Effects of Amyl Nitrite in Aortic Valvular and Muscular Subaortic Stenosis

By E. W. Hancock, M.D., and W. C. Fowkes, M.D.

Inhalation of amyl nitrite causes abrupt vasodilatation and increase in cardiac output and intensifies the murmur of aortic stenosis. The transaortic systolic pressure gradient increases because of the increased ejection rate through the stenotic orifice. In muscular subaortic stenosis this effect is particularly marked, not only because of the increased ejection rate but also because the diminished heart size apparently causes increase in the severity of obstruction in the outflow tract. Glyceryl trinitrate has a similar effect. Amyl nitrite is a convenient stimulus for increasing the pressure gradient in muscular subaortic stenosis and is widely used for this purpose during diagnostic cardiac catheterization. The relative effect of inhalation of amyl nitrite and infusion of isoproterenol and the extent to which the hemodynamic response to amyl nitrite differs in aortic valvular stenosis and muscular subaortic stenosis is not clear from previously published reports. The present report offers a comparative study and suggests that amyl nitrite provides the more potent, readily available provocative test for muscular subaortic stenosis. The responses in aortic valvular and muscular subaortic stenosis show qualitative and quantitative differences which are helpful in differential diagnosis.

Methods

The studies were carried out during transseptal

[Graph showing changes in systolic pressure and gradient before and after amyl nitrite inhalation for valvular and muscular stenosis.]

Figure 1
Changes in the left ventricular peak systolic pressure and in the left ventricular-brachial arterial peak systolic pressure gradient in 12 patients with aortic valve stenosis and five with muscular subaortic stenosis following inhalation of amyl nitrite.
left heart catheterization performed for diagnostic evaluation of aortic stenosis in 17 patients. Twelve patients had calcific stenosis of the aortic valve, confirmed by direct vision at operation in all but one. In the exception roentgenographic demonstration of aortic valve calcification and a slowly rising arterial pulse were taken to confirm the nature of the lesion. Five patients were diagnosed as having idiopathic muscular subaortic stenosis, a diagnosis supported by the absence of aortic ejection clicks and aortic valve calcification and the presence of a fast-rising arterial pulse with reduced pulse pressure or deformed pulse contour following post-extrasystolic pauses. Brachial ar-

Table 1

Measurements before and after Inhalation of Amyl Nitrite during Left Heart Catheterization in Twelve Patients with Aortic Valve Stenosis and Five Patients with Muscular Subaortic Stenosis

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, sex</th>
<th>Left ventricle*</th>
<th>Brachial artery†</th>
<th>Transaortic gradient</th>
<th>Heart rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Systolic/diastolic pressures, mm Hg.</td>
<td>Systolic/diastolic pressure, mm Hg.</td>
<td></td>
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</tbody>
</table>

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Arterial and left ventricular pressures were recorded continuously for 5 minutes after three deep breaths from a freshly broken amyl nitrite capsule. Cardiac output was measured by the dye-dilution method in two cases, one from each group, during the period of maximum fall in arterial pressure, ½ to 1 minute after the inhalation.

Results

The individual measurements before and during the amyl nitrite effect are given in table 1 and the mean and per cent changes are given in table 2. Both groups showed marked fall in systolic and diastolic arterial pressure and pulse pressure, the fall being a little more marked in the cases of muscular subaortic stenosis. The two groups showed a similar increase in heart rate of about 30%. The most striking differences in response were

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Aortic valve stenosis</th>
<th>Muscular subaortic stenosis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean change, mm Hg</td>
<td>% change</td>
</tr>
<tr>
<td>Left ventricle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-22</td>
<td>-11</td>
</tr>
<tr>
<td>End diastolic</td>
<td>-5</td>
<td>-42</td>
</tr>
<tr>
<td>Brachial artery</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>-39</td>
<td>-30</td>
</tr>
<tr>
<td>Diastolic</td>
<td>-16</td>
<td>-26</td>
</tr>
<tr>
<td>Transaortic gradient</td>
<td>+16</td>
<td>+25</td>
</tr>
<tr>
<td>Pulse pressure</td>
<td>-21</td>
<td>-29</td>
</tr>
<tr>
<td>Heart rate</td>
<td>+21</td>
<td>+30</td>
</tr>
</tbody>
</table>

Figure 2

Left ventricular and brachial arterial pressures before and after inhalation of amyl nitrite in a case of aortic valve stenosis (case 7). Both systolic pressures fall, the pressure gradient increases moderately, and the arterial pulse contour is only slightly altered. Double-pointed arrow in Figures 2 to 5 indicates 1 second.
seen in the left ventricular systolic pressure and the transaortic systolic pressure gradient (fig. 1). In the patients with valvular stenosis, the left ventricular systolic pressure decreased in every instance (range, 3 to 43; average, 22 mm Hg). The fall in left ventricular pressure was usually less than the fall in arterial pressure, so that the gradient increased in 11 of 12 instances, but the average increase in gradient was only 16 mm Hg. In the cases of muscular subaortic stenosis, the left ventricular systolic pressure either remained the same or increased. The gradient, therefore, increased markedly (range, 26 to 119; average, 68 mm Hg). Typical examples are illustrated in figures 2 to 4. Since the muscular subaortic cases usually had substantially smaller gradients at rest, the difference in response is particularly striking when the increase in gradient is expressed as a per cent of the resting gradient. The valvular cases showed an average increase of 25%, and the muscular subaortic cases an average increase of more than 400%. In case 16, with muscular subaortic stenosis with no pressure gradient at rest, after the amyl nitrite the gradient appeared in the first beat showing a fall in arterial pressure (fig. 5).

Left ventricular diastolic pressure remained the same or decreased in the valvular cases, with a mean fall of 5 mm Hg in the end-diastolic pressure, whereas there was a substantial rise in two of the five muscular subaortic cases with a negligible average change for the group.

In case 2, with valvular stenosis, where the gradient increased from 30 to 44 mm Hg, the cardiac output changed from 3.6 to 5.1 L/min/m², stroke volume rose from 43 to 53 ml/m², and the calculated orifice area remained the same at 0.8 sq cm. In case 14 with muscular subaortic stenosis, in which the gradient increased from 17 to 68 mm Hg, the cardiac output changed from 5.1 to 5.5 L/min/m², the stroke volume fell from 70 to 51 ml/m², and the calculated orifice area decreased from 2.3 to 0.7 cm. Thus, the increased gradient in the case of valvular stenosis reflected the increase of cardiac output and ejection rate, while in the case of muscular subaortic stenosis the degree of outflow tract obstruction was significantly increased.

The arterial pulse contour in aortic valve stenosis retained its slow-rising, single-peaked contour after amyl nitrite. The upstroke duration often shortened, sometimes to 0.10 sec.
ond, and a twin peak contour sometimes appeared, but in no instance was the appearance of a midsystolic dip and late systolic peak observed. In muscular subaortic stenosis, on the other hand, the arterial pulse became more quick rising, with a shortened upstroke duration of 0.05 to 0.09 second, and the midsystolic dip became deeper. The late systolic peak became markedly flattened, and in one instance later in timing. The altered pulse contour in muscular subaortic stenosis after amyl nitrite was particularly striking in postextrasystolic beats.

The increase in gradient which followed amyl nitrite in muscular subaortic stenosis was greater in four of five instances than the increase in gradient which was induced in the same patients by infusion of 2 μg of isopro-

**Figure 4**

*Left ventricular and brachial arterial pressures before and after inhalation of amyl nitrite in a case of muscular subaortic stenosis (case 15). Left ventricular systolic pressure increases slightly and the gradient increases markedly. Arterial pulse pressure is markedly narrowed and a sharp early systolic peak appears.*

**Figure 5**

*Continuous record of left ventricular and brachial arterial pressures in a case of muscular subaortic stenosis (case 16) during onset of the amyl nitrite effect. Left ventricular systolic pressure rises with the first cycle showing a fall in arterial pressure, before the heart rate increases.*

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These studies support the suggestion of Marcus, Perloff, and De Leon\(^3\) that amyl nitrite is more useful than isoproterenol in a provocative test for muscular subaortic stenosis during cardiac catheterization. Inhalation of amyl nitrite in our hands has a greater effect than intravenous injection of 2 μg of isoproterenol, is more easily administered, has a briefer action, and is less likely to induce adverse effects such as ventricular arrhythmias.

### Summary

The effects of amyl nitrite inhalation were observed in 12 patients with aortic valve stenosis and five patients with muscular subaortic stenosis during left heart catheterization. In aortic valve stenosis the left ventricular systolic pressure always fell, although less than the brachial arterial pressure, and the transaortic systolic pressure gradient rose by an average of 25% due to the increase in left ventricular ejection rate. In muscular subaortic stenosis, the left ventricular pressure always remained the same or rose despite a marked fall in brachial arterial pressure, and the average increase in transaortic systolic pressure gradient was more than fourfold. This effect was associated with a significant increase in the degree of outflow tract obstruction. The increase in outflow tract obstruction is thought to be due to a decrease in left ventricular volume, causing the hypertrophied walls of the left ventricle to become more closely apposed.

We believe that inhalation of amyl nitrite is superior to infusion of isoproterenol as a provocative test for muscular subaortic stenosis during cardiac catheterization and is probably the most potent stimulus available for this purpose.

### References

3. MARCUS, F. I., PERLOFF, J. K., AND DE LEON,
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Truth, if we can find it, belongs to every system; and to discover it, experimenters need free movement on every side, without feeling themselves stopped by the barriers of any system. Philosophy and science, then, must never be systematic: without trying to dominate one another, they must unite. Their separation could only be harmful to the progress of human knowledge. Striving ever upward, philosophy makes science rise toward the cause or the source of things. It shows science that there are questions beyond it, torturing humanity, which it has not yet solved. Solid union between science and philosophy is useful to both: it lifts the one and confines the other. But if the bonds uniting philosophy to science should break, philosophy, lacking the support or the counterpoise of science would rise out of sight and be lost in the clouds, while science, without guidance and without high aspiration, would sail at random.--Claude Bernard: An Introduction to the Study of Experimental Medicine. New York, The Macmillan Company, 1927, p. 224. Centenary of the First Publication, 1865.
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