Polygraphic studies of the effect of nitroglycerin in patients with ischaemic heart disease

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Polygraphic recordings were made before and after 0.6 mg of sublingual nitroglycerin in 20 normal subjects and in 20 patients with ischaemic heart disease.

The following effects of nitroglycerin were observed in both groups: shortening of ejection time, prolongation of pre-ejection period and also of isometric contraction time unrelated to decrease in systolic blood pressure, and increase in heart rate; in the apex cardiogram, retraction of the systolic wave and diminution in amplitude of the A wave which approached the ventricular wave; in the carotid arterial pulse, decrease in the level of the dicrotic notch, disappearance of the tidal wave, and augmentation of the dicrotic wave.

When compared with the normal group, pre-ejection period and isometric contraction time were significantly more prolonged (P<0.05) in the diseased group, the blood pressure was more reduced, and the heart rate showed a greater increase.

These alterations in polygraphic parameters after nitroglycerin reflect the decrease in stroke volume and blood pressure, and therefore of cardiac work, induced by the drug.

The data suggest that nitroglycerin more obviously reduces cardiac work (and presumably myocardial oxygen consumption) in the diseased group than in the normal group. A similar trend was evident after the administration of amyl nitrite in a study previously reported by the authors.

The value of noninvasive (polygraphic) methods for evaluating abnormalities of cardiac function in disease states may be enhanced by studying changes induced by vasoactive drugs. Nitroglycerin is of particular interest in this regard because its effects are largely on the peripheral circulation, and because it is in common clinical use.

Nitroglycerin is a ‘coronary dilator’ but the effectiveness of this agent in angina pectoris is largely due to its reduction of blood pressure, and therefore of cardiac work (Gorlin et al., 1959; Parker, West, and Giorgi, 1971). There have been some comparisons of the effects of this drug on the cardiovascular system in normal persons and in patients with ischaemic heart disease. However, all previous reports have used direct, invasive methods (Gorlin et al., 1959; Parker et al., 1971). There is, as yet, no report dealing with haemodynamic effects of the drug, as judged by noninvasive polygraphic methods.

In the present study, various parameters of polygraphic recordings were compared before and after the administration of nitroglycerin, and differences between the responses of normal subjects and of patients with ischaemic heart disease were studied.

Subjects and methods
Twenty normal men were selected for our study. They were over 40 years of age and had no heart disease as judged by precise physical and laboratory examination, including the Master’s double two-step test. Twenty men with ischaemic heart disease were selected for comparison. They all had past histories of myocardial infarction, or had angina of effort, and all had a positive Master’s test (using a criterion of 1 mm ST segment depression). They all had normal sinus rhythm without conduction disturbance, and had no congestive heart failure, hypertension, or valvular disease. Drugs that would directly influence cardiac function were discontinued before the study.

All studies were carried out with the subjects in the supine position and in a basal, postabsorptive state. In each subject, simultaneous recordings of the apex cardiogram, low- and middle-frequency phonocardiogram, electrocardiogram (lead II), and the indirect carotid pulse were made on a multichannel, jet writing unit (Elema-Schonander) at a paper speed of 100 mm/sec.
with time markers indicating 0.01 sec. Heart sounds and apex cardiogram were recorded over the apex with a contact microphone. The indirect carotid pulse was obtained with a crystal pick-up connected to a pulse transducer. A representative polygraph recording is shown in Fig. 1.

Tracings were recorded during a control period and then repeated at 4, 6, 8, 10, and 12 minutes after the administration of 0.6 mg nitroglycerin sublingually. In addition, blood pressure was measured at the end of each recording.

The following polygraphic data were obtained before and after nitroglycerin in both groups of subjects (see Fig. 1): systolic and diastolic blood pressure (BP; BPs and BPD); heart rate (HR); left ventricular ejection time and ejection time index (ETI = ET + 1.25 × HR); Q-U interval (from the Q wave to the upstroke of the carotid artery pulse); Q-U index ((Q-U) + 0.5 × HR); I-U interval (from the first heart sound to the upstroke of the carotid arterial pulse) and Q-I interval. The directly measured I-U and Q-U intervals were used instead of the standard isometric contraction time (ICT = interval from first to second heart sound minus ejection time), and pre-ejection period (PEP = Q-2 interval minus ejection time), to which they, respectively, correspond, in order to minimize errors in measuring ICT and PEP which are composed of multiple measurements. In addition, corrections for pulse transmission time are unnecessary when Q-U and I-U are used in the same subject, as when studying a drug intervention as in the current experiments. The values of the systolic time intervals were the averages of 5 consecutive cardiac cycles during the maximal effect of the drug. In addition, in the apex cardiogram, changes in the amplitude of the A wave, the atrioventricular interval (A-C interval, from the top of the A wave to the upstroke of the ventricular wave), and the shape of the ventricular wave were observed. Also, changes in wave shape of the carotid arterial pulse and in the level of the dicrotic notch were analysed.

**FIG. 1** A control tracing of the 5-channel polygram and 4 items measured directly on the tracing (R-R, Q-I, I-U, and ET). ACG, apex cardiogram; CAP, carotid artery pulse; PCG, phonocardiogram taken at the cardiac apex; ECG, electrocardiogram (lead V5).

### Results

1) Changes observed before and after nitroglycerin administration

The Table gives the average values of the maximal

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<thead>
<tr>
<th>TABLE</th>
<th>Maximal percentage changes in various haemodynamic items after administration of nitroglycerin to normal subjects and patients with ischaemic heart disease</th>
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<tr>
<td></td>
<td>Systolic blood pressure</td>
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<td>Normal (%)</td>
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<td>Mean</td>
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<td>SE(±)</td>
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<td>Ischaemic heart disease (%)</td>
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<td>SD(±)</td>
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<tr>
<td>SE(±)</td>
<td>1.5</td>
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<tr>
<td>P value</td>
<td>*</td>
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<td>Normal (vs ischaemic heart disease)</td>
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*Note: SD, standard deviation; SE, standard error. Other abbreviations, see text. *P < 0.05.*

Q-I is Q to first sound.
changes (%), with standard deviations and errors, of each item studied before and after the drug in the two groups of subjects (normal and ischaemic heart disease).

**A) Blood pressure and heart rate**  Blood pressure was decreased in the normal group (-10.7%) and in the ischaemic heart disease group (-16.5%); diastolic blood pressure was less decreased in the ischaemic heart disease group (-8.1%), but essentially unchanged in the normal group. Heart rate was increased by +20.4 per cent and +11.4 per cent in the two groups.

**B) Left ventricular systolic time intervals** Ejection time was shortened by -14.6 per cent in the normal group and by -12.5 per cent in the diseased group, while ejection time index was reduced by 6.5 per cent in both groups. On the other hand, Q-U and the Q-U index (representing the pre-ejection period and its index) were prolonged, as in the Table. The i-U (representing the isometric contraction time) was also prolonged (+2.9% and +12.8%), as was Q-i (+11.6% and +11.8%) in both groups.

**C) Wave shapes (Fig. 2 and 3)** In every case, the amplitude of the A wave of the apex cardiogram was reduced by nitroglycerin and it approached the ventricular wave (shortened A-C interval). In some cases, the A wave became indistinct or fused with the ventricular wave. The A wave and the atrial sound on the phonocardiogram changed in parallel. Further, the systolic wave showed a mid-systolic retraction, resulting in its steep fall from the E point.

The tidal wave of the carotid arterial pulse, which was distinctly evident before the drug administration, became indistinct afterwards, while the percussion wave became relatively peaked. The dicrotic wave increased, and the level of dicrotic notch declined. In some cases, the tidal wave disappeared completely, yielding a monophasic carotid wave.

2) **Comparison of changes occurring in two groups after drug administration**

Fig. 4 to 7 illustrate graphically the changes in

![Fig. 2 Polygraphic tracings recorded from a 51-year-old normal subject; a control tracing (left), and a tracing obtained 8 minutes after giving 0.6 mg nitroglycerin (right), showing a diminution of 'A' wave with mid-systolic retraction (retr) in the apex cardiogram, and a sharp fall with obscure tidal wave (TW) and with relative increase in dicrotic wave (DW) in the carotid artery pulse on the right.](http://heart.bmj.com/content/35/12/1234)
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FIG. 3 Polygraphic tracings recorded from a 56-year-old patient with old myocardial infarction showing similar changes after nitroglycerin as in Fig. 2.

FIG. 4 Maximal percentage changes (\%\Delta) in various haemodynamic parameters after nitroglycerin in the normal group (NL) and the diseased group (IHD), giving average value, standard error, and P value.
A) Blood pressure and heart rate (Fig. 4) The fall in both systolic and diastolic blood pressure in the group with ischaemic heart disease proved to be more pronounced (P < 0.05) than in the controls. On the other hand, the increase in heart rate was more pronounced (P < 0.05) in the normal group.

B) Left ventricular systolic time intervals (Fig. 5-7) The shortening of ejection time and ejection time index was not significantly different in the two groups (Fig. 5).

By contrast, the prolongation in Q-U, and i-U proved to be more pronounced (P < 0.05) in the ischaemic heart disease group (Fig. 6-7) but the prolongation of Q-I, and of the Q-U index, was not appreciably different in the two groups (Fig. 6-7).

Discussion

1) Changes in various parameters after nitroglycerin administration (Table)

The observed fall in blood pressure and rise in heart rate after nitroglycerin administration was consistent with previous reports (Gorlin et al., 1959;
Suggested that the effect of nitroglycerin on either the cardiac contractility, or on the left ventricular end-diastolic pressure, was greater in the diseased group. These results are similar to those obtained previously in studies using amyl nitrite (Sawayama et al., 1968, 1969). When amyl nitrite was inhaled, the cardiodepressant effect was greater in the diseased group than in the normal group. Further direct haemodynamic studies, correlated with left ventricular systolic time intervals, will be required to clarify the mechanism of these observed differences in the responses to the nitrite drugs.

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References


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