OBSERVATIONS ON THE
EFFECTS OF SOME ENVIRONMENTALLY INDUCED
MENTAL STRESSES ON THE HEART

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DECLARATION

Some of the initial work done for this thesis has been presented
in Proceedings of a Symposium "New Perspectives in Beta-Blockade"
Aarhus, Denmark, May, 1972.

Two papers have been submitted to the Lancet for publication; mention
has been made that they form part of this M.D. Thesis.
"My life is at the mercy of any scoundrel who chooses to put me in a passion".

JOHN HUNTER.

Hunter's death occurred during a dispute with the Governors of St. George's Hospital regarding the exclusion of students whom he considered to be the victims of a prejudice against the Scots.
SUMMARY

The cardiovascular effects of some environmentally induced mental stresses encountered in everyday life were studied in 33 normal healthy male subjects aged 23-56 years and in 12 male patients with ischaemic heart disease aged 35-60 years. Two studies were designed; the first to examine the effects of beta-adrenoreceptor suppression on the tachycardia induced by the mental stress of driving, by catecholamine infusion, and by treadmill exercise; the second study was designed to investigate the magnitude of the effects of some normal everyday environmental stresses on the heart rate and the degree of modulation of these responses induced by blockade of the heart rate beta-receptors. The heart rate was measured from a radiotelemetered electrocardiograph. The method of study included double-blind assessment and single-blind analysis with placebo control and 40 mg oral oxprenolol given in randomized order. The results in Study I indicated that relatively small doses of beta-receptor antagonists (40 mg oral oxprenolol) were capable of suppressing the heart rate increase induced by mental stress and catecholamines with much smaller effects on the response to physical exertion. The results in Study II showed that a number of everyday environmental situations were associated with substantial tachycardia and that these increases in heart rate were conspicuously reduced for up to 12 hours by 40 mg
oral oxprenolol. The association of everyday psychological or emotional stress with precocious coronary heart disease and the clinical implications of these observations in the treatment of emotionally induced anginal pain and the possible role of a relatively small dose of beta-receptor antagonist in suppressing the tachycardia associated with psychological stress is discussed.
INTRODUCTION

The possible patho-physiological effects of environmentally-induced psychological stress have recently attracted increasing attention. The interest has been stimulated by the assumption that the effects of such frequent stress may aggravate pre-existing athero-sclerotic heart disease and may even be an important factor in its pathogenesis. The evidence on which such important speculations are based require close examination. In the past the stimuli used to excite such cardiovascular reactions have often been unusual and frequently of such intensity as to bear little relationship to the emotional and mental stresses normally met in normal everyday life. There is little doubt that life in a Western urban society is associated with mental stress, but the frequency and magnitude of cardiovascular reactions to such stress are largely unknown. Furthermore, it is possible that the effects of such stresses may aggravate established coronary heart disease. It was the purpose of this study therefore to examine the effects on the heart of some of the psychological stresses usually met in everyday life in normal subjects and in patients with ischaemic heart disease.

HISTORICAL REVIEW

Emotionally induced tachycardia is a common personal experience and the cardiovascular responses to fear, sorrow, sexual arousal and other personal emotions have been the subject of extensive writings by many authors. A number of reports have documented the specific
circulatory changes occurring in a variety of mentally stressful situations.

Conspicuous changes in a number of circulatory variables have been observed in a variety of situations designed to cause mental stress.

1. In patients during provocative discussions of personal problems (Wolff, 1950). In 35 patients who complained of "praecordial symptoms" the author found that the "majority" showed "significant" changes in heart rate when discussing personal problems which aroused "anxiety" and "resentment". The tachycardia measured by electrocardiography, was "moderately severe" and "prolonged" in many of the subjects.

However, the author omitted to define "praecordial symptoms" or to state the exact number of subjects who showed changes in heart rate and the magnitude of these changes. In 18 of these patients, whom the author did not categorise clinically, he stated that the configuration of the electrocardiogram would have been interpreted as "abnormal" had they occurred during or after "standard exercise tests". The author also failed to define the abnormality, except to say that there were "T wave changes".

2. In normal individuals during heated arguments and electric shock stimuli (Bogdonoff et al 1959). Twenty male volunteer University students were studied during cardiac catheterisation. Two types of stimuli were used, "role enactment" and "electric shock". The role enactment procedure consisted of experiments either creating an atmosphere of concern about the subject's welfare or accusing the subject of failing
to co-operate properly, e.g. his inability to remain absolutely quiet.

The electric shock stimulus consisted of the application of an electrocardiographic lead plate to the lower extremity with the connection made to a small rheostat giving a 5-volt 3 ampere stimulus. The results were grouped according to the "quality" and "quantity" of "affect" change. The affect "quality" and "intensity" were measured by

1) the subjects ability to recall the experience
2) his ability to describe his feelings
3) the interpretation of the subjects statements by the interviewer.

The results indicated that the "intensity of affect" was directly correlated with the change in cardiac output and heart rate, the increase being most marked in the subjects in whom anxiety was greatest. The authors did not remark upon the obvious difficulty of defining alterations in or differences between affect changes in different subjects.

3. In medical students undergoing "particularly difficult and challenging" oral examinations.

(Bogdonoff et al, 1960). The situation chosen was a fifteen minute oral examination of sixteen 4th year medical students. An electrocardiogram using the limb leads was recorded throughout the examination. "Several" subjects showed a tachycardia ranging from 120 to 166 beats per minute. The degree of "affect arousal" (minimal, moderate or marked) was found to broadly correlated with the increase in heart rate. All students described some degree of tenseness, anxiety or fright.

However, the authors exact criteria of definition of "affect arousal" was not given, precluding such studies being repeated.
4. In house-officers presenting clinical problems at physicians' grand rounds (Moss and Wyner, 1970). The heart rate of ten house officers was measured by electrocardiography whilst they were presenting cases at grand rounds. The heart rate increased from an average control rate of 73 beats per minute up to an average of 154 beats per minute immediately before or during case presentation.

5. In lecturers speaking before a critical audience (Somerville et al, 1971). The authors stated that the heart rate increased to 100 to 120 beats per minute immediately before speaking; reached 150-170 beats per minute whilst speaking and decreased to 120 beats per minute during question time.

This paper was presented at a meeting of the British Cardiac Society. The authors did not mention the number of subjects studied, whether or not they were experienced speakers, the size and character of the audiences addressed, or whether the peaks in heart rate were associated with physical activity, such as moving across the lecture rostrum, gesticulations etc.

6. In subjects during aggressively monitored mental arithmetic (Brod et al 1959). A timed arithmetic exercise was used as the stressful stimulus in eight normotensive and ten hypertensive patients during cardiac catheterisation. After a period of control observations the subject was asked to subtract a two-figure number from the previous result every two seconds to a metronome. This stimulus was maintained for four minutes and the subjects were continuously and provocatively urged to keep the given pace. The authors stated that there was a "rise
in the heart rate", and documented the increase blood pressure and
cardiac output in all subjects.

Despite the comprehensive nature of these studies, an increase
in heart rate, from 60 to 90 beats per minute, is shown in only one
patient in a diagram.

7. In test pilots

(Roman 1965; Roman et al 1965). This author and his colleagues
reported two studies. Two-seater high altitude Mach 2F-104b fighter
aircraft were used in the first study. The average control heart rates
in six experienced pilots was 110 beats per minute when they were in
actual control of the aircraft and 96 beats per minute when they were
passengers in the same aircraft under similar conditions. In the
second study Roman and his colleagues demonstrated in a single test
pilot an increase in heart rate from a control value of 80 beats per
minute to 120 beats per minute during take-off and 105 beats per minute
during landing an F-100 aircraft. Heart rate measurements in these
studies were made from electrocardiographic recordings on magnetic
tape.

8. In commercial air-line pilots during take-off and landing

(Flying Personnel Research Committee Reports, 1965 and 1966;
Ruffel Smith 1967; Bateman et al 1970; Thomson 1971). In all
instances there was a conspicuous elevation of the heart rate during
take-off and landing. The heart rate was also increased by unexpected
difficulties and hazards during the remainder of the flying task, e.g.
manoeuvres requiring a high degree of skill, or when there was some
element of danger.

The pilots heart rate was measured on electrocardiographic magnetic tape recorders and analysed by computer.

9. Pilots training on a flight simulator

(Eliasch et al 1967; Bateman et al 1970). Eliasch and his colleagues studied the response of the heart rate, cardiac output, systemic blood pressure and plasma catecholamines to mental stress in 16 pilots performing simulated flights on a ground-based cockpit simulator. The average control heart rate was 73 beats per minute (range 55-86). During flight simulation the average heart rate increased to 92 beats per minute (range 71-120) (p<0.001). The blood pressure and cardiac output also increased by an average of 20 mm Hg. (p<0.001) and 2.6 l/min/sq.m. respectively (p<0.001).

Bateman and his colleagues studied the heart rate response of 12 volunteer training captains flying four different types of aircraft (Trident and Comet Jets, Vanguard and Viscount turbopropeller aircraft) in the following situations:

i) simulator training involving all phases of flight

ii) base training involving aircraft landing and

iii) line training that was a continuation of the work done during simulator and base training.

The average control heart rate was 66 beats per minute (range 59-75). During simulator training the average heart rate increased to 87 beats per minute (range 70-119); during base training the average heart rate increased to 91 beats per minute (range 76-112); during the line
training the average heart rate increased to 82 beats per minute (range 74-94); and during line flying the average heart rate increased to 85 beats per minute (range 73-107).

10. In ski-jumpers immediately before take-off

(Hanson and Tabaken 1964; Imhoff et al 1969). Hanson and Tabaken studied the heart rate in four experienced subjects by electrocardiography before the start of a 50 m. ski-jump. The control heart rates of 56 to 80 beats per minute increased to 87 to 118 beats per minute just before the jump. Imhoff and his colleagues measured the heart rate by radiotelemetry in nine experienced ski-jumpers. Two minutes before the start of the jump, during the jump and one minute after landing the average heart rates were 142, 145 and 128 beats per minute respectively.

11. In motor-racing drivers immediately before and during a race

(Collins 1966; Taggart et al 1969). Collins demonstrated that the heart rate increased immediately before the start of a motor race up to 170 to 200 beats per minute or more. This tachycardia was maintained or decreased only slightly during the race. The studies by Taggart and his colleagues involved ten racing drivers; the results were similar to those reported by Collins.

12. In motor-car drivers in heavy traffic

(Suenaga et al 1964; 1965a,1965b; Hoffman 1965; Dupius 1965; Collins et al 1965; Simonson et al 1968; Bellet et al 1968; Taggart and Gibbons 1969). Suenaga and his colleagues studied two healthy drivers in city traffic and found "large fluctuations" of pulse rate with increases of 40 beats per minute or more depending on road events and
speed. The average level of the pulse rate was 15 beats per minute higher at fast than at slow speeds.

Hoffman noted an increase in heart rate of 40 per cent or more of the control value in 8 per cent of 600 healthy drivers during city driving. Twenty six drivers with coronary artery disease showed similar changes.

Absolute values for heart rate were not given. The heart rate was measured from the E.C.G. telemetered to the laboratory. This limited the driving distance to within 30 Km.

Low density highway driving was associated with an increase in heart rate of up to 20 per cent. The heart rate increase was in excess of 20 per cent of the control value during urban driving in 28 per cent of drivers, rising to 42 per cent of healthy drivers during overtaking, sudden stops and other hazardous conditions.

The number of subjects and absolute values for heart rate were not given.

Dupius showed increases of pulse rate in healthy subjects in heavy traffic from 15 to 30 beats per minute and in overtaking up to 45 beats per minute. There was a sharp initial increase of the pulse rate at the start of driving (20 to 30 beats). The author does not state the number of subjects studied.

Collins and his associates in a study of three drivers also showed "high heart rates" with "large fluctuations" depending on road events in their published figures.

Simonson and his associates recorded the heart rate of the
driver and the passenger during the same ride on two consecutive periods of 30 minutes of city driving. The response of the driver and the passenger was nearly identical from a resting value of 75 to 85 beats per minute and the increase in heart rate correlated closely to critical road events.

Bellet and his colleagues studied 65 normal young men between 25-39 years and 66 subjects with proven coronary heart disease between 38-72 years, in city driving lasting two and a half hours, avoiding areas of heavy traffic. The electrocardiogram was recorded on magnetic tape. In the normal subjects the heart rate increased up to 145 beats per minute during driving and in subjects with ischaemic heart disease the heart rate increased to 155 beats per minute.

The central heart rates were not given in this study.

Seventeen per cent of the subjects with coronary artery disease developed ischaemic electrocardiographic changes consisting of S-T depression and multifocal ventricular ectopic beats.

Taggart and Gibbons studied 32 normal drivers and 24 drivers with ischaemic heart disease during drives of 20 minutes in central London. These drivers were experienced, driving their own cars along familiar but crowded traffic routes. Brief periods of tachycardia in excess of 140 beats per minute were recorded in both groups. Electrocardiographic "ischaemic S-T and T wave changes" occurred in 13, with "gross changes" in 6 subjects with ischaemic heart disease.

13. **In train drivers during operation of high-speed trains**

(Yoshio Noda 1965). The Japanese National Railways' New Tokaido Line was opened to traffic in October, 1964. This railway
line was specially built for high speed travel and drivers were specially trained for these high speeds. Heart rate measurements were conducted on a test section. At 150 km/hour the increase in heart rate was 106% of the control value. At a speed of 200 km/hour, the driver's heart rate increased to 111% of the control value. The author did not mention his method of heart rate measurement.

14. In male volunteers sorting ball-bearings to the accompaniment of distracting noise and lights

(Carlson et al 1967). In this study 33 male volunteers were divided into three groups of 11, matched for age, blood pressure and blood lipid content. One group acted as a control only listening to light music; the second group ingested 3 grams of nicotinic acid in six divided doses during the first 3 hours of the 6 hour experiment. This group and the third group sorted ball-bearings to the accompaniment of distracting noise and lights.

The heart rate was measured from an electrocardiograph and the blood pressure was measured from a direct left brachial artery catheter. The average resting heart rate of the control group was 65 beats per minute. The average heart rate in the group that ingested nicotinic acid rose to 79 beats per minute from a control value of 69 beats per minute; and the third group showed an average increase to 77 beats per minute from a resting heart rate of 63 beats per minute.

The control group showed no changes in blood pressure. In the "nicotinic acid group" the systolic blood pressure rose by 14 mm Hg and the diastolic blood pressure rose by 9 mm Hg. The remaining group showed a rise of 12 mm Hg in the systolic blood pressure and 9 mm Hg in diastolic blood pressure.
CONCLUSIONS

It is apparent that the majority of these studies were concerned with the circulatory response to intensely exciting or even unnatural psychological stresses. Many of the stimuli used are rarely met in normal everyday life. However, they do indicate the possible magnitude of the response of the heart and other circulatory variables to non-exertional stress. It is of some importance therefore to determine the range of cardiovascular responses to situations commonly occurring in everyday life. Many people drive motor-cars, but few undertake to subtract 17 from 1194 every two seconds to a metronome, watched by aggressive medical staff. It is these considerations that prompted the following studies.

The following programme of investigation was therefore designed to measure the cardiovascular effects of some of the more stressful environmental situations normally encountered in everyday life in normal healthy subjects and in patients with ischaemic heart disease and to examine the role of sympathetic stimulation of the heart in these responses.

Two studies were therefore undertaken.

The first study was undertaken to determine the relative contribution of sympathetic stimulation of the heart to the tachycardias associated with the mental stress of motor-car driving, catecholamine infusion and walking. This study was also designed to give information regarding the magnitude and duration of the suppression of these tachycardias achieved
by the oral beta-receptor antagonist oxprenolol.

The second study was designed to investigate the magnitude of the effects of some normal everyday environmental stresses on the heart rate and the degree of modulation of these responses induced by a similar degree of blockade of the heart rate beta-receptors as achieved in the first study.

ETHICAL CONSIDERATIONS

The ethical aspects of these studies were given careful consideration (Medical Research Council Annual Report, 1964; Ormrod, 1968). It was inherent in the design of these studies that the majority were carried out with inconspicuous electrocardiographic recordings during each patient's normal everyday activities; invasive techniques were not employed. A large number of clinical reports and general clinical experience has shown the relative freedom from side effects of the small doses of the beta-receptor antagonist oxprenolol used in these studies. In Study 1 invasive techniques were used for the isoprenaline infusion. In these studies the subjects were myself or my hospital colleagues, all of whom fully understood the aims and nature of the investigations and procedures involved.
STUDY 1

THE DIFFERENT EFFECTS OF ADRENERGIC BETA-RECEPTOR BLOCKADE ON THE HEART RATE RESPONSE TO MENTAL STRESS CATECHOLAMINES AND EXERCISE

INTRODUCTION

Emotional stress, catecholamines and physical exertion all induce an increase in heart rate. During recent studies of the effects of environmentally-induced psychological stress on the heart I noticed that small doses of the beta-receptor antagonist oxprenolol had a conspicuously greater effect on the tachycardia associated with mental stress than on the heart rate increase during walking. In view of the possible therapeutic implications of this observation the following study was designed to define more closely the quantitative relationship between the tachycardias due to these three stimuli in terms of their inhibition by beta-receptor antagonists.

METHOD

Subjects

Studies were made on six normal males aged 26 - 47 years. None had any symptoms of systemic disease and in all the blood pressure was within normal limits. I was one of the subjects; the remainder were professional colleagues who fully understood the aims and nature of the investigation.
Design of Study

Each subject was studied in three different test situations.

1. Driving a motor-car for 15 - 20 minutes in heavy city traffic.

2. In the supine position during a two-minute intravenous isoprenaline infusion sufficient to raise the heart rate to the levels observed during driving.

3. During treadmill walking of two minutes duration sufficient to raise the heart rate to similar levels.

Preliminary studies were carried out to familiarize each subject with the programme of investigation and determine the peak heart rate response regularly achieved by motor-car driving: the dose of intravenous isoprenaline and level of treadmill walking necessary to give a similar heart rate increase was then determined. Motor-car driving, carried out over a random route through Leeds city centre for 15 - 20 minutes repeatedly resulted in heart rate increments of 30 beats/min. or more in all subjects. The intravenous isoprenaline infusion rate necessary to induce a similar tachycardia varied between 3 - 7 ug/min. for two minutes in different subjects. A similar increase in heart rate was induced by treadmill walking at 3 m.p.h. on 10 - 15° incline for two minutes.

The definitive double-blind studies were commenced at 8.00 a.m. two hours after a light breakfast and one hour after a single oral tablet of 40 mg oxprenolol or matched placebo tablet. A control electrocardiogram was done with each subject sitting quietly at the wheel of his car. A 15 - 20 minute period of city driving was then
undertaken on a random route selected on an ongoing basis by an observer travelling as passenger. The subject then returned to the laboratory, and, after ten minutes rest, a two minute intravenous infusion of isoprenaline was given in a dose that had been determined beforehand would raise the heart rate in that subject by approximately 30 beats per minute. After a further ten minutes rest by which time the heart rate had returned to pre-isoprenaline infusion levels the treadmill exercise test was performed. Similar studies were repeated at 2, 4, 6, 8 and 12 hours. The programme was repeated three or four days later after placebo or oxprenolol.

Between the test periods each subject returned to his normal professional duties. No restriction was placed on their activities except that they were asked not to eat large meals or smoke within an hour of the subsequent test, as both have been shown to result in considerable increases in heart rate.

Active and placebo tablets were coded in pairs for each subject. The heart rate was measured from an electrocardiographic record taken blind into a closed container during the final 10 seconds of every minute of the study, and counted and checked by two uninvolved colleagues.

Techniques, Measurements and Statistics

The heart rate was measured from the record made on a portable electrocardiograph (Cambridge Transrite Model III). Values were averaged from the 15 - 20 one minute records taken during each driving period, averaged over the final ten seconds of the isoprenaline
infusion and during the final ten seconds of the second minute of treadmill exercise.

During the isoprenaline infusion and treadmill walking test the electrocardiogram was also displayed on an oscilloscope (S.E. Laboratories SEM 121).

Isoprenaline (Evans Medical Ltd) was given as a continuous intravenous infusion into a hand or arm vein via a subcutaneous needle by an electromechanical pump (Harvard Model 901) with a variation in rate of less than 2 per cent. The concentrations were arranged so that the volume of fluid infused was between 2 - 5 ml/min.

Walking was carried out on a treadmill (Quinton Instruments Model 18-54) with which the subjects were familiar. Subjects drove their own motor-cars, with manual gearboxes. Speed limits were obeyed.

The variability of the response to the test situation was calculated in each subject from the placebo results as a percentage (SEM/Mean) and averaged for the group.

RESULTS

The effects of 40 mg oral oxprenolol compared to placebo on the heart rate response to motor-car driving, isoprenaline infusion and treadmill walking in six normal subjects is presented in the accompanying figure I and tables 1, 2 and 3.

From the placebo results, the average variability about the mean increase in heart rate to driving, isoprenaline and exercise was 10 per cent (range 3.8 - 13.8), 3 per cent (range 3.1 - 3.9) and 3 per cent (range 3.0 - 3.4) respectively, Table 4. Compared to the
results with placebo, the tachycardia associated with motor-car
driving and isoprenaline infusion was conspicuously reduced for up
to 12 hours after 40 mg oral propranolol. In the same subjects, the
drug had much less effect on the heart rate response to exercise.

DISCUSSION

These results clearly demonstrate the different effects of a
similar degree of beta-receptor blockade on the increase in heart
rate associated with mental stress and catecholamine infusion
compared with the effect on a similar tachycardia induced by
exercise. Although the mechanism by which mental stress induces
an increase in heart rate is unknown, the similar suppression of the
tachycardia associated with motor-car driving and that due to infused
catecholamines by the same degree of beta-receptor blockade suggests
that both tachycardias are probably induced by a similar increase in
concentration of catecholamines at the cardiac beta-receptor sites
controlling the heart rate. Although it does not necessarily follow
that there is a similar increase in level of circulating catecholamines
an increase in the concentration of plasma catecholamines has been
observed in racing-car drivers in parallel with an increase in heart
rate (Taggart et al, 1968). At extreme levels of exertion the increase
in heart rate is predominantly due to direct sympathetic stimulation
of the cardiac heart rate receptors; the adrenomedullary catecholamines
appear to play little part in this response. But at the levels of exercise
used in the present studies, with heart rates of 100 - 120 beats per
minute, the tachycardia is due both to sympathetic stimulation and
vagal withdrawal (Donald and Shepherd, 1963; Robinson, 1966). In fact the results of the present studies indicate that the degree of direct sympathetic activity involved in the heart rate increase at this level of normal everyday exertion is probably small compared with the vagal withdrawal component. This is probably the most likely explanation for the different effects of small doses of beta-receptor antagonists on the heart rate response to the three stimuli observed in the present studies.

These findings have important clinical implications in the treatment of angina pectoris. One of the ideals of medical treatment is the establishment of a dose-response relationship, namely the administration of only sufficient drug as is necessary to achieve the desired effect. Although the mechanisms responsible for precipitating anginal pain in susceptible subjects are unknown (Robinson, 1971; Taylor, 1973), the onset of pain is closely correlated with an increase in heart rate (Robinson, 1971; Epstein et al, 1971; Taylor, 1973), whether this be induced by exercise or by the mentally stressful activities of everyday life. These results suggest that the dose of beta-receptor antagonist necessary to suppress the tachycardia in these different situations may differ widely. The single dose of propranolol or oxprenolol necessary to produce a near-maximum suppression of exercise tachycardia is 160 mg (Taylor et al, 1973). However, the maximum effectiveness of this dose in this respect is relatively short-lived and the majority of angina patients experience relief from exercise induced symptoms only with repeated daily doses of this order (Prichard and Gillam, 1971).
The present results suggest that anginal pain associated with anxiety or emotion may be controlled by much smaller doses of drug than those necessary to afford relief in exercise situation.

These studies were undertaken as an essential preliminary to the investigation of the cardiac response to everyday mental stress and its modulation by beta-receptor antagonists (Study II). The results indicate that the increase in the heart rate response to psychological stress may be largely suppressed throughout the waking hours by a dose of beta-receptor antagonist that has no detectable mental effects (Turner, 1972) and only small relatively short-lasting effects on the heart rate response to exercise.

**SUMMARY**

The magnitude and duration of effect of a single 40 mg oral tablet of oxprenolol on the tachycardias associated with motor-car driving, isoprenaline infusion and walking was measured in six normal subjects by a double-blind technique. The heart rate increase due to driving and isoprenaline was conspicuously reduced for more than 8 hours; the reduction in exercise tachycardia was substantially less. These results indicate that relatively small doses of beta-receptor antagonists will suppress the heart rate increase induced by mental stress and catecholamines with relatively little effect on the response to exercise. The clinical implications of these observations in the treatment of emotionally-induced anginal pain and their possible role in suppressing the tachycardia associated with psychological stress is discussed.
The effect of oral oxprenolol on the heart rate response to motor-car driving (△); isoprenaline infusion (○) and treadmill walking (O) in six normal subjects. 40 mg oral oxprenolol was given immediately after the control study (C). Data expressed as mean ± standard error of mean.
TABLE 1  INCREASE IN HEART RATE IN NORMAL SUBJECTS DURING MOTOR-CAR DRIVING IN CITY TRAFFIC
AND ITS MODULATION BY BETA-ADRENORECEPTOR BLOCKADE

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>TEST</th>
<th>CONTROL</th>
<th>TIME IN HOURS AFTER PLACEBO OR 40 mg OXPRENOLOL</th>
<th>INCREMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>PLACEBO</td>
<td>69</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>60</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>2</td>
<td>PLACEBO</td>
<td>65</td>
<td>37</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>56</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>PLACEBO</td>
<td>71</td>
<td>29</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>66</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>PLACEBO</td>
<td>76</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>68</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>PLACEBO</td>
<td>70</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>66</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>PLACEBO</td>
<td>73</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>62</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>MEAN ± SEM</td>
<td>PLACEBO</td>
<td>71 ± 2</td>
<td>34 ± 3</td>
<td>29 ± 3</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>63 ± 2</td>
<td>5 ± 2</td>
<td>5 ± 3</td>
</tr>
</tbody>
</table>

1 Heart rate during sitting period before test.
2 Values relate to increases in heart rate over control values.
3 Average heart rate increment over control value (Mean ± SEM).

* p < 0.05. Significance of differences relate to comparison with placebo value.
<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>TEST</th>
<th>CONTROL 1</th>
<th>TIME IN HOURS AFTER PLACEBO or 40 mg OXPRENOLOL</th>
<th>INCREMENT 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>PLACEBO</td>
<td>67</td>
<td>27</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>62</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>PLACEBO</td>
<td>64</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>58</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>PLACEBO</td>
<td>69</td>
<td>29</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>61</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>PLACEBO</td>
<td>67</td>
<td>28</td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>62</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>PLACEBO</td>
<td>71</td>
<td>32</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>65</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>PLACEBO</td>
<td>63</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>60</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>MEAN ± SEM</td>
<td>PLACEBO</td>
<td>68 ± 1</td>
<td>29 ± 1</td>
<td>31 ± 2</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>* 61 ± 1</td>
<td>0 ± 0</td>
<td>1 ± 0</td>
</tr>
</tbody>
</table>

1 Heart rate during control period lying supine before test
2 Values relate to increases in heart rate over control values
3 Heart rate increment over control value (Mean ± SEM)

* p < 0.001 Significance of differences relate to comparison with placebo value.
TABLE 3 INCREASE IN HEART RATE IN NORMAL SUBJECTS DURING TREADMILL WALKING AND ITS MODULATION BY Beta-ADRENORECEPTOR BLOCKADE

<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>TEST</th>
<th>CONTROL(^1)</th>
<th>TIME IN HOURS AFTER PLACEBO OR 40 mg OXPRENOLOL(^2)</th>
<th>INCREMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1</td>
<td>PLACEBO</td>
<td>94</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>71</td>
<td>20</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>PLACEBO</td>
<td>92</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>72</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>PLACEBO</td>
<td>76</td>
<td>32</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>63</td>
<td>17</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>PLACEBO</td>
<td>88</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>76</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>5</td>
<td>PLACEBO</td>
<td>84</td>
<td>30</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>70</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>6</td>
<td>PLACEBO</td>
<td>87</td>
<td>34</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>74</td>
<td>21</td>
<td>23</td>
</tr>
<tr>
<td>MEAN ± SEM</td>
<td>PLACEBO</td>
<td>* 87 ± 3</td>
<td>32 ± 1</td>
<td>31 ± 1</td>
</tr>
<tr>
<td></td>
<td>OXPRENOLOL</td>
<td>* 71 ± 2</td>
<td>19 ± 1</td>
<td>23 ± 1</td>
</tr>
</tbody>
</table>

\(^1\) Heart rate during control period standing still for two minutes before test

\(^2\) Values relate to increases in heart rate over control values

\(^3\) Heart rate increment over control value (Mean ± SEM)

\(* p < 0.001\) Significance of differences relate to comparison with placebo value.
<table>
<thead>
<tr>
<th>SUBJECT</th>
<th>Motor Car Driving</th>
<th>Isoprenaline Infusion</th>
<th>Treadmill Walking</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3.8</td>
<td>3.4</td>
<td>3.2</td>
</tr>
<tr>
<td>2</td>
<td>13.3</td>
<td>3.1</td>
<td>3.4</td>
</tr>
<tr>
<td>3</td>
<td>9.7</td>
<td>3.3</td>
<td>3.2</td>
</tr>
<tr>
<td>4</td>
<td>4.2</td>
<td>3.9</td>
<td>3.1</td>
</tr>
<tr>
<td>5</td>
<td>13.8</td>
<td>3.3</td>
<td>3.2</td>
</tr>
<tr>
<td>6</td>
<td>12.0</td>
<td>3.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Average</td>
<td>9.5</td>
<td>3.4</td>
<td>3.2</td>
</tr>
</tbody>
</table>

Variability calculated as \( \frac{\text{SEM}}{\text{Mean}} \times 100 \) of heart rate increments at 1, 2, 4, 6, 8, and 12 hours during placebo studies.
STUDY II

INTRODUCTION

Reports concerned with the measurement of some of the effects of emotional and environmental stress on the heart have already been reviewed. However, as pointed out in the introduction, the majority of these studies were concerned with the responses to stress that were often extreme and frequently unnatural in the context of everyday life. The present study was therefore designed with a different attitude, namely to examine the magnitude and duration of the effects of normal everyday stimuli on the heart.

METHODS

Subjects: The following groups of subjects were studied:

1. Normal Subjects:

   These consisted of a group of eight healthy male subjects who were either business acquaintances and professional staff of the hospital. Their ages ranged between 26 - 56 years. None were obese or diabetic, systemic arterial blood pressure was normal in all, and none had any symptoms or signs of systemic disease.

2. Patients with Ischaemic Heart Disease

   Studies were also made on twelve company directors and business executives suffering from proven ischaemic heart disease.

   A) Six were suffering from exercise-induced angina pectoris.

      Their ages ranged from 35 - 60 years. None of them were obese, hypertensive, diabetic or suffering from signs and symptoms of systemic disease.

The diagnosis of angina pectoris was based on the following criteria:
i) no electrocardiographic S-T segment depression at rest but a depression of the J point of more than 0.1 mV during exercise induced pain with a prompt return of the S-T segment to the isoelectric line on stopping exercise (Fig 2)

ii) a left ventricular end-diastolic pressure of less than 12 mm Hg at rest increasing to more than 25 mm Hg at the onset of exercise.

B) Six had suffered a definite myocardial infarction between 6 and 12 months previously for which they had been admitted to the Coronary Care Unit of Leeds General Infirmary. None of them were obese, hypertensive, diabetic or suffering from signs of systemic disease. Their ages ranged between 36 - 60 years.

The diagnosis of myocardial infarction was based on the following criteria:

i) electrocardiographic changes consisting of Q waves greater than 1 mm, S-T segment elevation and T wave inversion with reciprocal changes in the opposite leads. The evolution of the infarct followed the normal pattern of regression of the S-T segment elevation with residual Q waves and T wave inversion in these.

ii) Serum enzymes done serially over days 1, 2 and 3 showed a raised level of at least two of them on the second day.

The serum glutamic oxalacetic transaminase, serum glutamic pyruvic acid transaminase, creatinine phosphokinase and lactic acid dehydrogenase were measured in the hospital chemical pathology laboratory by autoanalyser methods. The normal
range of values for this laboratory is:

8 - 22 IU/L,

4 - 203 IU/L.

less than 60 IU/L and

150 - 480 IU/L respectively.

3. Bus Drivers

Following the demonstration that motor-car driving induced substantial increases in the heart rate both during city and motorway driving, the study was extended to include observations on bus drivers. Two groups of experienced bus-drivers were studied:

A) Thirteen during long-distance travel. Their ages ranged between 30 - 58 years. They were of normal height and weight and none had signs or symptoms of any systemic disease.

B) Six during city bus-driving. Their ages ranged between 26 - 40 years and they were of normal height and weight. None of them had any signs or symptoms of systemic disease.

4. Two B.B.C. radio and television commentators and performers were studied; one during professional soccer matches and the other during variety programmes.

The radio and television commentator was a male aged 36 years, of normal height and weight and had no symptoms of systemic disease. He belonged to a regular sports programme and gave live commentaries frequently during the soccer season.

The radio and television performer was a male aged 48 years, of
normal height and weight with no symptoms or signs of systemic disease. He has a regular "pop" music programme which is recorded the day before the live transmission. The audience comprises of about 150 teenagers.

5. Four normal subjects who claimed that they were particularly excited by watching horror, mystery, thriller and live boxing television programmes were studied. Their ages ranged between 23 - 50 years. None had any symptoms or signs of systemic disease and none were obese, diabetic or suffering from systemic hypertension.
DESIGN OF INVESTIGATION

The measurement of cardiovascular responses to everyday stress imposes considerable technical restrictions and it is mandatory that they fulfil certain limiting criteria:

1. The measurements should be capable of detecting changes in those variables which directly reflect alterations in sympathetic influence on the circulation.

2. They should be capable of continuous, extended and repeated use.

3. They should be so unappreciated by the subject that they in no way interfere with his normal activities.

Furthermore, in order to describe the cardiac response to as full a spectrum of environmental and psychological stress as is usually met in everyday life it was considered that more valuable information would be obtained by studying the effects of stress on the heart serially in a group of subjects than the effects of different stresses in separate larger groups.

Normal subjects and patients with ischaemic heart disease were therefore studied serially under the following situations:

1. Motor-car driving on a motorway.

2. Motor-car driving in city traffic.


4. Rail passenger

5. Aircraft passenger

6. Spectator at football matches

7. Television viewing of comedy, drama and documentary film.
8. Radio and Television commentators and performers.


The reasons for the choice of these situations were that the psychological stress involved formed part of the subject's normal everyday life-pattern and was unlikely to be accompanied by physical exertion. The studies were extended to include bus drivers, rail and aircraft travel and radio commentators after the early results had shown the conspicuous effects on heart rate of motor-car drivers and passengers and radio and television viewing.

It was decided to study the effects of blockade of the heart rate beta-receptors for two reasons:-

1) to assess how much of the tachycardia was due to a sympathetic stimulation;

2) to explore the possible therapeutic usefulness of these drugs in these situations.

The technical difficulties involved in measuring variables other than the heart rate reliably and continuously in normal subjects and patients with ischaemic heart disease have already been mentioned. Similarly there was considerable difficulty for logistic reasons in carrying out a double-blind assessment in every instance.

Double-blind measurements would require continuous electrocardiographic recording over extended periods of time which was impractical as there was no apparatus available capable of such recording when the study commenced. Therefore, the majority of this study was of necessity single-blind as the observer recording the results
could detect the heart rate response of the subject. In order to eliminate the influence of suggestion one of the studies was carried out after the ingestion of an oxprenolol matched placebo tablet containing Sucrose, 192 mgs, Tricalcium Phosphate 14 mgs, Wheat Starch, 70.59 mgs, Bitrex perfume 0.01 mg, Magnesium Stearate 1.40 mg, Kallidon 25.8 mgs and Talc 14 mgs. The other study was carried out one hour after taking 40 mg oral oxprenolol. The order of administration of the tablets was randomised in pairs. However, a short double-blind study was initially carried out to examine any differences that may have been introduced by subject suggestion or observer bias.

In order to determine the circulatory response to environmental and psychological stresses during normal everyday activities, frequently over many hours, and serially on a number of occasions (e.g. during different modes of travel before and after beta-receptor antagonists) non-invasive extravascular methods were mandatory. Extravascular monitoring of the heart rate was the only method which would fulfil these criteria in intact man. The extravascular measurement of heart rate by radiotelemetry offers perhaps the optimum method in that the heart rate directly reflects the degree of sympathetic stimulation of the heart and by this method it can be measured continuously, repeatedly and for extended periods of time without physical appreciation by the subject under study. It has the added advantage that in these circumstances the heart rate is linearly related to the level of exogenously infused catecholamines.
in individuals at rest (Wexler et al 1971; Majid et al 1973; Taylor et al 1973) and it also appears to be the predominant variable aggravating the symptoms of ischaemic heart disease (Robinson 1971; Taylor 1973). Repetative measurement of the blood pressure by sphygmomanometer was found to be impractical under many conditions and distracting to the subject under study; continuous measurement from indwelling arterial cannulae was similarly impractical for extended periods in the real-life situations envisaged. For these reasons heart rate alone was chosen to monitor the degree of cardiac sympathetic activity. This in no way detracts from the criticism that the measurement of changes in a single variable can do little more than indicate the direction of changes in sympathetic influence, that such measurements cannot be used to indicate either quantitative changes in sympathetic drive or to indicate the overall influence of such changes on the heart and vascular system. But the gain in the facility with which the measurements of heart rate can be made far outweigh the disadvantages of using more cumbersome and distracting methods.

TECHNIQUES

Heart rate was measured electrocardiographically by a radiotelemeter (Parks Electronics Laboratory, Beverton, Oregon, U.S.A.), (Figs 3 and 4).

The apparatus consisted of:-

1. **Receiver** (Model RD-27) - a small battery operated unit (26 x 16.5 x 10 cm) with a frequency matched to the transmitter and an output voltage of 1 to 5 millivolts, suitable for the input to a variety of E.C.G. recorders.
2. **Transmitter** (Model 27) - a frequency modulated transmitter

(16 x 9.4 x 4 cm) powered by two 9 volt transistor radio batteries.

The transmitter was attached to the subject's belt with two leads to the chest electrodes; strapped in the vicinity of the right shoulder so that its end was free and inconspicuous.

3. **Ratemeter** (Model 503 - E) - this was battery powered and was able to operate either directly from the subject or from the telemetry receiver. The ratemeter and electrocardiograph could be used on the receiver at the same time. It has a 250 beats per minute scale with an alarm signal and cumulative counter.

The telemetry system was able to operate satisfactorily with an outside range of 100 to 200 yards but in buildings with steel mesh under the plaster the range was severely restricted. The battery life was about 16 hours.

The condition of the batteries was checked by the meter on the telemetry receiver and the ratemeter.

The radiotelemeter system picked up potentials from the electrodes and sent them by radio to the receiver for recording on the electrocardiograph or ratemeter.

Two bipolar silver chloride electrodes were used (Becton Dickinson U.K. Limited) with the following specifications:

- Electrode-to-skin offset voltage as low as 300 microvolts with an electrode to skin impedance as low as 100 ohms where the epidermis was pricked.

The electrode lead cables were plugged into the transmitter. The electrodes consisted of a reservoir for the electrode paste;
Industrial Medical Instruments adhesive washers securely held electrodes to the skin. To make a firm contact the electrodes were applied to skin which had been shaved. One electrode was placed on top of the sternum and the second electrode below the left nipple, usually about 2 inches from the nipple both below and towards the anterior axillary line. The electrical resistance (measured by an ohmmeter) between two electrodes on the chest was ideally around 3000 ohms or lower. The resistance was lowered by abrading the skin and rubbing a small amount of electrode paste into the skin at the contact point with a cotton-tipped applicator. Industrial Medical Instruments skin cleaner swabs were most efficient for preparing the skin for electrode sites. The swab was a combination of ingredients including isopropyl alcohol and skin emulsifiers absorbed into a mildly abrasive unit. The swabs had been specially formulated to:

1. remove all the insulating elements from the skin surface and
2. actually deposit a conductive film on the skin.

The heart rate was monitored continuously and plotted at 30 or 60 second intervals depending on the variation of the monitored changes observed. The fidelity of the apparatus was measured by recording directly from the transmitter and separately from an electrocardiograph machine. The fidelity was found to be absolute (Fig. 5).

A Philips School’s 24” Television Receiver (Model No 8692) suitably modified to show video-taped programmes was used for the viewing of the comedy, dramas and documentary films.
The Philips Type LDL 1000/00 video-machine used a \( \frac{3}{4} \) inch video-tape (Philips VER 6 8945 002 06002) on a 6 inches diameter spool, which ran over one and a half hours.
Diagnostic changes in the exercise electrocardiogram in a patient with angina pectoris.
FIGURE 3

Photograph of the radiotelemeter apparatus. (Parks Electronics Laboratory, Beverton, Oregon, U.S.A.)

2. Transmitter 5. Ratemeter
FIGURE 4

Photograph of one of the subjects connected to the radio-telemetry system.
1. Chest electrodes
2. Transmitter
3. Antennae wire
4. Receiver
5. Ratemeter
MATCHED SEGMENTS OF ECG RECORDINGS TAKEN DIRECTLY ON A MINGOGRAP 34 ECG MACHINE AND ECG SIGNALS FROM A TELEMETRY RECEIVER TO DEMONSTRATE FIDELITY.

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**FIGURE 5**

Electrocardiographic record showing the **ABSOLUTE** fidelity of the telemeter transmitter.
RESULTS

The results are discussed under the respective sections with a selection of illustrative figures and tables. The remainder of the individual figures of the results are included in the Appendix.

A summary of the results is included at the end of the chapter.
TRAVEL BY MOTOR-CAR

Motor-car journeys were made throughout the year under various weather conditions; these ranged from clear summer and spring days to dark, rainy, foggy days and with occasional winter snow and sleet. The majority of the studies were done between Leeds and London, a distance of approximately 200 miles on the M1 motorway. Other studies were carried out during driving on the A1 and A1/M1 trunk roads between Leeds and Newcastle (approximately 120 miles). All of these journeys were done as part of the normal everyday duties of the businessmen concerned. The journeys were done in normal saloon cars and one high powered coupe.

Studies of the effects on the heart rate of motor-car driving in city traffic were carried out in Leeds at times when traffic density was usually high, during the early morning (6 - 9 a.m.) and evening (5 - 6 p.m.) rush hours. Journeys lasted from 15 - 25 minutes.

In order to eliminate the influence of suggestion, the study was carried out in a single-blind fashion. One of the studies was carried out after the ingestion of an oxprenolol matched placebo tablet. The other study was carried out one hour after taking orally a 40 mg tablet of oxprenolol.

A) Motor-car drivers

1) Motorway driving

a) normal subjects - (Fig. 6 and 7; Table 5)

The heart rate was recorded during continuous driving in varied weather conditions from the centre of Leeds to the centre of London, (approximately 200 miles) or between Leeds and Newcastle (approximately
Driving was commenced one hour after taking 40 mg oxprenolol or a matched placebo tablet, the order of administration being randomized in pairs. During control studies, i.e. after taking the placebo tablet, the conspicuous peaks of heart rate were found to be usually related to the usual motorway hazards, e.g.

i) bunching of cars in the fast lane
ii) overtaking or being overtaken without warning
iii) sudden showers of rain
iv) potentially hazardous moves by other drivers
v) short bursts of high speed
vi) driving through unexpected mist or fog patches
vii) unexpected appearance of police vehicles

The ingestion of 40 mg oxprenolol taken one hour before a journey carried out under similar conditions conspicuously reduced the peak responses in heart rate observed in the placebo studies.

b) Patients with ischaemic heart disease (Figs. 8 and 9; Table 6)

A similar pattern of peaks of tachycardia was seen throughout the journey undertaken after ingestion of placebo. The peaks of heart rate observed in these patients were associated with similar travelling events to those detailed for the normal subjects. Similarly these peaks of tachycardia were completely suppressed after 40 mg oral oxprenolol taken one hour after the start of the journey.

2) City Driving

a) Normal Subjects (Figs. 10 and 11; Table 7)

This commuter study was done in high density traffic in Leeds.
city. Significant peaks of tachycardia were seen with a high total cumulative heart rate one hour after taking a placebo tablet. The peaks of tachycardia were related to the hazards that often occur during driving in congested city traffic e.g.

i) taking sudden avoidance action when pedestrians suddenly step into the street.

ii) trying to avoid the results of hazardous manoeuvres by other drivers.

iii) a potentially dangerous move by the driver himself

iv) the frustration of driving behind a long queue especially when late for an appointment

v) the sudden changing of lights necessitating emergency braking on the part of the driver.

The cumulative heart rate was reduced and the peaks of tachycardia significantly reduced after 40 mg oral oxprenolol taken one hour before the journey.

b) Patients with ischaemic heart disease (Figs 12 and 13; Table 8)

A similar pattern of peaks of tachycardia as were seen in the normal subjects were observed in all patients after placebo. These peaks were associated with similar traffic events as were seen in the normal subjects and were similarly suppressed after 40 mg oral oxprenolol.

B) Motor-car Passengers

a) Normal Subjects (Figs 14 and 15; Table 9)

When the same normal subjects were travelling as motor-car
passengers lesser levels of tachycardia and smaller peaks of heart rate responses were observed throughout the journey one hour after taking placebo. The basal level of heart rate was reduced and the peaks of tachycardia suppressed by 40 mg oral oxprenolol in all subjects.

b) Patients with ischaemic heart disease (Figs 16 and 17; Table10):

The peaks of tachycardia in these patients were similar to those observed in the normal subjects after placebo. Similarly 40 mg oral oxprenolol resulted in a significant reduction in these peaks of tachycardia.
TRAVEL BY TRAIN

These journeys were undertaken for routine business purposes to London by British Rail inter-city express. Journeys were undertaken throughout the year and the usual journey time was 2 1/2 – 3 1/2 hours. The heart rate response was recorded an hour after taking a 40 mg oxprenolol or a matched placebo tablet; the order of administration was randomized in pairs.

RAILWAY TRAIN PASSENGERS

a) Normal Subjects (Figs 18 and 19; Table 11)

The pattern of the heart rate response travelling by train was much more subdued with few peaks throughout the inter-city journey between Leeds and London as compared to that observed in the same normal subjects during motor-car travel on the motorway and commuter traffic. The basal heart rate was lowered by 40 mg oral oxprenolol taken one hour before the start of the journey, but the response to the drug was much less conspicuous than during motor-car travel.

b) Patients with ischaemic heart disease (Figs 20 and 21; Table 12)

The heart rate response during train travel after placebo was similar to that of the normal subjects. The heart rate response was subdued after 40 mg oral oxprenolol, taken one hour before commencement of the journey.
TRAVEL BY AIRCRAFT

Flights were made throughout the year and covered a wide range of weather conditions. During the summer and spring, days were often ideal for flying with a cloudless blue sky. But, during the autumn and winter adverse conditions were often met with thick fog, low clouds and the aircraft frequently had to fly entirely by instruments and make blind landing approaches. Frequently the cloud base extended from 2000 ft to 12000 ft so that the whole journey involved blind flying in turbulent conditions. Two types of aircraft were used for these journeys. Vickers Viscount turbopropeller aircraft with 73 seats and Hawker-Siddeley Trident jet aircraft with 123 seats both run by North-East Airlines. The turbopropeller aircraft journey from Leeds to London, an approximate distance of 200 miles, was usually flown in the routine aircraft corridor at an altitude of 12000 feet and speed of 300 m.p.h. with a flight time of approximately 55 minutes. The jet journey was from Newcastle to London, a distance of approximately 330 miles and was flown at an altitude of 29000 feet at 600 m.p.h. with a usual flight time of 40 minutes.

It was not possible to use a double-blind method of study for two reasons. The 12 hour duration of the anti-stress effects of oxprenolol determined from the previous study precluded a study based on a single return flight. And the costs involved ruled out two separate return flights in each individual (with an observer). A single blind study was used in preference to open trial to obviate the effects of subject suggestion. However, one patient, who suffered a myocardial infarction six months prior to the study, was given an oxprenolol matched
placebo tablet on both the outward and return journey on the turbo-
propeller flight (Fig. 22).

The first study was carried out on the outward journey one hour
after the ingestion of placebo. The return flight was carried out one
hour after taking a 40 mg tablet of oral oxprenolol.

1) Leeds - London by Viscount Turbopropeller aircraft

a) Normal Subjects (Figs 23 and 24; Table 13)

Travel by these aircraft from Leeds to London after placebo
was associated with conspicuous peaks of tachycardia throughout the flight
but particularly during:

i) take-off and landing

ii) during air turbulence

iii) in response to unusual noises

iv) attitude of the aircraft

v) hazard warnings by the captain or crew

vi) captain's announcements of diversions of the aircraft to
another airport.

After 40 mg oral oxprenolol taken one hour before the return flight the
peaks and cumulative heart rate were much reduced despite similar test
conditions.

b) Patients with ischaemic heart disease (Figs. 25 and 26; Table 14)

These subjects showed a similar response to that observed in
normal subjects; the peaks of tachycardia observed during the placebo
test were conspicuously reduced after 40 mg oral oxprenolol, despite the
very similar test situation.
2) **Newcastle-London by Trident Jet aircraft**

   a) **Normal Subjects** (Figs 27 and 28, Table 15);

   Travel by jet aircraft from Newcastle to London after placebo showed conspicuous peaks of tachycardia throughout the flight and in particular during take-off, landing and during adverse flying conditions similar to those experienced during the flights by turbopropeller aircraft.

   40 mg oral oxprenolol taken one hour before the return flight abolished the peaks of tachycardia and decreased the total cumulative heart rate.

   b) **Patients with ischaemic heart disease** (Figs 29 and 30; Table 16);

   These subjects showed a similar response to the normal subjects and the peaks of tachycardia were completely suppressed on the return flight one hour after 40 mg oral oxprenolol. The total cumulative heart beats were also decreased.
SPECTATOR VIEWING

Live viewing at Football Matches

This was a study of the heart rate response of spectators during live football matches. These matches were played in different and varying weather conditions either on a Wednesday evening or a Saturday afternoon, and involved First Division matches with Leeds United's first team. The subjects studied were all interested in football and the local Leeds United team in particular. Some of the studies were done an hour after the ingestion of an oxprenolol matched placebo tablet and the other study an hour after the ingestion of 40 mg oral oxprenolol; the order of taking the tablets being reversed in pairs, in randomised order. In other studies 40 mg oral oxprenolol was ingested after the first 30 minutes of the match and the effects on the heart rate was monitored throughout the subsequent 60 minutes. The resting heart rates were taken over a 15 minute period before the start of the match with the subject sitting quietly reviewing the programme.

a) Normal subjects

Watching soccer matches one hour after the ingestion of an oxprenolol matched placebo tablet as spectators (Figs 31 and 32, Table 17) was often associated with conspicuous peaks of tachycardia. These were associated with:

i) goal scoring

ii) near misses

iii) fouls on home-side players

or iv) misinterpreted decisions by the referee.

40 mg oxprenolol taken orally one hour before the start of a soccer match completely suppressed the peaks of tachycardia and the total cumulative
heart beats. The action of onset of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match can be seen in Fig. 35 during passive soccer viewing. The suppression of the peaks of tachycardia could be seen 30 minutes after ingestion of 40 mg oral oxprenolol.

b) **Patients with ischaemic heart disease**

The heart rate response during passive spectator viewing (Figs 37 and 38 Table 18) was similar to the normal subjects both after the ingestion of the placebo tablet and after 40 mg oral oxprenolol.

**Television viewing of Football Matches**

The television viewing soccer programme involved watching B.B.C.'s live transmission of national or international soccer matches. 40 mg oral oxprenolol was given after the first 30 minutes of the game.

a) **Normal Subjects**

Watching soccer matches during live television transmission was associated with conspicuous peaks of tachycardia (Figs 33 and 34). The suppression of the peaks of tachycardia could be seen 30 minutes after the ingestion of 40 mg oral oxprenolol (Fig. 36.)

Passive viewing of soccer matches was associated with a greater tachycardia than watching live television transmission.

b) **Patients with ischaemic heart disease**

The heart rate response during live television transmission was similar to the normal subjects before and after the ingestion of 40 mg oral oxprenolol (Figs 39 and 40).

These illustrations of the individual responses were consistent for all subjects studied whether normal or patients with known ischaemic heart disease. The response to 40 mg oral oxprenolol was equally consistent in all individuals in all situations.
TELEVISION VIEWING

Normal subjects and patients with ischaemic heart disease were shown videotaped films of a Drama, Comedy or Documentary on each of successive two evenings in randomized order during the normal viewing hours after 6.00 p.m. None of the subjects had seen the programme before, neither were they aware that these were videotaped series. One of the programmes was seen an hour after the ingestion of an oxprenolol matched placebo tablet and a similar programme of the same series was seen an hour after 40 mg oral oxprenolol; the order being randomly varied.

The Drama series consisted of an hour's viewing of the tragic and suspense ridden "Scales of Justice". The series were re-enactments of true crimes; of the trial that followed and of the passing of the sentence which was suspect in a lot of cases. The subjects reported feelings of anger, agitation and excitement throughout the performance.

The stimulus chosen for the Comedy series was the pleasant and charming comedy of "Doctor in the House". This was a series of 30 minutes of hilarious comedy depicting the mischief and the trials and tribulations of a group of hospital interns under a dominating consultant. There was much laughter and the subjects reported being very amused.

The Documentary series was a programme of 25 minutes on the
During watching the subjects reported anger and concern for the casualties of the war.

Resting heart rates were taken over 10 minutes prior to the start of the programme with the subject sitting quietly in a comfortable chair.

a) Normal Subjects (Figs 41, 42 and 43; Table 19).

Watching videotaped programmes of Drama, Comedy or Documentary on television during the normal viewing hours at 6.00 p.m. produced conspicuous peaks of tachycardia one hour after the ingestion of an oxprenolol matched placebo tablet. The least degree of tachycardia occurred while watching documentary programmes. 40 mg oral oxprenolol taken one hour before the programme suppressed the peaks of tachycardia and substantially lowered the cumulative heart rate.

Subjects sensitive to either thriller, horror or live boxing films monitored in their own homes exhibited high peaks of tachycardia one hour after the ingestion of placebo. Three of the four subjects became very tense and anxious, complained of palpitations and switched off their television sets. 40 mg oral oxprenolol taken one hour before a similar programme by the subjects suppressed the peaks of tachycardia and decreased the total cumulative heart rate (Figs. 44, 45 and 46).

b) Patients with ischaemic heart disease (Figs 47, 48 and 49; Table 20)

These subjects showed a similar heart rate response as the normal subjects. Some of the patients with angina pectoris
complained of retrosternal discomfort during exciting moments in the televised programmes after taking the placebo tablet. This sensation did not occur after taking 40 mg oral exprenolol one hour prior to the start of viewing.
RADIO AND TELEVISION COMMENTATORS
AND PERFORMERS

The emotional reactions of radio and television commentators reporting live sports events followed the natural swings in the excitement of the game. A greater degree of "emotional stress" was involved in a radio and television personality involved in the popular "Top of the Pops" teenage "pop" music show, shown on B.B.C. television on Thursday nights.

The heart rate response was studied one hour after taking an oxprenolol matched placebo tablet, and one hour after taking 40 mg oral oxprenolol before the start of the programme on separate occasions. The television personality study on the "pop" music show was repeated on another occasion without the ingestion of any tablets. Resting hearts were taken over 15 minutes an hour prior to the start of the programme.

Conspicuous tachycardia with high peak heart rates occurred throughout the commentary and performance of the radio and television personalities after the placebo tablet and also without the ingestion of any tablets in the "pop" music artist. This was accompanied with a high basal cumulative heart rate. One hour following the ingestion of 40 mg oral oxprenolol the tachycardia and peak heart rates were significantly reduced with a low basal cumulative heart rate. There was no apparent adverse effect on their individual performances. (Figs 50, 51 and 52; Table 21).
BUS DRIVERS

Long Distance Driving (Figs 53, 54 and 55, Table 22).

Experienced long distance bus drivers were studied during the summer when good weather conditions usually prevailed and the roads were congested with holiday traffic. These trips involved journeys of between 130 - 480 miles and the buses conveyed holiday makers to their respective destinations. Driving was confined predominantly to the towns with short motorway runs.

In order to obviate the effects of suggestion this study was done one hour after the taking of a placebo tablet. Oral exprenolol was not given to these drivers.

This is the record of almost continuous driving mainly confined to towns with short motorway runs. The pattern of heart rate changes in these experienced bus drivers is similar to that of motor car drivers in similar circumstances. Significant peaks of tachycardia are seen throughout the journey; especially through towns and during hazardous motorway and poor weather conditions.

City Driving (Figs 56, 57 and 58, Table 23).

This study was confined to drivers, experienced in driving in London, on their own familiar bus routes. The study was undertaken during the summer; traffic conditions in London are poor with overcrowded roads and pedestrian hazards. The heart rate response is shown by continuous tachycardia and high peak
rates, entirely correlated to the hazards of city driving, throughout the journey.
FIGURE 6

Records of the heart rate in a normal subject driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol
FIGURE 7

Record of the heart rate in a normal subject driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
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1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 8

Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
FIGURE 9

Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
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1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 10

Record of the heart rate during city driving in a normal subject before and after 40 mg oral oxprenolol.
FIGURE II

Record of the heart rate during city driving in a normal subject before and after 40 mg oral oxprenolol.
TABLE 7 HEART RATE RESPONSE OF NORMAL CITY DRIVERS AND ITS MODIFICATION BY ORAL OXPRENOLOL

| Subjects | Control Heart Rate \(^1\) per minute | Peak Heart Rate \(^2\) | Cumulative Heart Rate \(^3\) \\
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<td>SEM ±</td>
<td>±2</td>
<td>±2</td>
<td>±4</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test  
2. Values relate to the maximal heart rate during the trip  
3. The total heart rate over the journey.
FIGURE 12

Record of heart rate during city driving in a patient with ischaemic heart disease before and after 40 mg oral exprenolol.
FIGURE 13

Record of heart rate during city driving in a patient with ischaemic heart disease before and after 40 mg oral oxprenolol.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate&lt;sup&gt;1&lt;/sup&gt; per minute</th>
<th>Peak Heart Rate&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Cumulative Heart Rate&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>JR</td>
<td>70</td>
<td>65</td>
<td>130</td>
</tr>
<tr>
<td>LG</td>
<td>80</td>
<td>60</td>
<td>120</td>
</tr>
<tr>
<td>AS</td>
<td>70</td>
<td>60</td>
<td>120</td>
</tr>
<tr>
<td>SB</td>
<td>75</td>
<td>60</td>
<td>150</td>
</tr>
<tr>
<td>JM</td>
<td>80</td>
<td>70</td>
<td>120</td>
</tr>
<tr>
<td>DM</td>
<td>75</td>
<td>70</td>
<td>105</td>
</tr>
<tr>
<td>McCaa</td>
<td>75</td>
<td>70</td>
<td>125</td>
</tr>
<tr>
<td>GA</td>
<td>70</td>
<td>65</td>
<td>120</td>
</tr>
<tr>
<td>MEAN</td>
<td>74</td>
<td>65</td>
<td>124</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 1</td>
<td>± 2</td>
<td>± 5</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test.
2. Values relate to the maximal heart rate during the trip.
3. The total heart rate over the journey.
FIGURE 14

Record of the heart rate in a normal motor car passenger between Leeds and London during placebo and after 40 mg oral oxprenolol.
FIGURE 15

Record of heart rate in a normal motor-car passenger between Leeds and London during placebo and after 40 mg oral oxprenolol.
TABLE 9 HEART RATE RESPONSE OF NORMAL MOTOR CAR PASSENGERS DURING MOTORWAY DRIVING AND 
ITS MODIFICATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate $^1$</th>
<th>Peak Heart Rate $^2$</th>
<th>Cumulative Heart Rate $^3$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>SHT</td>
<td>70</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>HT</td>
<td>60</td>
<td>55</td>
<td>90</td>
</tr>
<tr>
<td>MKM</td>
<td>60</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>MP</td>
<td>80</td>
<td>60</td>
<td>110</td>
</tr>
<tr>
<td>PH</td>
<td>70</td>
<td>60</td>
<td>105</td>
</tr>
<tr>
<td>GAP</td>
<td>80</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>GHK</td>
<td>80</td>
<td>60</td>
<td>110</td>
</tr>
<tr>
<td>MEAN</td>
<td>71</td>
<td>59</td>
<td>99</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 3</td>
<td>± 1</td>
<td>± 4</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test.
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 16

Record of the heart rate in a passenger with ischaemic heart disease between Leeds and London, during placebo and after 40 mg oral oxprenolol.
FIGURE 17

Record of the heart rate in a passenger with ischaemic heart disease between Leeds and London during placebo and after 40 mg oral oxprenolol.
TABLE 10 HEART RATE RESPONSE OF PASSENGERS WITH ISCHAEMIC HEART DISEASE AND ITS MODIFICATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate</th>
<th>Peak Heart Rate</th>
<th>Cumulative Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>JR</td>
<td>80</td>
<td>65</td>
<td>120</td>
</tr>
<tr>
<td>LG</td>
<td>75</td>
<td>60</td>
<td>95</td>
</tr>
<tr>
<td>AS</td>
<td>75</td>
<td>70</td>
<td>90</td>
</tr>
<tr>
<td>SB</td>
<td>70</td>
<td>60</td>
<td>120</td>
</tr>
<tr>
<td>JM</td>
<td>70</td>
<td>65</td>
<td>90</td>
</tr>
<tr>
<td>SD</td>
<td>80</td>
<td>60</td>
<td>135</td>
</tr>
<tr>
<td>MEAN</td>
<td>75</td>
<td>63</td>
<td>108</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 2</td>
<td>± 2</td>
<td>± 8</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 18

Record of the heart rate in a normal subject travelling by rail between Leeds and London before and after 40 mg oral oxprenolol.
Record of the heart rate in a normal subject travelling by rail between Leeds and London before and after 40 mg oral oxprenolol.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3 Total Heart Rate</th>
<th>Heart Rate per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
<td>Oxprenolol</td>
</tr>
<tr>
<td>SHT</td>
<td>75</td>
<td>60</td>
<td>95</td>
<td>80</td>
</tr>
<tr>
<td>MKM</td>
<td>50</td>
<td>45</td>
<td>60</td>
<td>50</td>
</tr>
<tr>
<td>MP</td>
<td>70</td>
<td>65</td>
<td>80</td>
<td>70</td>
</tr>
<tr>
<td>AF</td>
<td>65</td>
<td>60</td>
<td>90</td>
<td>70</td>
</tr>
<tr>
<td>PH</td>
<td>75</td>
<td>60</td>
<td>90</td>
<td>70</td>
</tr>
<tr>
<td>GAP</td>
<td>65</td>
<td>60</td>
<td>65</td>
<td>60</td>
</tr>
<tr>
<td>MEAN</td>
<td>67</td>
<td>58</td>
<td>80</td>
<td>67</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 4</td>
<td>± 3</td>
<td>± 6</td>
<td>± 4</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
Record of the heart rate in a subject with ischaemic heart disease travelling by rail between Leeds and London during placebo and after 40 mg oral oxprenolol.

FIGURE 20
FIGURE 21

Record of the heart rate in a subject with ischaemic heart disease travelling by rail between Leeds and London during placebo and after 40 mg oral oxprenolol.
TABLE 12 HEART RATE RESPONSE OF PATIENTS WITH ISCHAEMIC HEART DISEASE DURING RAIL TRAVEL AND ITS MODIFICATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate per minute</th>
<th>Peak Heart Rate</th>
<th>Cumulative Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxrenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>JR</td>
<td>75</td>
<td>65</td>
<td>90</td>
</tr>
<tr>
<td>LG</td>
<td>70</td>
<td>70</td>
<td>85</td>
</tr>
<tr>
<td>JM</td>
<td>75</td>
<td>65</td>
<td>80</td>
</tr>
<tr>
<td>JB</td>
<td>70</td>
<td>60</td>
<td>85</td>
</tr>
<tr>
<td>DM</td>
<td>70</td>
<td>65</td>
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</tr>
<tr>
<td>GA</td>
<td>72</td>
<td>60</td>
<td>80</td>
</tr>
<tr>
<td>MEAN</td>
<td>72</td>
<td>64</td>
<td>84</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 1</td>
<td>± 4</td>
<td>± 2</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 22

Record of the heart rate in a patient with ischaemic heart disease travelling by turbopropeller aircraft between Leeds and London during placebo on both the outward and return journeys.
FIGURE 23

Record of the heart rate in a normal subject travelling by passenger turbo-propeller aircraft between Leeds and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
FIGURE 24

Record of the heart rate in a normal subject travelling by passenger turbo-propeller aircraft between Leeds and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
### TABLE 13 HEART RATE RESPONSE OF NORMAL TURBO-PROPELLER AIR-FLIGHT PASSENGERS AND ITS MODIFICATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate</th>
<th>Peak Heart Rate</th>
<th>Cumulative Heart Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>per minute</td>
<td></td>
<td>Total Heart Rate</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>SHT</td>
<td>70</td>
<td>60</td>
<td>140</td>
</tr>
<tr>
<td>MKM</td>
<td>60</td>
<td>50</td>
<td>150</td>
</tr>
<tr>
<td>MP</td>
<td>70</td>
<td>60</td>
<td>150</td>
</tr>
<tr>
<td>AF</td>
<td>75</td>
<td>60</td>
<td>115</td>
</tr>
<tr>
<td>PH</td>
<td>60</td>
<td>50</td>
<td>100</td>
</tr>
<tr>
<td>GAP</td>
<td>75</td>
<td>60</td>
<td>130</td>
</tr>
<tr>
<td>MEAN</td>
<td>68</td>
<td>57</td>
<td>131</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 3</td>
<td>± 2</td>
<td>± 3</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 25

Record of the heart rate in a patient with ischaemic heart disease travelling by turbo-propeller aircraft between Leeds and London during placebo and one hour after 40 mg oral oxprenolol.
FIGURE 26

Record of the heart rate in a patient with ischaemic heart disease travelling by turbo-propeller aircraft between Leeds and London during placebo and one hour after 40 mg oral oxprenolol.
**TABLE 14** HEART RATE RESPONSE OF PATIENTS WITH ISCHAEMIC HEART DISEASE TRAVELLING BY TURBO-PROPELLER AIRCRAFT AND ITS MODIFICATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3 Total Heart Rate Heart Rate per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>JR</td>
<td>70</td>
<td>55</td>
<td>100</td>
</tr>
<tr>
<td>LG</td>
<td>75</td>
<td>60</td>
<td>120</td>
</tr>
<tr>
<td>JM</td>
<td>75</td>
<td>70</td>
<td>120</td>
</tr>
<tr>
<td>McCaa</td>
<td>75</td>
<td>60</td>
<td>140</td>
</tr>
<tr>
<td>GA</td>
<td>70</td>
<td>65</td>
<td>125</td>
</tr>
<tr>
<td>MEAN</td>
<td>73</td>
<td>62</td>
<td>126</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 1</td>
<td>± 2</td>
<td>± 7</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 27

Record of the heart rate in a normal subject travelling by jet aircraft between Newcastle and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
FIGURE 28

Record of the heart rate in a normal subject travelling by jet aircraft between Newcastle and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
# Table 15: Heart Rate Response of Normal Jet Air Flight Passengers and Its Modification by Oral Oxprenolol

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate per minute</th>
<th>Peak Heart Rate</th>
<th>Cumulative Heart Rate Total Heart Rate Heart Rate per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>SHT</td>
<td>70</td>
<td>65</td>
<td>110</td>
</tr>
<tr>
<td>MKM</td>
<td>60</td>
<td>50</td>
<td>90</td>
</tr>
<tr>
<td>PH</td>
<td>75</td>
<td>65</td>
<td>100</td>
</tr>
<tr>
<td>GAP</td>
<td>75</td>
<td>65</td>
<td>115</td>
</tr>
<tr>
<td>MEAN</td>
<td>70</td>
<td>61</td>
<td>104</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±4</td>
<td>±4</td>
<td>±6</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
Record of the heart rate in a patient with ischaemic heart disease travelling by jet aircraft between Newcastle and London during placebo and one hour after 40 mg oral oxprenolol.
FIGURE 30

Record of the heart rate in a patient with ischaemic heart disease travelling by jet aircraft between Newcastle and London during placebo and one hour after 40 mg oral oxprenolol.
TABLE 16 HEART RATE RESPONSE OF PATIENTS WITH ISCHAEMIC HEART DISEASE TRAVELLING BY JET AIRCRAFT AND ITS MODULATION BY ORAL OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>JR</td>
<td>70</td>
<td>65</td>
<td>115</td>
</tr>
<tr>
<td>LC</td>
<td>75</td>
<td>70</td>
<td>100</td>
</tr>
<tr>
<td>JM</td>
<td>70</td>
<td>60</td>
<td>119</td>
</tr>
<tr>
<td>GA</td>
<td>60</td>
<td>55</td>
<td>90</td>
</tr>
<tr>
<td>MEAN</td>
<td>69</td>
<td>63</td>
<td>104</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±3</td>
<td>±3</td>
<td>±6</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to the maximal heart rate during the trip
3. The total heart rate over the journey.
FIGURE 31

Record of the heart rate in a normal subject watching a soccer match after the ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 32

Record of the heart rate in a normal subject watching a soccer match after the ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 33

Record of the heart rate in a normal subject watching a televised live football match and the effect of 40 mg oral oxprenolol.
FIGURE 34

Record of the heart rate in a normal subject watching a televised live football match and the effect of 40 mg oral oxprenolol.
FIGURE 35

Record of the heart rate in a normal subject watching a soccer match and its modification produced by 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 36

Record of the heart rate in a normal subject watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>SHT</td>
<td>75</td>
<td>60</td>
<td>115</td>
</tr>
<tr>
<td>MKM</td>
<td>80</td>
<td>70</td>
<td>130</td>
</tr>
<tr>
<td>MP</td>
<td>80</td>
<td>70</td>
<td>120</td>
</tr>
<tr>
<td>PH</td>
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<td>105</td>
</tr>
<tr>
<td>CNR</td>
<td>75</td>
<td>60</td>
<td>125</td>
</tr>
<tr>
<td>GAP</td>
<td>80</td>
<td>70</td>
<td>130</td>
</tr>
<tr>
<td>GHK</td>
<td>70</td>
<td>65</td>
<td>110</td>
</tr>
<tr>
<td>MEAN</td>
<td>77</td>
<td>67</td>
<td>119</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±1</td>
<td>±2</td>
<td>±4</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting quietly 30 minutes before the match.
2. Values relate to maximal heart rate during the match.
3. Total heart rate during the match.
FIGURE 37

Record of the heart rate in a patient with ischaemic heart disease watching a soccer match and the modulation of the response by 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 38

Record of the heart rate in a patient with ischaemic heart disease watching a soccer match and the modulation of the response by 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 39

Record of the heart rate in a patient with ischaemic heart disease watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 40

Record of the heart rate in a patient with ischaemic heart disease watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2 per minute</th>
<th>Cumulative Heart Rate 3 Total Heart Rate</th>
<th>Heart Rate per minute</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
<td>Oxprenolol</td>
</tr>
<tr>
<td>JR</td>
<td>70</td>
<td>65</td>
<td>120</td>
<td>75</td>
</tr>
<tr>
<td>LG</td>
<td>80</td>
<td>70</td>
<td>125</td>
<td>95</td>
</tr>
<tr>
<td>JM</td>
<td>75</td>
<td>60</td>
<td>90</td>
<td>60</td>
</tr>
<tr>
<td>SD</td>
<td>70</td>
<td>60</td>
<td>120</td>
<td>70</td>
</tr>
<tr>
<td>DM</td>
<td>80</td>
<td>70</td>
<td>130</td>
<td>80</td>
</tr>
<tr>
<td>McCaa</td>
<td>75</td>
<td>65</td>
<td>140</td>
<td>85</td>
</tr>
<tr>
<td>GA</td>
<td>75</td>
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<td>120</td>
<td>80</td>
</tr>
<tr>
<td>MEAN</td>
<td>75</td>
<td>64</td>
<td>121</td>
<td>78</td>
</tr>
<tr>
<td>SEM ±</td>
<td>± 2</td>
<td>± 2</td>
<td>± 6</td>
<td>± 4</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting quietly 30 minutes before the match
2. Values relate to maximal heart rate during the match.
3. Total heart rate during the match.
FIGURE 41

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 42

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 43

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
Record of the heart rate in a sensitive subject watching a mystery television film and the modulation of the response by 40 mg oral oxprenolol taken one hour before a similar programme.
Record of heart rate in a sensitive subject watching a horror television film after 40 mg oral oxprenolol.

FIGURE 45
FIGURE 46

Record of the heart rate in a sensitive subject watching a televised live boxing match, after 40 mg oral oxprenolol.
## TABLE 19

**HEART RATE RESPONSE OF NORMAL SUBJECTS TO TELEVISION VIEWING AND ITS MODIFICATION BY OXPRENOLOL**

<table>
<thead>
<tr>
<th>Subjects</th>
<th>CONTROL HEART RATE 1 PER MINUTE</th>
<th>PEAK HEART RATE 2</th>
<th>CUMULATIVE HEART RATE 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drama (60 min)</td>
<td>Comedy (30 min)</td>
<td>Documentary (25 min)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>O</td>
<td>P</td>
</tr>
<tr>
<td>MKM</td>
<td>60</td>
<td>55</td>
<td>60</td>
</tr>
<tr>
<td>MP</td>
<td>72</td>
<td>65</td>
<td>72</td>
</tr>
<tr>
<td>AF</td>
<td>80</td>
<td>75</td>
<td>80</td>
</tr>
<tr>
<td>PH</td>
<td>70</td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>GAP</td>
<td>82</td>
<td>65</td>
<td>82</td>
</tr>
<tr>
<td>GHK</td>
<td>84</td>
<td>70</td>
<td>80</td>
</tr>
<tr>
<td>MEAN</td>
<td>76</td>
<td>65</td>
<td>75</td>
</tr>
<tr>
<td>SEM ±</td>
<td>+4</td>
<td>±3</td>
<td>±3</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test.
2. Values relate to maximal heart rate during television viewing.
3. Total heart rate during television viewing.

P - Placebo
O - Oxprenolol
Record of the heart rate in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
Record of the heart rate in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.

FIGURE 48
FIGURE 48

Record of the heart rate in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>CONTROL HEART RATE (^1) PER MINUTE</th>
<th>PEAK HEART RATE (^2)</th>
<th>CUMULATIVE HEART RATE (^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Drama (60 min)</td>
<td>Comedy (30 min)</td>
<td>Documentary (25 min)</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>O</td>
<td>P</td>
</tr>
<tr>
<td>JR</td>
<td>70</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>AS</td>
<td>80</td>
<td>65</td>
<td>76</td>
</tr>
<tr>
<td>SB</td>
<td>70</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>JM</td>
<td>70</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>SD</td>
<td>72</td>
<td>65</td>
<td>70</td>
</tr>
<tr>
<td>JB</td>
<td>72</td>
<td>60</td>
<td>70</td>
</tr>
<tr>
<td>DM</td>
<td>74</td>
<td>66</td>
<td>74</td>
</tr>
<tr>
<td>GA</td>
<td>75</td>
<td>60</td>
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</tr>
<tr>
<td>MEAN</td>
<td>73</td>
<td>62</td>
<td>72</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±1</td>
<td>±1</td>
<td>±1</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before test
2. Values relate to maximal heart rate during television viewing
3. Total heart rate during television viewing.

P - Placebo
O - Oxprenolol
FIGURE 50

Record of heart rate of a radio and television commentator during a live football match and the modification of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 51

Record of heart rate in a radio and television personality during a "pop" music show after ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar show.
FIGURE 52

Record of heart rate in the radio and television "pop" personality during a show without the ingestion of any tablets.
TABLE 21 HEART RATE RESPONSE OF RADIO AND TELEVISION COMMENTATORS AND PERFORMERS
AND ITS MODIFICATION BY OXPRENOLOL

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
<td>Oxprenolol</td>
<td>Placebo</td>
</tr>
<tr>
<td>B.D.</td>
<td>80</td>
<td>60</td>
<td>150</td>
</tr>
<tr>
<td>J.S.</td>
<td>76</td>
<td>60</td>
<td>160</td>
</tr>
<tr>
<td>&quot;pop&quot; artist</td>
<td>(65)*</td>
<td>(160)*</td>
<td></td>
</tr>
</tbody>
</table>

* Denotes heart rate response without ingestion of any tablets.

1. Heart rate during control period sitting still for 30 minutes before broadcasting/performance.
2. Values relate to maximal heart rate during broadcasting/performance.
3. Total heart rate during broadcasting/performance.
LONG DISTANCE BUS DRIVING

FIGURE 53
Record of heart rate during long distance bus driving.
FIGURE 54

Record of heart rate during long distance bus driving.
LONG DISTANCE BUS DRIVING

EXCURSION BUS DRIVER
480 MILES

FIGURE 55
Record of heart rate during long distance bus driving.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Control Heart Rate per minute</th>
<th>Peak Heart Rate</th>
<th>Cumulative Heart Rate</th>
<th>Increment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total Heart Rate</td>
<td>-HR/min</td>
</tr>
<tr>
<td>JB</td>
<td>78</td>
<td>150</td>
<td>64200 (600 mins)</td>
<td>107</td>
</tr>
<tr>
<td>JC</td>
<td>80</td>
<td>145</td>
<td>57643 (600 mins)</td>
<td>96</td>
</tr>
<tr>
<td>PJ</td>
<td>74</td>
<td>140</td>
<td>57893 (600 mins)</td>
<td>96</td>
</tr>
<tr>
<td>BC</td>
<td>68</td>
<td>150</td>
<td>48960 (480 mins)</td>
<td>102</td>
</tr>
<tr>
<td>BB</td>
<td>78</td>
<td>140</td>
<td>45450 (480 mins)</td>
<td>95</td>
</tr>
<tr>
<td>HS</td>
<td>80</td>
<td>150</td>
<td>53260 (600 mins)</td>
<td>89</td>
</tr>
<tr>
<td>SW</td>
<td>82</td>
<td>145</td>
<td>48800 (540 mins)</td>
<td>90</td>
</tr>
<tr>
<td>JS</td>
<td>72</td>
<td>155</td>
<td>62846 (600 mins)</td>
<td>105</td>
</tr>
<tr>
<td>HS</td>
<td>76</td>
<td>130</td>
<td>2428 (240 mins)</td>
<td>100</td>
</tr>
<tr>
<td>JB</td>
<td>78</td>
<td>130</td>
<td>9720 (90 mins)</td>
<td>108</td>
</tr>
<tr>
<td>HS</td>
<td>82</td>
<td>145</td>
<td>31600 (300 mins)</td>
<td>105</td>
</tr>
<tr>
<td>JCC</td>
<td>80</td>
<td>140</td>
<td>29586 (300 mins)</td>
<td>99</td>
</tr>
<tr>
<td>SW</td>
<td>80</td>
<td>120</td>
<td>11520 (120 mins)</td>
<td>96</td>
</tr>
<tr>
<td>MEAN</td>
<td>77</td>
<td>140</td>
<td>99</td>
<td>20</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±1</td>
<td>±3</td>
<td>±2</td>
<td></td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before start of journey.
2. Values relate to maximal heart rate during journey.
3. Total heart rate during trip.
4. Percentage heart rate increment over control value during journey.
FIGURE 56

Record of heart rate during bus-driving in London.
LONDON BUS DRIVING

FIGURE 57

Record of heart rate during bus-driving in London.
Record of heart rate during bus-driving in London.
<table>
<thead>
<tr>
<th></th>
<th>Control Heart Rate 1 per minute</th>
<th>Peak Heart Rate 2</th>
<th>Cumulative Heart Rate 3</th>
<th>Increment 4</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total Heart Rate</td>
<td>HR/min</td>
</tr>
<tr>
<td>DP</td>
<td>80</td>
<td>140</td>
<td>11760 (120 mins)</td>
<td>98</td>
</tr>
<tr>
<td>TML</td>
<td>76</td>
<td>130</td>
<td>12780 (120 mins)</td>
<td>107</td>
</tr>
<tr>
<td>MJ</td>
<td>75</td>
<td>120</td>
<td>13240 (120 mins)</td>
<td>110</td>
</tr>
<tr>
<td>AC</td>
<td>74</td>
<td>140</td>
<td>14720 (120 mins)</td>
<td>123</td>
</tr>
<tr>
<td>AW</td>
<td>78</td>
<td>140</td>
<td>10200 (90 mins)</td>
<td>113</td>
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<tr>
<td>JS</td>
<td>70</td>
<td>130</td>
<td>9360 (90 mins)</td>
<td>104</td>
</tr>
<tr>
<td>MEAN</td>
<td>76</td>
<td>133</td>
<td>12010</td>
<td>109</td>
</tr>
<tr>
<td>SEM ±</td>
<td>±1</td>
<td>±3</td>
<td>±3</td>
<td>±2</td>
</tr>
</tbody>
</table>

1. Heart rate during control period sitting still before start of journey.
2. Values relate to maximal heart rate during journey.
3. Total heart rate during trip.
4. Percentage heart rate increment over control value during journey.
SUMMARY OF RESULTS

The following conclusions can be drawn from these studies:

1) A number of everyday environmental situations were associated with a substantial increase in heart rate, i.e. motor-car and bus driving on a motorway and in city traffic, motor-car, rail and aircraft passenger, live and television viewing of soccer matches, television viewing of comedy, drama and documentary films, and radio and television commentators and performers.

2) These peaks of tachycardia were conspicuously reduced for up to 12 hours by 40 mg oral oxprenolol.

3) The peaks of tachycardia observed during motor-car driving were similarly suppressed by the same degree of beta-blockade as that resulting from the infusion of catecholamines.

4) None of the subjects noticed any appreciable effect on mental performance or any detectable change in their everyday skills after oxprenolol.
DISCUSSION

The discussion is arranged under the following headings:

1. CRITIQUE of Method.
2. INTERPRETATION of the Results
3. CONCLUSIONS
CRITIQUE OF METHOD

In order that these studies may be placed in proper clinical perspective, it is important that their design and execution are critically examined. They may be criticised from the following viewpoints:

1) It may be argued that in the absence of a double-blind study the interpretation of the effects of oxprenolol is less valid. However, as was discussed in Study 1 a completely double-blind study undertaken during the stress of city motor driving showed that 40 mg oral oxprenolol conspicuously modified the peaks of tachycardia for up to 12 hours. It is impossible to hide the marked reductions in heart rate to a trained observer; only continuous blind E.C.G. recording would have answered the problem and this was impractical both technically and economically at the time. However, in the other more extensive single blind studies, the responses were measured objectively and were similar in all subjects, confirming their validity.

2) Ideally in the study of environmental stress on the heart, E.C.G. recordings over 24 hours and over several days is mandatory and would allow far more detailed study of the sympathetic stimulation of the heart. Unfortunately, during the time of this study, no such recording apparatus was available.

3. The heart rate response recorded may have not been solely psychologically induced by in part the results of unnoticed
physical exertion. This criticism could be answered by the fact that the tachycardia response of the heart to psychologically induced stress (motor-car driving) and to the infusion of catecholamines was largely suppressed for up to 12 hours following 40 mg oral oxprenolol; the tachycardia induced by exercise in the same subjects was much less affected by the drug both in magnitude and duration (Study 1). Similar small doses of propranolol have also been shown to have relatively little effect on the tachycardia associated with isometric contraction of skeletal muscles, such as might be expected in gripping the arms of a chair (McDonald et al, 1966). Therefore the major portion of the tachycardia observed in these situations is a reaction to psychological stress and unassociated with significant physical exertion.

4) It could be argued that this pilot study consisted of a small number of male subjects. There is no reason to believe that the heart rate response to stress or its modulation by sympathetic antagonists is different in female subjects. Moreover, the environmental stresses studied were those frequently experienced by the same patients and subjects; all were studied during their normal everyday activities and none were subject to abnormal situations as many of the previous studies in the literature. Against this it
could be argued that because of extreme individual variations in the heart rate response to environmental stress, this pilot study should be extended to incorporate a larger cross-section of the population.

5) There is a valid argument that the whole spectrum of environmental stress on the heart should be studied; this was by necessity a limited survey. It was not possible in such a pilot study to measure effects of all situations in everyday life. The situations chosen were thought to be the most stressful in the everyday life situation.

6) Anxiety is accompanied not only by an increase in heart rate but perhaps also by an increase in cardiac output and the systemic arterial pressure. Changes other than heart rate were not measured as they were precluded by the design of the study. Even the taking of the blood pressure by the cuff method besides being unreliable would have caused some further anxiety under the circumstances of study. All methods of measurement of cardiac output involve procedures that can reasonably be expected to result in additional mental stress. Therefore, although the measurement of heart rate alone limits the interpretation of these results, at least the non-invasive methods used were innocuous in this respect.

**INTERPRETATIONS OF THE RESULTS**

Accepting the validity of the foregoing criticisms of the methods used the results of the present studies are clear-cut.

Many forms of everyday travel were consistently associated with
conspicuous peaks in heart rate. In this respect motor-car, bus
driving and air travel were associated with greater tachycardia than motor
car travel as a passenger; rail travel was by far the least disturbing.
High peaks in heart rate were found on television viewing of drama and comedy
films than during documentary programmes. Similar responses were seen
in live radio and television commentators. There was no apparent
difference between the responses in normal subjects and patients with proven
ischaemic heart disease. The tachycardia found during these situations
was conspicuously suppressed by 40 mg oral oxprenolol in all subjects. The
rapidity of action of the drug was illustrated by observations during
spectator viewing whilst the exciting stimuli was maintained; the heart
rate increase was abolished within thirty minutes of its ingestion. The
modulation of stress-induced tachycardia by this dose of drug was
maintained for up to 12 hours.

**Cardiac Work during Mental Stress**

What do these repetitive increases in cardiac sympathetic activity
mean in terms of increase in cardiac work?

There is little doubt that increases in heart rate are directly responsible
for substantial increments in myocardial oxygen consumption (Yeo, 1885;
Evans and Matsuoka, 1915; Laurent et al, 1956; Van Citters et al, 1957;
Maxwell et al, 1958; Mitchell et al, 1963; Van der Veen and Willebrands
1967; Boerth et al, 1969). But there are few comprehensive circulatory
studies of the overall haemodynamic consequences of emotionally induced
stress. Anxiety in subjects undergoing circulatory investigation has been
shown to be accompanied by increases in heart rate, cardiac output and
systemic arterial pressure (Grollman, 1928; Stead et al, 1945; Hickman
et al, 1948; Stevenson et al, 1949). These changes are increased by any
further psychological stress, such as forced mental arithmetic (Brod et al., 1959). The tachycardia, increase in cardiac output and blood pressure are accompanied by vasoconstriction in the skin and renal circulation (Brod et al., 1954; French et al., 1959) and by metabolically independent vasodilatation in muscle (Blair et al., 1959; Barcroft et al., 1960; Brod et al., 1962). These circulatory changes observed during stress imply substantial increases in left ventricular work. It must also be pointed out that the cardiac changes measured in these studies were in response to relatively mild stressful conditions which may give some indication of the extent and magnitude of the circulatory changes that may result from more stressful situations.

The heart rate is one of the predominant variables related to the production of symptoms of myocardial ischaemia in patients with coronary heart disease (Robinson, 1971; Taylor, 1973), and is probably of more importance in this respect than changes in systemic arterial pressure (Sharma et al., 1973).

A further factor that must be taken into account in this respect is that in the majority of circumstances in which such measurements were made, the tachycardia associated with psychologically induced stress was accompanied by a high concentration of plasma catecholamines, particularly nor-adrenaline (Taggart et al., 1969; Taggart and Carruthers, 1971) or by their increased urinary secretion (Bogdonoff et al., 1960). It is perhaps relevant in this respect to point out that catecholamines appear to increase myocardial oxygen consumption over and above that purely related to their positive chronotropic and inotropic effects (Raab et al., 1962). Thus, there would appear to be no reasonable doubt that
stress induced by emotional or psychological factors results in substantial increases in cardiac work; these increases are probably underestimated by the use of the heart rate index alone. The peaks of tachycardia observed in these studies were of a similar order to those known to be associated with the production of myocardial ischaemia in patients in whom the coronary arterial blood supply is limited. Yet these were associated with normal everyday conditions of living. Whilst the effects of such increases in heart rate may be borne with impunity by the heart with normal arterial supply, it can be expected with reasonable confidence that the heart limited by coronary arterial disease will outstrip its available blood supply at these rates. In fact, this is the basis of the diagnostic atrial pacing test for the precipitation of angina pectoris. Furthermore, these heart rates imply very considerable sympathetic stimulation of the heart. The resulting direct increase in myocardial contractility can be expected to result in an increase in myocardial oxygen consumption considerably greater than that directly due to the increased rate alone. This is the clinical basis for the provocative isoprenaline infusion test for ischaemic heart disease. (Wexler et al, 1971).

Pathophysiological effects of Stress on the Heart

Are such increases in cardiac work immediately hazardous to the heart?

There are no haemodynamic studies which would suggest that the stress induced in subjects under cardiac investigation are associated
with impairment of left ventricular function; no direct measurements of left ventricular activity during emotional stress appear to have been made. The catheter studies of Hickman et al, 1948 can be used as a guide; anxiety induced in five "normal" subjects was not accompanied by any abnormal increase in pulmonary artery pressure. But there was a rise of 12 mm Hg in the mean pulmonary artery pressure without change in the cardiac output (2.2 4 min/sq.m) in a patient in congestive heart failure during induced anxiety. Although changes in pulmonary artery pressure are at best an insensitive indicator of changes in left ventricular filling pressure, directional changes in both pressures are similar (Bakon et al, 1972). Thus it is possible that mental anxiety may adversely affect the pumping function of the failing or ischaemic heart.

The heart rate peaks repeatedly seen during these everyday stressful activities can with reasonable confidence, be expected to precipitate a state of myocardial ischaemia in many patients with obstructive coronary artery disease.

Of more definite relevance to my studies are the studies of electrocardiographic changes in subjects during induced psychological stress. The evidence that the type of stressful situation under consideration in this thesis induced pathological changes in the electrocardiogram of "normal" subjects is difficult to evaluate. Electrocardiographic changes suggestive of myocardial ischaemia have been reported in association with the tachycardia induced by fear.
Mainze and Krause (1940) described electrocardiographic changes suggestive of myocardial ischaemia in 16 of 25 patients without other evidence of ischaemic heart disease and 8 of 12 patients with definite evidence of such disease during the anxiety immediately before surgical operations; the changes disappeared after induction of anaesthesia. A number of reports have also described electrocardiographic changes during spontaneous anxiety states in otherwise normal patients (Loftus et al., 1946; Heyer et al., 1947; Magendantz and Shortsleeve, 1951) and during anxiety induced by cardiovascular investigations (Stevenson et al., 1949). Even more relevant to my study was the demonstration of a close association between the heart rate and electrocardiographic ischaemic changes during motor car driving. Hoffman (1965) in an extensive study of 600 healthy male drivers and 26 drivers with coronary artery disease, claimed to have demonstrated no "pathological" electrocardiographic changes in healthy drivers as compared to changes in 12 per cent in subjects with coronary heart disease driving in low traffic densities. In city driving, with high traffic density "pathological" changes occurred in 16 per cent of healthy drivers and 46 per cent of drivers with coronary disease. Unfortunately, the clinical categorization of the patients studied, the exact definition of electrocardiographic evidence of abnormality and the observer variation in interpretation of the electrocardiographic findings was not given. Simonson and his colleagues (1968) described "T-wave changes" during long distance motor car driving in five
healthy males aged 26 – 77 years with normal post-exercise electrocardiograms. However, "T-wave changes" are not pathognomonic of myocardial "hypoxia" although they have been observed during infusion of adrenaline (Mitchell and Shapiro, 1954; Lepeschkin et al, 1960) and it has been claimed that such changes are a reflection of subendocardial ischaemia (Sodi Polares et al, 1971) there is no categoric evidence of this supposition particularly in the presence of high heart rates. Bellet and his co-markers (1968) reported that no significant changes were noticed in the electrocardiogram recorded continuously in 65 normal subjects during a period of two and a half hours driving in "favourable conditions". In similarly easy driving conditions electrocardiographic changes probably significant of myocardial ischaemia, e.g. S-T segment depression multifocal premature contractions, ventricular bigeminal or trigeminal rhythm, were observed in 11 of 66 patients with known coronary heart disease. More recently Taggart et al (1969) reported a close association between the heart rate and electrocardiographic ischaemic changes during motor car driving in dense commuter traffic in 13 of 24 patients with ischaemic heart disease and 3 of 32 normal subjects. Furthermore, it should not be ignored that it is common clinical experience that many patients with established ischaemic heart disease suffer typical anginal symptoms during the stress of motor car driving, during the excitement of live football matches, watching exciting television programmes or viewing mystery films.
Despite the variability in observer recognition and oral interpretation of electrocardiographic changes, certain conclusions can be drawn from these and my studies. Although the increase in cardiac sympathetic stimulation associated with extremely stressful situations may give rise to myocardial ischaemia even in the normal heart, there is no conclusive evidence that this results from everyday emotional stimuli. However, in patients with coronary heart disease, even such common everyday tasks such as motor car or bus driving may precipitate myocardial ischaemia, and it is of relevant interest that similar symptomatic and electrocardiographic changes may be produced in such patients by raising the heart rate to similar levels by the infusion of catecholamines (Wexler et al, 1971).

This evidence, together with that of the foregoing, suggests that while the everyday psychological stresses met in modern urban existence probably have no immediately deleterious effects on the normal heart, there is reasonable evidence that they result in myocardial ischaemia in subjects with coronary artery disease.

There was a conspicuous suppression of the tachycardia associated with stressful situations in all subjects after 40 mg oral oxprenolol. Both studies confirm this conclusion.

Study I suggests the similarity in the magnitude and duration of the stress and isoprenaline tachycardia to the same degree of beta-receptor antagonism suggests that the heart rate response to both stimuli may be due to the same mechanism, namely stimulation of
the cardiac beta-receptors by circulating catecholamines. Although such a supposition should be susceptible to direct proof by the measurements of circulating catecholamines the practical and technical difficulties in making such measurements precludes their valid use at the present time. The quite different pattern of response of exercise tachycardia to the same degree of beta-receptor blockade would suggest that a difference mechanism is responsible for heart rate response to exertion. This differential effect of beta-receptor antagonism on the cardiac response to psychological stress and exercise has also been observed in other situations. Eliašch et al., (1967) observed that propranolol inhibited the heart rate increase during simulated flight in pilots but had much less effect on the tachycardia of exercise. Imhoff and his colleagues (1969) found similar differential effects of oxprenolol on the tachycardia associated with pre-jump anxiety and that associated with the physical exertion of ski-jumping. The response of the heart rate to exercise in this range of exertion is preponderantly due to vagal withdrawal (Donald and Shepherd, 1963; Robinson, 1966). Thus the small doses of oral oxprenolol that completely suppressed catecholamine or stress induced tachycardia had relatively little effect on exercise performance of the heart. Thus the effects on the heart of such environmental stresses as were studied in the present investigation may be largely suppressed with doses of beta-receptor antagonists that could be expected to have little noticeable effect on patients' exercise.
capability during normal everyday life.

The Effect of Emotional Stress on the Course of Established Ischaemic Heart Disease

Do these responses aggravate the course of established ischaemic heart disease? The factors associated with the progression of established coronary heart disease are unknown. There is, at present, no evidence that the frequency of emotionally induced or exercise induced myocardial ischaemia has any bearing on the natural history of the disease. But as the pain sometimes associated with ischaemic heart disease is often accompanied by enzyme changes in the peripheral blood probably indicative of myocardial cell death, and as the majority of patients dying from ischaemic heart disease usually exhibit widespread myocardial fibrosis, there is every reason to suppose that recurrent attacks of myocardial ischaemia, however induced, are deleterious in the long term. Even more speculative is the association between these circulatory responses and the 'sudden death' associated with coronary artery disease. In an autopsy study of the causes of sudden natural death in motor car drivers, Peterson and Petty (1962) found the large majority of deaths to be associated with severe coronary heart disease or actual myocardial infarction. Chiang and his colleagues (1969) found distinct correlation between the prevalence of ventricular premature contractions, coronary artery disease and sudden death. It is of interest that extrasystoles are commonly noted in anxiety states, are frequently precipitated by
catecholamine infusions (Lapeschkin et al, 1960) and have been noticed during motor car driving (Taggart et al, 1969). Although this evidence relating mental stress, its effects on the heart and sudden death is speculative, it is based on reasonable logic. Fortunately, the beta-receptor antagonists provide a socially acceptable medical tool for putting this important thesis to the test.

The Relationship between Mental Stress and Precocious Coronary Heart Disease

Despite many speculative hypotheses and assertions (Wolff, 1950; Morris and Crawford, 1958; Carruthers, 1969), there is, as yet, no acceptable evidence that stress and coronary heart disease are casually related. A number of studies on bus drivers, train drivers, aircraft pilots and subjects in sedentary occupations have all claimed a connection between occupation and an increased incidence of ischaemic heart disease. But the validity of these conclusions is in serious doubt due to two main factors: the personal characteristics of the subjects in each occupational group and the basis on which the clinical diagnosis of coronary heart disease was made. These problems are highlighted by the early studies of Morris and his colleagues (1953). These authors concluded that there was an increased incidence of "coronary heart disease" in London bus drivers as compared to bus conductors. But the clinical diagnoses were "obtained from general practitioners" and "hospital certificates" or from medical officers' reports of examinations carried out 28 days or more after the illness.
The quality of such information, presumably much of it subjective, is unacceptable for the present day diagnosis of ischaemic heart disease. Later it was reported that at the time of taking up their occupation, the bus drivers were already considerably fatter men than the conductors (Morris et al., 1956). It may be that the recurrently high heart rate of bus drivers does indeed predispose them to coronary heart disease, but there is no convincing evidence of such a relationship. A similar argument may be levelled at the claim that stress on telephonists predisposes them to precocious coronary heart disease as compared to postmen (Morris et al., 1953). However, although such critical reasoning is essential if such findings are to be placed in proper clinical and social perspective, it is equally important that the potential value of such studies in the evaluation of the effects of urbanized living on the heart is not ignored.

Although the demonstration of such a relationship does not necessarily implicate a cause-effect relationship, the findings in this thesis that small doses of beta-receptor antagonists completely suppress the cardiac effects of such stress, again suggests that these drugs may provide a useful tool in the test of such a hypothesis.

CONCLUSION

The results of this study of the effects of emotional and psychological stress on the heart must be placed in clinical and social perspective. Although the observations made raise many exciting questions in the coronary heart disease scene, their interpretation
must be tempered by critical consideration of the design and objective findings of the study. The results of any single report such as this, designed as a limited pilot study, must necessarily be treated with reserve until confirmed by observations in a larger population. The stresses selected for study were arbitrarily chosen from a wide range of possible situations; the effects of many other types of everyday stress require similar evaluation. These results concern only changes in heart rate; other less accessible circulatory variables must be measured before the full spectrum of the circulatory responses to everyday life situations are known. But within these critical limitations these studies indicate that the stresses of everyday life, many of which are accepted as normal in a Western urbanized society result in substantial sympathetic stimulation of the heart. There is no evidence that such psychological or emotional stresses are damaging to the normal heart or associated with precocious coronary heart disease. But there are suggestive indications that such responses may be harmful to the heart afflicted by coronary artery obstruction. However, there is as yet no evidence that suppression of these effects stays or reverses the natural course of ischaemic heart disease. Furthermore, these studies have shown that the effect of such stresses on the heart may be completely prevented by small doses of beta-receptor antagonists which have little effect on everyday exercise performance. The beneficial effects of such agents on the amelioration of symptoms in angina pectoris is
well established. The results of this study, if confirmed, would suggest that their evaluation in progressive ischaemic heart disease and perhaps in its prevention is also worthy of serious consideration.
APPENDIX

1. Summary Tables of the subject studied.

2. Remaining illustrations from the results of the main text.
<table>
<thead>
<tr>
<th>Subjects</th>
<th>Age</th>
<th>Height in ft and ins.</th>
<th>Weight in stones</th>
<th>B.P.</th>
<th>Occupation</th>
</tr>
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<tbody>
<tr>
<td>SHT</td>
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<td>11.00</td>
<td>120/80</td>
<td>Consultant Physician</td>
</tr>
<tr>
<td>MKM</td>
<td>35</td>
<td>5' 10&quot;</td>
<td>11.80</td>
<td>115/75</td>
<td>Physician</td>
</tr>
<tr>
<td>MP</td>
<td>28</td>
<td>5' 11&quot;</td>
<td>11.50</td>
<td>120/70</td>
<td>Senior Technician</td>
</tr>
<tr>
<td>AF</td>
<td>26</td>
<td>5' 9&quot;</td>
<td>10.50</td>
<td>120/70</td>
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<td>PH</td>
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<td>5' 11&quot;</td>
<td>11.00</td>
<td>115/70</td>
<td>Senior Technician</td>
</tr>
<tr>
<td>CNR</td>
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<td>5' 10&quot;</td>
<td>12.00</td>
<td>130/80</td>
<td>Physician</td>
</tr>
<tr>
<td>GAP</td>
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<td>5' 9&quot;</td>
<td>12.00</td>
<td>125/80</td>
<td>Company Director</td>
</tr>
<tr>
<td>GHK</td>
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<td>11.00</td>
<td>120/80</td>
<td>Physician</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Subjects</th>
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<th>Weight in stones</th>
<th>B.P.</th>
<th>Occupation</th>
</tr>
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<tbody>
<tr>
<td>JS</td>
<td>23</td>
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<td>11.00</td>
<td>120/80</td>
<td>School Teacher</td>
</tr>
<tr>
<td>AC</td>
<td>25</td>
<td>5' 9&quot;</td>
<td>10.00</td>
<td>115/80</td>
<td>Salesman</td>
</tr>
<tr>
<td>WL</td>
<td>50</td>
<td>5' 8&quot;</td>
<td>10.00</td>
<td>130/70</td>
<td>Works Foreman</td>
</tr>
<tr>
<td>AC</td>
<td>30</td>
<td>5' 9&quot;</td>
<td>10.50</td>
<td>115/75</td>
<td>Salesman</td>
</tr>
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</table>
### A) Patients with Exercise induced Angina Pectoris

<table>
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<tr>
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<th>Wt. in stones</th>
<th>B. P.</th>
<th>Occupation</th>
<th>Clinical Diagnosis</th>
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<td>JR</td>
<td>35</td>
<td>5' 10''</td>
<td>12.00</td>
<td>110/80</td>
<td>Company Director</td>
<td>Exercise induced angina pectoris for 12 months.</td>
</tr>
<tr>
<td>LG</td>
<td>60</td>
<td>5' 8''</td>
<td>11.50</td>
<td>135/80</td>
<td>Business Executive</td>
<td>Exercise induced angina pectoris for six months.</td>
</tr>
<tr>
<td>AS</td>
<td>53</td>
<td>5' 11''</td>
<td>13.00</td>
<td>140/80</td>
<td>Company Director</td>
<td>Exercise induced angina pectoris for nine months.</td>
</tr>
<tr>
<td>JB</td>
<td>60</td>
<td>5' 6''</td>
<td>10.50</td>
<td>130/70</td>
<td>Business Executive</td>
<td>Exercise induced angina pectoris for nine months.</td>
</tr>
<tr>
<td>JO</td>
<td>40</td>
<td>5' 10''</td>
<td>11.75</td>
<td>140/75</td>
<td>Company Director</td>
<td>Exercise induced angina pectoris for 12 months.</td>
</tr>
<tr>
<td>DB</td>
<td>45</td>
<td>5' 9''</td>
<td>11.00</td>
<td>135/80</td>
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<td>Exercise induced angina pectoris for six months.</td>
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</table>

### B) Patients with Myocardial Infarction

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<th>Wt. in stones</th>
<th>B. P.</th>
<th>Occupation</th>
<th>Clinical Diagnosis</th>
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<td>SB</td>
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<td>5' 9''</td>
<td>11.00</td>
<td>110/70</td>
<td>Retired Business Executive</td>
<td>Posterior Myocardial Infarction 9 months prior to study; confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>JM</td>
<td>35</td>
<td>5' 8''</td>
<td>12.00</td>
<td>120/80</td>
<td>Company Director</td>
<td>Anterior myocardial infarction 6 months prior to study; confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>SD</td>
<td>38</td>
<td>5' 8''</td>
<td>12.50</td>
<td>130/75</td>
<td>Branch Manager of Motor Factory</td>
<td>Anterolateral Infarction 12 months prior to study confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>DM</td>
<td>36</td>
<td>5' 10''</td>
<td>13.00</td>
<td>120/80</td>
<td>Works Manager British Leyland</td>
<td>Inferior myocardial Infarction 12 months prior to study; confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>McCaig</td>
<td>50</td>
<td>5' 11''</td>
<td>12.25</td>
<td>130/80</td>
<td>Factory Director</td>
<td>Inferior myocardial Infarction 12 months prior to study; confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>GA</td>
<td>50</td>
<td>5' 9''</td>
<td>11.00</td>
<td>130/80</td>
<td>Company Director</td>
<td>Anterior myocardial Infarction 6 months prior to study; confirmed by E.C.G. changes and elevated serum enzymes.</td>
</tr>
<tr>
<td>Subjects</td>
<td>Age</td>
<td>Height in ft and ins.</td>
<td>Weight in stones</td>
<td>B.P.</td>
<td>Subjects</td>
<td>Age</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>----------------------</td>
<td>------------------</td>
<td>--------</td>
<td>----------</td>
<td>-----</td>
</tr>
<tr>
<td>JB</td>
<td>50</td>
<td>5' 8&quot;</td>
<td>10.00</td>
<td>135/85</td>
<td>DP</td>
<td>32</td>
</tr>
<tr>
<td>JC</td>
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<td>5' 10&quot;</td>
<td>12.00</td>
<td>120/80</td>
<td>TML</td>
<td>30</td>
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<tr>
<td>PJ</td>
<td>48</td>
<td>5' 9&quot;</td>
<td>11.50</td>
<td>120/75</td>
<td>MJ</td>
<td>26</td>
</tr>
<tr>
<td>BC</td>
<td>36</td>
<td>5' 8&quot;</td>
<td>9.75</td>
<td>130/70</td>
<td>AC</td>
<td>28</td>
</tr>
<tr>
<td>BB</td>
<td>36</td>
<td>5' 11&quot;</td>
<td>10.50</td>
<td>120/75</td>
<td>AW</td>
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<tr>
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<td>5' 10&quot;</td>
<td>12.00</td>
<td>130/80</td>
<td>JS</td>
<td>36</td>
</tr>
<tr>
<td>SW</td>
<td>32</td>
<td>5' 8&quot;</td>
<td>10.00</td>
<td>115/70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JS</td>
<td>46</td>
<td>5' 10&quot;</td>
<td>11.75</td>
<td>120/80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS</td>
<td>46</td>
<td>5' 7&quot;</td>
<td>10.00</td>
<td>125/80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JB</td>
<td>30</td>
<td>5' 9&quot;</td>
<td>12.00</td>
<td>115/80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HS</td>
<td>30</td>
<td>5' 7&quot;</td>
<td>11.00</td>
<td>120/80</td>
<td></td>
<td></td>
</tr>
<tr>
<td>JCC</td>
<td>45</td>
<td>5' 8&quot;</td>
<td>9.75</td>
<td>130/70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SW</td>
<td>50</td>
<td>5' 10&quot;</td>
<td>12.00</td>
<td>130/85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject</td>
<td>Age</td>
<td>Height in ft. ins.</td>
<td>Weight in stones</td>
<td>B.P.</td>
<td>Occupation</td>
<td></td>
</tr>
<tr>
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<td>-------------------</td>
<td>------------------</td>
<td>------</td>
<td>-----------------------------</td>
<td></td>
</tr>
<tr>
<td>BD</td>
<td>36</td>
<td>5' 10&quot;</td>
<td>11.00</td>
<td>120/75</td>
<td>Radio and Television Commentator</td>
<td></td>
</tr>
<tr>
<td>JS</td>
<td>48</td>
<td>5' 9&quot;</td>
<td>10.50</td>
<td>130/80</td>
<td>Radio and Television Performer</td>
<td></td>
</tr>
</tbody>
</table>
Records of the heart rate in a normal subject driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.

**FIGURE 59**

MOTOR-CAR DRIVING
FIGURE 60

Records of the heart rate in a normal subject driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
MOTOR-CAR DRIVING

FIGURE 61

Records of the heart rate in a normal subject driving a motor-car between Leeds and Newcastle before and after 40 mg oral oxprenolol.
FIGURE 62

Records of the heart rate in a normal subject driving a motor-car between Leeds and Newcastle before and after 40 mg oral oxprenolol.
Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and London before and after 40 mg oral oxprenolol.
Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and Newcastle before and after 40 mg oral oxprenolol.
Record of the heart rate in a patient with ischaemic heart disease driving a motor-car between Leeds and Newcastle before and after 40 mg oral oxprenolol.
FIGURE 67

Record of the heart rate during city driving in a normal subject before and after 40 mg oral oxprenolol.
FIGURE 68

Record of the heart rate during city driving in a normal subject before and after 40 mg oral oxprenolol.
FIGURE 69

Record of heart rate during city driving in a patient with ischaemic heart disease before and after 40 mg oral oxprenolol.
Record of heart rate during city driving in a patient with ischaemic heart disease before and after 40 mg oral oxprenolol.
FIGURE 71

Record of the heart rate in a normal motor car passenger between Leeds and London during placebo and after 40 mg oral oxprenolol.
FIGURE 72

Record of the heart rate in a normal motor car passenger between Leeds and London during placebo and after 40 mg oral oxprenolol.
FIGURE 73

Record of the heart rate in a normal motor car passenger between Leeds and London during placebo and after 40 mg oral oxprenolol.
Record of the heart rate in a passenger with ischaemic heart disease between Leeds and London, during placebo and after 40 mg oral oxprenolol.

FIGURE 74
Record of the heart rate in a passenger with ischaemic heart disease between Leeds and London, during placebo and after 40 mg oral oxprenolol.

FIGURE 75
FIGURE 76

Record of the heart rate in a passenger with ischaemic heart disease between Leeds and London, during placebo and after 40 mg oral oxprenolol.
FIGURE 77

Record of the heart rate in a normal subject travelling by rail between Leeds and London before and after 40 mg oral oxprenolol.
Record of the heart rate in a normal subject travelling by rail between Leeds and London before and after 40 mg oral oxprenolol.
FIGURE 79

Record of the heart rate in a normal subject travelling by rail between Leeds and London before and after 40 mg oral oxprenolol.
Record of the heart rate in a subject with ischaemic heart disease travelling by rail between Leeds and London during placebo and after 40 mg oral oxprenolol.
FIGURE 81

Record of the heart rate in a subject with ischaemic heart disease travelling by rail between Leeds and London during placebo and after 40 mg oral oxprenolol.
RAILWAY PASSENGER

FIGURE 82

Record of the heart rate in a subject with ischaemic heart disease travelling by rail between Leeds and London during placebo and after 40 mg oral oxprenolol.
FIGURE 83

Record of the heart rate in a normal subject travelling by passenger turbo-propeller aircraft between Leeds and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
FIGURE 84

Record of the heart rate in a normal subject travelling by passenger turbo-propeller aircraft between Leeds and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
Record of the heart rate in a normal subject travelling by passenger turbo-propeller aircraft between Leeds and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
Record of the heart rate in a patient with ischaemic heart disease travelling by turbo-propeller aircraft between Leeds and London during placebo and one hour after 40 mg oral oxprenolol.
Record of the heart rate in a patient with ischaemic heart disease travelling by turbo-propeller aircraft between Leeds and London during placebo and one hour after 40 mg oral oxprenolol.

FIGURE 87
Figure 88

Record of the heart rate in a patient with ischaemic heart disease travelling by turbo-propeller aircraft between Leeds and London during placebo and one hour after 40 mg oral oxprenolol.
FIGURE 89

Record of the heart rate in a normal subject travelling by jet aircraft between Newcastle and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
Record of the heart rate in a normal subject travelling by jet aircraft between Newcastle and London and the modulation of the response by 40 mg oral oxprenolol taken one hour before the flight.
Record of the heart rate in a patient with ischaemic heart disease travelling by jet aircraft between Newcastle and London during placebo and one hour after 40 mg oral oxprenolol.
FIGURE 92

Record of the heart rate in a patient with ischaemic heart disease travelling by jet aircraft between Newcastle and London during placebo and one hour after 40 mg oral oxprenolol.
FIGURE 93

Record of the heart rate in a normal subject watching a soccer match after the ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 94

Record of the heart rate in a normal subject watching a soccer match after the ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 95

Record of the heart rate in a normal subject watching a soccer match after the ingestion of placebo and the modulation of the response produced by 40 mg oral oxprenolol taken one hour before a similar match.
FIGURE 96

Record of the heart rate in a normal subject watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the start of the match.
FIGURE 97

Record of the heart rate in a normal subject watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the start of the match.
FIGURE 98

Record of the heart rate in a patient with ischaemic heart disease watching a soccer match and the modulation of the response by 40 mg oral oxprenolol taken 30 minutes after the start of the match.
Record of the heart rate in a patient with ischaemic heart disease watching a soccer match and the modulation of the response by 40 mg oral oxprenolol taken 30 minutes after the start of the match.
FIGURE 100

Record of the heart rate in a patient with ischaemic heart disease watching a soccer match and the modulation of the response by 40 mg oral oxprenolol taken 30 minutes after the start of the match.
FIGURE 101

Record of the heart rate in a patient with ischaemic heart disease watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 102.

Record of the heart rate in a patient with ischaemic heart disease watching a televised live football match and the effect of 40 mg oral oxprenolol taken 30 minutes after the commencement of the match.
FIGURE 103

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 104

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 105

Record of the heart rate in a normal subject watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 106

Record of heart rate in a sensitive subject watching a television thriller film and the modulation of the response by 40 mg oral oxprenolol taken one hour before a similar programme.
FIGURE 107

Record of the heart in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 108

Record of the heart rate in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 109

Record of the heart rate in a patient with ischaemic heart disease watching programmes of Drama, Comedy and Documentary on television during placebo and the modification of the response by 40 mg oral oxprenolol taken one hour before the programme.
FIGURE 110

Record of heart rate during long distance bus driving.
LONG DISTANCE BUS DRIVING

LONG DISTANCE BUS DRIVING
350 MILES

Cumulative Total
44000

Time min.

FIGURE III
Record of heart rate during long distance bus driving.
LONG DISTANCE BUS DRIVING

EXCURSION BUS DRIVER
480 MILES

FIGURE 112
Record of heart rate during long distance bus driving.
FIGURE 113

Record of heart rate during long distance bus driving.
Record of heart rate during long distance bus driving.
FIGURE 115

Record of heart rate during long distance bus driving.
FIGURE 116

Record of heart rate during bus-driving in London.
FIGURE 117

Record of heart rate during bus-driving in London.
FIGURE 118

Record of heart rate during bus-driving in London.
FIGURE 119

Heart rate records of experienced bus drivers during motorway driving between Leeds and London.
Heart rate records of experienced bus drivers during motorway driving between Leeds and London.

Figure 120
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