degree of severity of the muscular hypertrophy.

Anatomically, the left ventricle is diffusely hypertrophied in patients with hypertrophic subaortic stenosis, but the septal wall forming the left ventricular outflow tract is usually even more prominent than the rest of the chamber; this configuration has led to the pathologic designation of "asymmetric ventricular hypertrophy." It is not difficult to visualize that some variations in the degree of prominence of the hypertrophied muscle forming the left ventricular outflow tract could occur in the hearts of different patients with the same basic disease, and that this variation could lead to a large intraventricular pressure gradient in some patients and to no gradient in others. Support for this view is found in the study of Paré and colleagues, who recently described a large family, many members of which had evidence of idiopathic ventricular hypertrophy. Postmortem examinations were carried out on three patients in this family. In two of the hearts there was extensive asymmetric hypertrophy, involving particularly the upper portion of the ventricular septum and the subvalvular portion of the free wall of the left ventricle. Although left heart catheterizations were not carried out in these patients, it would seem likely from the description of the specimens that hemodynamically significant obstruction was present during life. In contrast, the ventricular hypertrophy in the heart obtained from a third member of this same family showed concentric hypertrophy, which the authors thought had probably not resulted in an intraventricular pressure gradient during life.
IV. Involvement of Opposite Ventricles in Members of the Same Family

Although the initial description of idiopathic hypertrophic subaortic stenosis focused failure without any evidence of outflow tract attention on the involvement of the left ventricle, it is now clear that bulging of the ventricular septum into the right ventricular outflow tract and a systolic gradient in this region are not unusual.1,16 In the majority of patients the gradients were substantially greater within the left than the right ventricle. In one family observed, however, one member was found to have obstruction primarily to right ventricular outflow, while his two brothers showed the more common picture of left ventricular involvement alone. In another family that we have studied, an 8-year-old boy was found to have a 20-mm. Hg systolic gradient in the left ventricle, but no right ventricular gradient. This child died suddenly and the diagnosis of idiopathic hypertrophic stenosis was confirmed at post-mortem examination. Five years later, examination of his 7-year-old brother revealed physical findings which were essentially identical. However, in the second child there was no left ventricular gradient, but a 40-mm. Hg systolic gradient within the right ventricular outflow tract which was associated with diffuse narrowing of this region on angiocardiographic study.

As a result of such observations it becomes tempting to speculate that the basic disease process in some patients with ventricular hypertrophy of unknown etiology in whom there is no clinical or hemodynamic evidence of obstruction to ventricular outflow may be similar to that present in the patients with hypertrophy and a significant intraventricular pressure gradient, i.e., in the patients with idiopathic hypertrophic subaortic stenosis. Studies in three patients during the past year have lent some support to this possibility. The first of these is a 39-year-old woman who presented with left ventricular failure as well as enlargement of this chamber on clinical examination, by x-ray, and by electrocardiogram. Her sister had died several years earlier, at the age of 39 years, with clinical and laboratory findings that were essentially identical to those of our patient. Right and left heart catheterization in the latter revealed hemodynamic findings of ventricular obstruction. The other two patients are asymptomatic and unrelated boys of 17 and 22 years, each with clear-cut left ventricular hypertrophy of obscure etiology and without an intraventricular pressure gradient. In all three patients angiocardiography has shown a configuration of the left ventricle similar to that which we have seen repeatedly in patients with idiopathic hypertrophic subaortic stenosis, i.e., a small left ventricular cavity, an indentation of its inferior surface, a greatly thickened left ventricular wall, and the cone-shaped outflow tract during systole.1 On the basis of these considerations, the possibility is suggested that the same basic disease process may, in different patients, be responsible for a variety of clinical and hemodynamic pictures. When obstruction to ventricular outflow is present, the designation "hypertrophic subaortic or subpulmonic stenosis" would seem to be appropriate.

At this time we are aware of no method of management that can specifically and favorably influence the course of a patient with idiopathic ventricular hypertrophy. When congestive heart failure is present the usual therapeutic measures have been found helpful, but when there is also hemodynamic evidence of severe obstruction to left ventricular ejection, the digitalis glycosides may be contraindicated.11 In such patients a surgical procedure designed to relieve the obstruction to outflow should be seriously considered.7,12,13 It is clear that the basic disease process in hypertrophic subaortic stenosis is not amenable to surgical correction, but the initial results of operation have been sufficiently encouraging to warrant continuing application and evaluation of this form of treatment.

EUGENE BRAUNWALD
EDWIN C. BROCKENBROUGH
ANDREW G. MORROW

Circulation, Volume XXVI, August 1962
EDITORIAL

References


When we hear that Alcuin ordered the formal teaching of medicine, it was under the name of "Physics"; and not until the Physics of Aristotle came to light did the various branches of natural history become in their turn not only definite studies but also self-sufficient, aside from the art of healing. To this day the healer keeps the name of "physician"; and the subject at Cambridge the name of Physie. It is well to be reminded that although the soldiers of truth must be separated into several regiments, nevertheless for its edification the healing art must draw, directly or indirectly, on all natural science.—Thomas Clifford Allbutt, M.D. Science and Medieval Thought. London, C. J. Clay and Sons, 1901, p. 52.

Circulation, Volume XXVI, August 1964
Editorial: Hypertrophic Subaortic Stenosis—A Broadened Concept
EUGENE BRAUNWALD, EDWIN C. BROCKENBROUGH and ANDREW G. MORROW

Circulation. 1962;26:161-165
doi: 10.1161/01.CIR.26.2.161

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1962 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/26/2/161.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org//subscriptions/