The systolic murmur in hypertrophic obstructive cardiomyopathy
and the nature of the obstruction

M. NELLEN

Cardiac Clinic, Department of Medicine, Groote Schuur Hospital,
and Council for Scientific and Industrial Research Cardiovascular-Pulmonary Research Group,
Department of Medicine, University of Cape Town

PATIENTS with hypertrophic obstructive cardiomyopathy present with dyspnoea, angina pectoris, palpitations, fatigue or syncope, but the systolic murmur should draw attention to the condition. The murmur begins after the first heart sound, has a crescendo–decrecendo configuration and has its maximum intensity to the right of the mid-systolic point. It is best heard in the fourth left intercostal space, radiates to the apex and base of the heart and has a harsh, low-pitched quality. It varies in intensity from moment to moment—occasionally it is loud, at other times it may be soft or absent. Other notable features on auscultation are the striking fourth heart sound, a softer third heart sound, and left and right-sided mid-diastolic flow murmurs due to inflow obstruction and occasionally paradoxical or partial paradoxical splitting of the second heart sound due to prolonged left ventricular ejection. An aortic early diastolic murmur is occasionally heard and may be due to distortion of the aortic valve ring by asymmetrical hypertrophy (Braunwald et al., 1954a, b; Tucker et al., 1966; Goodwin, 1967).

We do not know whether the hypertrophy or gradient in the cases where right ventricular involvement has been described either alone or with left ventricular disease is sufficient to cause a systolic murmur within the right ventricular system, but this is probable. In a recently described case of apparently purely right ventricular involvement, a harsh loud ejection systolic murmur was heard best at the left sternal border and apex (Falcone, Moore & Lambert, 1967). However, even though no left ventricular gradient was found there may have also been involvement of the left ventricle which may become more apparent in the future. The apical site of the murmur would, however, suggest a left ventricular origin of the murmur even in this case.

While the systolic murmur may occur at a time when there is no pressure gradient as shown by intraventricular phonocardiogram (Goodwin, 1967), the intensity of the murmur appears from our studies to vary with the gradient. That the increase in gradient is associated with increase in systolic murmur intensity does not exclude mitral incompetence as the cause of the murmur because the hypertrophy of the septum and papillary muscle cause both the gradient and mitral incompetence. Mitral insufficiency almost invariably accompanies hypertrophic obstructive cardiomyopathy (Wigle, Marquis & Auger, 1967) However, we agree with Goodwin (1967, 1968) that there are probably several reasons for the systolic murmur in hypertrophic obstructive cardiomyopathy. Thus obstruction within the left ventricle, mitral incompetence and probably turbulence within the strongly and rapidly contracting ventricle may all play a part in its production.

We have shown that amyl nitrite markedly diminishes the regurgitant murmur of rheumatic valvar mitral incompetence and that phenylephrine intensifies the murmur (Vogelpoel et al., 1959; Beck et al., 1961). Amyl nitrite intensifies the systolic murmur in hypertrophic obstructive cardiomyopathy (Nellen et al., 1965) and increases the gradient (Wigle et al., 1964) and phenylephrine abolishes or markedly reduces the murmur and gradient; isoproterenol increases the gradient and murmur (Nellen et al., 1965). These findings do not rule out incompetence of the mitral valve (Fig. 1) as a factor in the production of the systolic murmur. The cause of the mitral incompetence in hypertrophic obstructive cardiomyopathy is papillary dysfunction due to papillary and septal hypertrophy and not a pure valve mechanism. These drugs by altering the internal diameter and mechanics of the obstructive hypertrophy in the left ventricular chamber affect the murmur in opposite directions to their effect in pure valvar mitral incompetence.
Further support for the view that the obstruction causes the mitral incompetence is that pharmacological abolition of the stenosis also abolishes the mitral incompetence (Wigle et al., 1967).

In contrast to the marked lessening in intensity or disappearance of the systolic murmur in hypertrophic obstructive cardiomyopathy with intravenous phenylephrine we have shown that the murmur of aortic stenosis is hardly affected. It usually lessens only slightly but may actually intensify—this may be a useful bedside test as the two conditions may mimic each other (Nellen et al., 1965) (Fig. 2).

The studies of Marcus, Perloff & DeLeon (1964) and Hancock & Fowkes (1966) show that inhalation of amyl nitrite is more useful than isoproterenol as a provocative test for hypertrophic obstructive cardiomyopathy. Inhalation of amyl nitrite has a greater effect than intravenous injection of 2 mg of isoproterenol, is more readily administered, has a briefer action and is less likely to induce adverse effects such as ventricular arrhythmias.

The effect of prompt squatting on the systolic murmur

Prompt squatting provides a simple bedside method of acutely increasing venous return, effective filling pressure of the heart, stroke output and systemic arterial pressure and resistance (Sharpey-Shafer, 1955).

We have therefore studied the effect of this manoeuvre on the systolic murmur in twelve patients with hypertrophic obstructive cardiomyopathy (Nellen et al., 1967), and we have compared the effect of this manoeuvre in eight patients with fixed valvar aortic stenosis and in five patients with mitral valvar incompetence as the systolic murmurs in these cases may resemble that of hypertrophic obstructive cardiomyopathy.

In hypertrophic obstructive cardiomyopathy we found that this manoeuvre abolished the murmur in three, and softened it markedly in seven. In one, the murmur softened slightly and in one the effect was variable (Figs. 3 and 4). In no case did the murmur intensify. In all the cases of valvar aortic stenosis and mitral incompetence the systolic murmur increased in loudness. To help in the assessment of the mechanism of squatting we studied the effect of this procedure on the murmur of pulmonary stenosis. The systolic murmur in this condition also quickly intensified on squatting. In this condition the increase in mean arterial pressure and in peripheral arterial resistance would not be expected to increase the murmur, whereas increase in venous return and effective cardiac output would be useful. The systolic murmurs in these patients were acutely intensified by squatting.
ventricular volume, the gradient lessens due to
the increase in ventricular dimension which
reduces the degree of obstruction. Additionally
the raised arterial pressure and peripheral resis-
tance, the bradycardia and reduction of left
ventricular contractility would reduce the
gradient and thus the intensity of the murmur.

The nature of the obstruction
Braunwald et al. (1964a, b) attributed the
haemodynamic findings and the murmur to ob-
struction of left ventricular outflow; Goodwin
(1964) broadened the concept and added im-
pedance to inflow in the right and left ventercle
as a cause of the diastolic murmurs. Criley et
al. (1965) questioned obstruction to the outflow
region and suggested that the hourglass silhouette
observed at angiocardiology is a diastolic
event due to inflow of non-opaque blood from
the left atrium. They proposed that the high
ventricular pressure gradients resulted from sus-
tained contraction and absence of flow in
obliterated portions of the left ventricular cavity.
The hypertrophi ed ventercle empties more com-
pletely and faster than the unobstructed normal
ventercle, with marked apical obliteration. They
also suggested that the systolic murmur is due
to mitral incompetence from abnormal align-
ment of the papillary muscles in the greatly
hypertrophi ed left ventercle.

Ross et al. (1966) showed the presence of
definite outflow-tract obstruction during systole,
70% of the systolic blood volume is ejected
during a period when a gradient is present,
whilst 30% of the forward stroke volume is
ejected early when no significant pressure gradient
is present. These workers showed that isometric
pressure development and early ventricular eje-
tion proceed more rapidly than normally, this
early systolic period being responsible for the
sharp upstroke of the arterial pulse. These
workers have thus prepared a strong brief in
support of the postulate that an obstructive fac-
tor exists in the haemodynamic hypertrophic left
ventercle syndrome.

The studies of Wigle et al. (1967) support the
views of Ross et al. (1966). These authors stress
the importance of the outflow tract as being the
site of obstruction in hypertrophic obstructive
cardiomyopathy and show by retrograde and trans-septal catheterization that the obstruction
is caused by systolic apposition of the ventercular
septum and anterior leaflet of the mitral valve.
They show how an abnormally high pressure at
the apex of the ventercular chamber can be ob-
tained by 'imbedding' or 'catheter entrapment'
in various conditions including hypertrophic ob-

<table>
<thead>
<tr>
<th>3</th>
<th>Murmur abolished</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Murmur softens markedly</td>
</tr>
<tr>
<td>1</td>
<td>Murmur softens slightly on propranolol</td>
</tr>
<tr>
<td>1</td>
<td>Variable response</td>
</tr>
</tbody>
</table>

Fig. 4. Effect of squatting on the murmur of hyper-
trophic obstructive cardiomyopathy in twelve patients.
Obstructive cardiomyopathy (Wigle et al., 1967; Cross & Salisbury, 1963; Martin, Hackel & Sieker, 1963; DeBono, Proctor & Brock, 1965; Martin et al., 1965; White, Lewis & Criley, 1965; Morrow et al., 1965; Tobin et al., 1965; Wilson et al., 1967). In these latter conditions (except for hypertrophic obstructive cardiomyopathy) the inflow tract pressure will equal the aortic pressure whereas in hypertrophic obstructive cardiomyopathy the pressure is higher in the inflow tract than in the outflow tract and aorta.

Conclusions
There are probably several reasons for the systolic murmur in hypertrophic obstructive cardiomyopathy. Obstruction within the left ventricle, mitral incompetence and turbulence within the strongly and rapidly contracting ventricle may all play a part.

The systolic murmur (and gradient) is abolished or lessens markedly in intensity with intravenous phenylephrine, in contrast to the increase in loudness of the murmur of valvar mitral incompetence and little significant change in fixed valvar aortic stenosis. In hypertrophic obstructive cardiomyopathy amyl nitrite inhalation and intravenous isoproterenol intensify the murmur and the gradient. Amyl nitrite is probably the best provocative test for the diagnosis of the condition—being safer and easier to administer than isoproterenol and having a greater effect than the usual 20 μg dose of the latter β-stimulating catecholamine.

Prompt squatting has proved to be an excellent bedside test in this condition—the systolic murmur never increases but is either abolished or decreases markedly in intensity in most cases, in contrast to the intensification of the systolic murmur of valvar mitral incompetence and fixed valvar aortic stenosis.

The obstruction causes a true gradient within the outflow tract of the left ventricle and interferes also with papillary muscle function, causing in most cases some mitral incompetence. The problem of ‘entrapment’ or ‘imbedding’ of the catheter in the apex has been referred to.

We would agree that although there is a tremendous amount of information on the condition of hypertrophic obstructive cardiomyopathy ‘The citadel holding the ultimate truth of the syndrome, is still to be taken’ (Burchell, 1966).

Acknowledgments
We wish to thank Professor V. Schrive and our colleagues in the Cardiac Clinic, and our laboratory staff for assistance with the catherization procedures, and Dr J. G. Burger, Superintendent of Groote Schuur Hospital, for permission to publish. We acknowledge with thanks the continued financial support of the Council for Scientific and Industrial Research and the City Council of Cape Town.

Figs. 1 and 3 are taken from Nellen et al. (1967) Brit. med. J. ii, 340, with permission of the Editor.

References


A modified index of phosphate excretion

B. E. C. NORDIN  
L. BULUSU

Medical Research Council Mineral Metabolism Research Unit,  
General Infirmary, Leeds

There are several ways of looking at the excretion of phosphorus, or for that matter of any element in the urine. For certain purposes, it is most appropriate to consider the total daily or weekly excretion and relate it to the dietary intake and faecal output as part of a balance study, the object of which is to establish whether the subject is in negative or positive balance on a particular dietary intake. In the study of kidney stone disease, the important criterion is probably the concentration of the different phosphate ion species in the urine and these can be calculated from a knowledge of urinary pH and total phosphorus concentration (the organic phosphorus content of the urine being negligible). In relation to many other aspects of calcium and phosphorus metabolism, however, the physiological parameter of particular interest is the tubular reabsorption of phosphorus, both because it is a large factor in the regulation of the plasma phosphorus level and because it is under the control of the parathyroid glands.

There are various ways of assessing tubular reabsorption of phosphorus, the simplest being the measurement of phosphate clearance (which is inversely related to tubular reabsorption) (Kyle, Schaaf & Canary, 1958) and the most sophisticated the measurement of the maximum tubular reabsorptive capacity (Anderson & Parsons, 1963). Between these extremes is the phosphate/creatinine clearance ratio which indicates the proportion of filtered phosphate that is not reabsorbed by the tubules; it tends to be raised in hyperparathyroidism and reduced in hypoparathyroidism (Milne, Stanbury & Thompson, 1952; Nordin & Fraser, 1954).

Unfortunately, the phosphate/creatinine clearance ratio is itself governed not only by tubular function but also by the filtered load of phosphorus itself since there is a very high correlation between the plasma phosphorus level and the phosphate/creatinine clearance ratio in normal subjects (Lambert, van Kessel & Leplat, 1947). For this reason, Nordin & Fraser (1960) suggested that any particular value of \( C_p/C_\text{cr} \) should always be related to the plasma phosphorus level and that the extent to which the observed value differed from the predicted value could be used as a measure of tubular reabsorption of phosphorus. They called this value the phosphate excretion index, established the limits \( \pm 0.09 \) and showed that higher values were associated with states of hyperparathyroidism and low values with states of parathyroid insufficiency.

The general validity of the phosphate excretion index has since been confirmed. It is generally raised in primary hyperparathyroidism (Nordin & Smith, 1965) and frequently also in the secondary hyperparathyroidism of osteomalacia (Nordin & Fraser, 1960), renal failure and high phosphate feeding (Smith & Nordin,
The systolic murmur in hypertrophic obstructive cardiomyopathy and the nature of the obstruction.

M. Nellen and M. S. Gotsman

*Postgrad Med J* 1968 44: 89-93
doi: 10.1136/pgmj.44.507.89