Functional Aortic Stenosis
A Malformation Characterized by Resistance to Left Ventricular Outflow
without Anatomic Obstruction

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When the clinical findings of aortic stenosis are present and a pressure gradient is demonstrated between the left ventricle and aorta, a discrete site of obstruction, generally amenable to surgical correction, has been assumed. The fallacy of this widely held concept is emphasized by the operative and hemodynamic findings in 3 patients described.

It has generally been assumed that the demonstration of a systolic pressure gradient between the left ventricle and the aorta always results from stenosis of the aortic valve, the presence of a localized ring of fibrous tissue immediately beneath the aortic annulus (congenital subaortic stenosis) or, rarely, from a constriction of the aorta itself a short distance above the valve. These lesions are, in general, amenable to surgical correction and patients have been selected for operation on the basis of the magnitude of the pressure gradient across the stenotic orifice. We have recently studied 2 patients in whom significant pressure gradients were demonstrated preoperatively but in whom no anatomic site of outflow obstruction could be detected at the time of open-heart operation. A third patient is described in whom functional obstruction to left ventricular outflow was demonstrated and found to regress gradually after the complete division of a discrete subvalvular stenosis. The clinical and hemodynamic findings in these patients are summarized in the present report.

Clinical Summaries
Case 1. E. Z., a 27-year-old white man was asymptomatic until the age of 16 when he began to have precordial pain with severe exertion. At the age of 20 a precordial murmur was noted in the course of a routine physical examination. At age 25 exertional dyspnea, orthopnea, and paroxysmal nocturnal dyspnea first appeared, persisted, and progressed in severity. Angina pectoris became more prominent and eventually disabling. In June 1957 he was studied by Drs. E. M. Nanson, L. Horlick, and J. E. Merriman at the University Hospital Saskatoon, Saskatchewan, where the clinical diagnosis of congenital aortic stenosis was made. Combined right and transbronchial left heart catheterizations demonstrated a normal cardiac index and a pulmonary artery pressure of 51/32 mm. Hg. In the course of left heart catheterization the catheter was passed into the aorta and upon being withdrawn traversed 2 zones of ventricular pressure. In the distal zone the pressure was essentially equal to the radial artery pressure but in the proximal one it exceeded the radial artery pressure by a mean systolic gradient of 85 mm. Hg. The left atrial and ventricular end-diastolic pressures were elevated to 20 mm. Hg. These findings were interpreted as indicative of the presence of subaortic stenosis.

In the ensuing year, the patient's symptoms progressed to some extent. He was admitted to the National Heart Institute in June 1958. There was no evidence of heart failure. The blood pressure was 120/70. The heart was enlarged and a prominent left ventricular lift was noted outside the midclavicular line. A faint, short systolic thrill at the apex was noted by only one of several examiners. No thrill was palpable at the base of the heart or in the carotid vessels. The rhythm was regular. The second heart sound was normally split with respiration. A grade IV holosystolic murmur was heard at the apex and along the left sternal border. A fainter, shorter ejection-type systolic murmur was heard at the base and radiated into the neck. A diastolic gallop and a short mid-diastolic murmur were present at the apex. The phonocardiogram is shown in figure 1. The electrocardiogram (fig. 2 Top) revealed left atrial and left ventricular hypertrophy. Fluoroscopic and radiographic examinations of the heart demonstrated slight generalized cardiac enlargement with prominence of the left ventricle (fig. 3). The

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ascending aorta did not appear to be dilated and no intracardiac calcification was noted.

The results of right heart catheterization are summarized in table 1. There was moderate elevation of the pulmonary artery pressure at rest and with exercise both the pulmonary arterial and pulmonary capillary pressures rose significantly. The cardiac output, normal at rest, did not rise normally with exercise. Left heart catheterization was carried out by the transbronchial route. The left atrial mean pressure was 16 mm. Hg and its contour was normal and did not suggest mitral valve disease. The catheter was manipulated into the aorta (pressure 118/71 mm. Hg) and upon withdrawal again traversed 2 zones of pressure with ventricular contour; in the distal one the systolic pressure was equal to that in the aorta. Proximally the ventricular pressure was 192/37 mm. Hg, resulting in a peak systolic gradient of 74 mm. Hg. The cardiac index at this time (indicator-dilution method) was 2.96 L/min./M.² The calculated stenotic orifice area was 0.30 cm.²/M.² B.S.A.

A selective angiocardio gram with pulmonary artery injection revealed normal pulmonary vasculature and a normal-sized left atrium. The left ventricular cavity was small. No site of outflow

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**Table 1.—Right Heart Catheterization**

<table>
<thead>
<tr>
<th>Position</th>
<th>Pressure, mm. Hg, systolic/diastolic, mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC*</td>
<td>Rest†</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>PA</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>RV</td>
<td>45/4</td>
</tr>
<tr>
<td>RA</td>
<td>5/1, 2</td>
</tr>
<tr>
<td>PA N₂O test</td>
<td>1%</td>
</tr>
<tr>
<td>Ventilation</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>QO₂, ml./min./M.²</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>R. Q.</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>Cardiac index</td>
<td>Rest</td>
</tr>
<tr>
<td></td>
<td>Exercise</td>
</tr>
<tr>
<td>Arterial O₂ saturation</td>
<td>95.8%</td>
</tr>
</tbody>
</table>

*PC, PA, RV, and RA refer to pulmonary artery wedge position, pulmonary artery, right ventricle, and right atrium.
†Measurements in the resting state are the average of 2 determinations in every instance.
obstruction could be visualized. The aorta was normal in size and contour.

On the basis of the studies outlined, the diagnosis of congenital subaortic stenosis seemed substantiated and operation for its relief was recommended and carried out on June 19, 1958. The aorta was of normal size and a systolic thrill of moderate intensity was felt within it. The left atrium was enlarged and tense and upon digital exploration of the mitral valve, moderate mitral regurgitation was palpable. The mitral leaflets were not thickened and palpation within the left ventricular inflow tract did not reveal a site of obstruction. With cardiopulmonary bypass and elective cardiac arrest induced with potassium citrate, the ascending aorta was widely opened. The aortic valve was normal and the leaflets were thin and mobile. No subvalvular stenosis was seen and a finger could be passed to the apex of the left ventricle with ease. The left atrium was then reentered and a bimanual examination of the entire ventricle carried out. Its wall was considerably thickened but no obstruction could be found and palpating fingers from the aorta and atrium met in the ventricular cavity. The left ventricular endocardium did not appear or feel abnormal. Postoperatively the patient's course was uncomplicated.

Case 2. C. G., a 20-year-old man, was first admitted to the National Heart Institute in July 1957 with the symptom of progressive exertional dyspnea. He was apparently normal at birth and in the course of many examinations by the family physician before the age of 12, the family was never told of the presence of a murmur. At this time, during a routine school examination, a murmur was detected and he was seen by a cardiologist who made the clinical diagnosis of ventricular septal defect. He had always complained of mild exertional dyspnea and this became gradually more severe after age 15. At about 14 he began to experience squeezing chest pain on exertion and he found it necessary to limit physical activity. He had had several attacks of vertigo but no true syncope.

Physical examination was normal except for the heart. The blood pressure was 110/70. The heart was enlarged with the apical impulse in the fifth intercostal space just within the anterior axillary line. There was a prominent left ventricular lift as well as a systolic thrill along the left sternal
border. No thrill was palpable to the right of the sternum or in the carotid vessels. The rhythm was regular and the second heart sound was louder in the aortic than in the pulmonic area. A harsh grade IV systolic ejection-type murmur (fig. 4) was best heard along the left sternal border and at the apex. It was less prominent over the aortic area and was only faintly heard over the neck vessels. A prominent protodiastolic gallop was heard at the apex. The electrocardiogram (fig. 2, *Bottom*) revealed left axis deviation and left ventricular hypertrophy. Fluoroscopic and radiographic examinations revealed moderate cardiac enlargement with fullness of the left ventricular and left atrial contours (fig. 5). There was no evidence of poststenotic dilatation of the aorta.

The results of right heart catheterization are summarized in table 1. The pulmonary artery pressure was normal and as the catheter was withdrawn across the outflow tract, the pressure contour indicated mild subvalvular pulmonary obstruction (fig. 6). Percutaneous puncture of the left ventricle was performed and 2 distinct left ventricular systolic pressures were recorded, one equal to systemic pressure and one exceeding it by 75 mm. Hg. Following this procedure the patient developed cardiac tamponade which was relieved by the aspiration of 250 ml. of blood from the pericardial space. Subsequent left heart catheterization by the transbronchial route revealed a left atrial pressure of 14 mm. Hg (mean) and a normal pulse contour. The catheter was passed into the aorta where a pressure of 111/71 mm. Hg was recorded. Upon withdrawal, 2 distinct ventricular systolic pressures were encountered; distally the pressure was 113/20 and more proximally it was 185/20 (fig. 7). The cardiac index at this time was 3.63 L/min./M.2 and the calculated orifice area was 0.36 cm.2/M.2 B.S.A. The preoperative diagnosis of congenital subaortic stenosis again seemed substantiated and operation was recommended but deferred for 1 year at the patient's request. In the year between study and operation the patient's symptoms and findings had remained unchanged.

Operation was carried out on August 15, 1958. Only a mild systolic thrill was palpable in the aorta which was of normal size and did not show poststenotic dilatation. No thrill was felt over the left atrium, which was somewhat enlarged. The mean left atrial pressure during operation was 20 mm. Hg. By direct needle puncture, a gradient of 50 mm. Hg between the inflow portion of the left ventricle and the radial artery was recorded. With the aid of total cardiopulmonary bypass and elective cardiac arrest the aorta was widely opened. The valve leaflets were entirely normal and palpation through the annulus did not reveal any subvalvular stenosis; a finger and a large Brock dilator could be passed with ease to the apex of the heart. The left ventricular wall was considerably thickened and there were prominent muscular trabeculations. The ventricular endocardium was not thickened. Following restoration of the circulation digital examination of the left atrium and mitral
functional aortic stenosis

Fig. 4. Phonocardiogram of patient C.G. 2 ICS RSE, placement of the microphone in the second intercostal space at the right sternal edge.

valve revealed normal leaflets and inflow portion of the ventricle. A mild jet of mitral regurgitation was noted. Postoperatively the patient's course was uneventful.

Three months after operation the patient returned for postoperative study. He felt well and his activity had been virtually unlimited. A selective angiocardiogram with left ventricular injection was carried out by the percutaneous method. These films revealed an enlarged left ventricle and demonstrated incompetence of the mitral valve. The outflow portion of the ventricle appeared to become markedly narrowed in systole (fig. 8, Top left) but to open to some extent during diastole (fig. 8, Top right). The left ventricular cavity appeared in both projections to be encroached upon and almost divided by an intrinsic mass, presumably hypertrophied cardiac muscle (fig. 8, Bottom).

Case 3. J. R., a 16-year-old boy, was admitted to the National Heart Institute in August 1956. A heart murmur had been first noted at the age of 9 at which time he had first noted anginal pain. This had persisted, become incapacitating and had recently been accompanied by severe attacks of headache and vertigo. He presented the classic physical findings of aortic stenosis and in addition had a blowing decrescendo diastolic murmur along the left sternal border. The electrocardiogram revealed left ventricular hypertrophy and strain and x-rays showed left ventricular enlargement. There was poststenotic dilatation of the aorta. The results of right heart catheterization were normal. At transbronchial left heart catheterization the catheter was passed into the aorta where the pressure was 122/75 mm. Hg. Upon withdrawal it first traversed an area of left ventricle with a pressure of 122/15 and then entered the main ventricular cavity where a pressure of 24/15 mm. Hg was recorded. The peak systolic gradient was 122 mm. Hg. An open-heart operation under general hypothermia was carried out on September 6, 1956. The aortic valve leaflets were not stenotic and a thin subvalvular fibrous ring just beneath the aortic annulus was divided and dilated, apparently completely. Three weeks after operation another left heart catheterization revealed the left ventricular pressure to be 193/8 mm. Hg and a gradient of 70 mm. Hg was still present. The patient's symptoms improved during a follow-up period of 18 months. At this time a third left heart catheterization demonstrated that the left ventricular pressure had fallen to a normal level, 115/7 mm. Hg, and that no gradient between the left ventricle and aorta existed. Representative pressure tracings obtained at the 3 left heart catheterizations are shown in figure 9.
Functional obstruction to ventricular ejection is not a new concept. A systolic pressure gradient across the outflow tract of the right ventricle may develop as a result of severe right ventricular hypertrophy associated with such lesions as stenosis of the pulmonary valve or ventricular septal defect.6-11 Proof that this form of obstruction is secondary in nature is provided by the observations of Gasul et al.,11 who noted its development in patients with ventricular septal defect and by the increasing number of reports of the regression of the subvalvular gradient when the primary stimulus to ventricular hypertrophy is removed by pulmonary valvulotomy.6-10

The development of similar secondary obstruction to left ventricular outflow was described by Brock.12 He noted in certain patients with valvular aortic stenosis that even though a satisfactory valvular opening was apparently accomplished, a pressure gradient persisted after operation. This phenomenon was attributed by him to the occurrence of a muscular subvalvular stenosis in the grossly hypertrophied left ventricular outflow tract. Proof of the validity of this hypothesis is afforded by the catheterization data obtained in the third patient described in the present report. A substantial gradient was proved to persist after the anatomic obstruction had been abolished. It seems clear that this gradient was due to functional aortic stenosis since, with the gradual regression of the hypertrophy of the ventricle and without further mechanical intervention, it disappeared completely (fig. 9).

Another etiology of left ventricular hypertrophy resulting in functional aortic stenosis is systemic arterial hypertension. In 1 patient described by Brock12 this seems clearly to be the case since severe systemic hypertension had been well documented in the patient’s immediate history. He also postulated this mechanism in the other patient described in his report although an elevated arterial pressure had never been recorded. Hypertension can certainly not be invoked as the causative factor for the left ventricular hypertrophy

**DISCUSSION**

In the patients described, the hemodynamic evidence of obstruction to left ventricular outflow is unequivocal; in the first 2 patients a systolic pressure difference between the left ventricle and aorta was demonstrated on 2 separate occasions and was definitely localized to an area within the ventricle. On the other hand, it is equally evident that none of the usual forms of aortic stenosis is present since the absence of discrete supravalvular, valvular, or subvalvular obstruction was clearly proved at open-heart operation. In these 2 patients it must, therefore, be concluded that the obstruction to ventricular outflow is of such a nature that it is only operative in the contracting heart and was not apparent during the diastolic paralysis induced by potassium citrate. These features can only be explained by muscular hypertrophy of the left outflow tract of sufficient severity that flow is actually impeded during contraction.

**Fig. 6.** Pressure tracings obtained in the pulmonary artery (P.A.), right ventricular (R.V.) outflow tract and main right ventricular cavity in patient C.G.

**Fig. 7.** Pressures recorded sequentially from the aorta, left ventricular outflow tract (subvalvular chamber), and main left ventricle in patient C.G. (Reproduced by permission from Morrow, A. G., Braunwald, E., and Sharp, E. H.: Clinical features and surgical treatment of congenital aortic stenosis. Progress in Cardiovascular Disease 1: 80, 1958.)
and functional aortic stenosis in our first 2 patients. The etiology of the ventricular hypertrophy in these patients remains obscure. There was no gross evidence of endocardial fibroelastosis and the myocardium appeared normal in color and consistency. Although both patients had mitral regurgitation it would seem unlikely that this lesion could have produced severe ventricular changes with the left atrial pressure pulse remaining normal in contour. Until complete pathologic study of these hearts is carried out, we must attach to them the well-worn label of "idiopathic left ventricular hypertrophy."
A recent report of Bercu et al.\textsuperscript{13} a similar patient is described. A systolic pressure gradient of 130 mm Hg was recorded and at open operation under hypothermia no obstruction was encountered. At autopsy this patient was found to have massive symmetrical hypertrophy of both ventricles and "most remarkable was the reduction of both ventricular cavities to mere uniform slits throughout their entire length.\textsuperscript{13} No cause for the ventricular hypertrophy was apparent on histologic study. If a similar process, involving both the left and right ventricles, is present in patient C.G. described above, a ready explanation is afforded for the physiologically established subvalvular stenosis in the right ventricular outflow tract (fig. 6).

The recognition of functional aortic stenosis is of considerable importance since this lesion is at present not amenable to surgical correction and an unnecessary exploration of the ventricle and valve in such a patient is hazardous indeed.\textsuperscript{12, 13} The diagnosis may be suggested by certain features present in both the patients described herein as well as in the one reported by Bercu et al. The systolic thrill and murmur were most prominent at the apex and lower left sternal border and less apparent in the aortic area. The thrill was not transmitted to the carotid vessels. Phonocardiography in patient E.Z. revealed a loud holosystolic murmur at the apex with a softer ejection murmur at the base of the heart. C.G. on the other hand had a typical ejection murmur only. In none of the patients was post-stenotic dilatation of the aorta demonstrable. This latter finding is in contrast to that in patients proved to have the more usual form of congenital subvalvular aortic stenosis.\textsuperscript{3}

In both patients at left heart catheterization the obstruction was demonstrated to lie beneath the aortic valve, as in Brock’s patients with functional obstruction secondary to hypertension.\textsuperscript{12} Thus it would seem that the diagnosis of functional aortic stenosis can be excluded by the demonstration of a pressure difference across the valve and must be suspected when the site of stenosis is shown to be below it. For this reason complete left heart and aortic catheterization would seem preferable to simple ventricular puncture in the study of patients with aortic stenosis. It is probable that selective left ventricular angiography will prove the most definitive diagnostic technic in distinguishing this lesion from the other forms of aortic stenosis and will also reveal any accompanying mitral insufficiency.

The persistence of a large pressure gradient following the complete relief of a localized subvalvular obstruction in patient J.R. can only be attributed to functional aortic stenosis, the hemodynamic effects of which disappeared during the 19 months after operation. This would indicate that the results of late postoperative studies may be of greatest value in the assessment of operative results.

**Summary**

Three patients are described in whom functional obstruction to left ventricular outflow was present. In 2 a significant pressure gra-
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dient was shown to exist between the left ventricle and aorta and the obstruction was localized within the left ventricle. At the time of open-heart operation, however, no localized stenotic area was found and the obstruction must be attributed to systolic narrowing of the ventricular outflow tract resulting from massive muscular hypertrophy, the cause of which is obscure. Such narrowing was subsequently demonstrated in 1 patient by selective angiocardiography with left ventricular injection. In a third patient functional aortic stenosis was present after surgical relief of a discrete subvalvular stenosis and regressed in the postoperative period. The clinical and hemodynamic features which distinguish this lesion from the more usual forms of aortic stenosis are emphasized.

SUMMARIO IN INTERLINGUA
Es describite tres patientes in qui obstructione functional del effluxo sinistro-ventricular esseva presente. In duos, un significative gradiente de tension esseva constatat inter le ventriculo sinistr e le aortae, e le obstructione esseva localisata intra le ventriculo sinistre. Tamen, al tempore del operation, effectuate a corde aperte, nulle area de stenosis localisata esseva trovate, e le obstructione debe esseva attribuit a restriction systolic del via de effluxo ventricular como resultato de un massive hypertrophia muscular. Le causa de iste hypertrophia es obscure. Un tal restriction esseva demonstrate subsequentemente in un patiente per medjo de angiocardiographia selective con injection sinistro-ventricular. In un tertie patiente, stenosis aortica functional esseva presente post le alleviamento chirurgic de un discrete stenosis subvalvular. Illo regredeva durante le periodo postoperatori. Es signalate le caracteristicas clinic a hemodynamic que distinguish iste lesion ab le formas plususual de stenosis aortica.

REFERENCES
Functional Aortic Stenosis: A Malformation Characterized by Resistance to Left Ventricular Outflow without Anatomic Obstruction
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