Papers and Originals

Disturbances of Pulmonary Function after Acute Myocardial Infarction

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The studies of MacKenzie *et al.* (1964), McNicol *et al.* (1965), and Valentine *et al.* (1966) and observations of our own (Sloman *et al.*, 1966) have shown a high incidence of arterial hypoxaemia in patients studied after myocardial infarction. McNicol *et al.* suggested that pulmonary congestion with veno-arterial shunting was the basic cause of this hypoxaemia and that treatment with diuretics would improve blood oxygenation presumably by removing transudated fluid from the lungs.

This paper reports studies carried out in an attempt to further elucidate the mechanisms responsible for disturbed pulmonary function after myocardial infarction. Measurements of arterial blood gases, uniformity of ventilation, ventilation-perfusion relations, and pulmonary haemodynamics were made shortly after the onset of myocardial infarction.

Materials and Methods

The subjects, aged 39 to 77, were patients with a clinical diagnosis, subsequently confirmed by electrocardiograms and serum enzyme abnormalities, of acute transmural myocardial infarction. Studies were undertaken within four hours of admission to a coronary-care ward and within 12 hours of the onset of infarction. Throughout the procedures the patient was horizontal, with the head supported by one pillow. Papaveretum intravenously (10 mg.) was used to relieve pain if necessary.

Blood Gases.—Arterial blood was sampled from a nylon catheter placed in one brachial artery. Care was taken to keep this catheter patent with heparin-saline solution, and the dead space of the catheter was always flushed with blood before taking the actual samples. These were taken with the subject breathing room air and after the administration of 100% oxygen for 10 minutes. Patients were allowed to breathe in their natural pattern. The blood was drawn into 10-ml. syringes with their dead space filled with heparin-saline, capped, and immediately placed in a flask containing ice and water. Determination of the oxygen tension (Pao_2), carbon dioxide tension ($Paco_2$), and *p*H was performed within 20 minutes by means of a Beckman triple electrode module at 37° C. and physiological gas analyser 160. The oxygen electrode was calibrated, wet gases (commercial nitrogen, 7% O_2, room air, and 40% O_2) being used. The Po_2 measured was multiplied by 1.06 or 1.08 (depending on the level of Po_2) to correct for the blood-gas difference with this electrode and the use of polpropylene membrane. To correct for the fall in Po_2 due to delay in analysis of the high oxygen samples, 30 mm. Hg was added to the Po_2 measured. This figure had been previously derived by multiple sampling and analysis after varying intervals. The Pco_2 electrode was calibrated with two known CO_2–O_2 mixtures and the *p*H electrode calibrated with two freshly prepared buffers.

Pulmonary Ventilation-perfusion Relationships.—With the subject breathing room air, and at the time of taking the arterial blood sample, a three-minute collection of expired gas was made via a Collins one-way valve system of dead space 94 ml. The expired-gas tensions were measured with the electrodes, and the minute-volume was measured with a Wright anemometer. With the respiratory rate and the above data, the ratio of physiologic dead space to tidal volume (V_D/V_T ratio) and the ideal alveolar-arterial oxygen tension gradient were calculated, using standard formulae (Riley and Cournand, 1949). With an assumed arteriovenous oxygen content difference of 5 volumes per 100 ml., the approximate venous admixture and venoarterial shunt, both expressed as a percentage of the total blood flow, were obtained from the air-breathing and oxygen-breathing analyses respectively.

Uniformity of Ventilation.—This was assessed in 18 of the subjects by a multibreath nitrogen washout technique (Fowler *et al.*, 1952) with a Nitralyser 105 (Medical Science Electronics) and a potentiometric single-channel recorder (Texas Instruments). The meter was calibrated, 100% oxygen and room air being used. The output of the Nitralyser is non-linear, and this was corrected from a calibration curve previously plotted by means of multiple intermediate nitrogen-oxygen mixtures derived from a proportional gas-mixing pump (H. Wosthoff-Bochum). The corrected end-expired nitrogen concentration during the nitrogen washout was then plotted against the number of breaths on semilogarithmic paper. Patients were connected to the oxygen circuit at the end of quiet expiration. The clearance curve obtained was assessed visually for linearity. This was regarded as sufficient to describe the washout as being linear or alinear, and multicompartment analysis of alinear curves was not performed.

Haemodynamic Measurements.—In 17 subjects measurements of pulmonary artery or right ventricular pressure and cardiac output were made. Whenever possible these were performed within four hours of admission, but in six patients these measurements were separated by up to 24 hours from the gas-exchange measurements. Right heart pressures were measured with a fine polyethylene catheter (P.E. 60) 80 cm. long, which was passed percutaneously from a median cubital vein. With a Sanborn transducer (267A), preamplifier, and direct-writing recorder (296), the dynamic response is flat (±5%) to 4 c.p.s. Cardiogreen (5 mg.) was injected into the right atrium, and blood from the brachial artery was passed through a Waters densitometer (XP 302). Cardiac output was calculated from dye-curve analysis.

All the above procedures were not performed in every subject. Of the 33 patients studied, 29 had blood-gas analysis and

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ventilation-perfusion ratio analysis, 18 had blood-gas analysis and a nitrogen washout procedure, 19 had blood analysis, gas-exchange study, and haemodynamic measurements.

In 11 patients arterial blood samples were taken one hour after the intravenous injection of 80 mg. of frusemide.

Results

Blood Gases.—The common finding of arterial hypoxaemia during air breathing is indicated in Table I. The mean value for Pa_{O_2} was 62 mm. Hg, with a range of 44 to 78 mm. Hg (normal value in our laboratory is 85–100 mm. Hg). The mean Pa_{CO_2} was normal at 39 mm. Hg, and the *p*H was also normal at 7.43. Table I indicates that in none of the subjects was the *p*H below 7.32, and this is a reflection of patient-selection, since studies were not performed on very ill patients requiring resuscitation. Ten minutes of breathing oxygen produced a rise in arterial P_{O_2}, but in all cases this was below the normal response. The mean Pa_{O_2} was 400 mm. Hg (range 100 to 510 mm. Hg). In the absence of abnormal venoarterial shunting of blood, the Pa_{O_2} after 10 minutes of oxygen breathing is above 640 mm. Hg. All subjects therefore showed an abnormal amount of blood passing through the lungs but not coming into contact with ventilated alveoli. Changes in carbon dioxide tension and *p*H after oxygen breathing were not significant.

TABLE I.—*Results of Arterial Blood Analyses Performed During Air-breathing and After 10 Minutes of Oxygen Breathing. Grade of Severity of Infarction According to Robinson and Sloman* (1965)

Subject	Breathing Air			Breathing 100% Oxygen			
	Pa_{O_2}	Pa_{CO_2}	*p*H	Pa_{O_2}	Pa_{CO_2}	*p*H	Grade
1	65	38	7·43	460	40	7·41	Mild
2	68	38	7·43	420	39	7·42	,,
3	71	41	7·48	460	45	7·43	Severe
4	66	46	7·39	470	49	7·36	Mild
5	68	38	7·43	490	40	7·41	,,
6	59	33	7·47	390	29	7·49	,,
7	64	41	7·40	520	33	7·46	,,
8	61	34	7·44	480	39	7·41	,,
9	78	36	7·41	505	28	7·46	Severe
10	72	39	7·46	450	38	7·47	Mild
11	50	37	7·42	370	43	7·38	Severe
12	46	44	7·40	290	54	7·36	,,
13	64	50	7·32	420	49	7·33	Mild
14	59	45	7·38	480	45	7·38	Severe
15	62	47	7·38	440	48	7·36	,,
16	65	34	7·49	460	36	7·47	Mild
17	64	43	7·39	400	45	7·38	Severe
18	54	41	7·43	370	46	7·39	Mild
19	44	37	7·43				Severe
20	60	31	7·51	330	32	7·50	,,
21	62	34	7·44	320	41	7·40	,,
22	77	36	7·44	510	37	7·43	Mild
23	73	30	7·44	490	22	7·54	,,
24	68	41	7·41	450	45	7·42	,,
25	70	37	7·39	240	42	7·36	,,
26	50	35	7·49	340	31	7·50	Severe
27	70	43	7·40	360	46	7·38	,,
28	65	38	7·46	360	40	7·48	Mild
29	50	38	7·43	100	43	7·39	Severe
30	67	45	7·38	420	34	7·43	,,
31	65	38	7·40	340	40	7·39	Mild
32	45	40	7·44	310	42	7·43	,,
33	54	36	7·42	420	34	7·46	Severe
Mean	62	39	7·43	400	40	7·42	
Range	44–78	30–50	7·32–7·51	100–520	22–54	7·33–7·54	

Ventilation-perfusion Ratio Relationships (Table II).—The mean value for the V_D/V_T ratio (corrected for apparatus dead space) was 0.38, with a range of 0.23 to 0.57. Elevation of this ratio above the upper limit of normal (0.3) reflects the presence of regions of the lungs which are overventilated in relation to the regional blood flow. The alveolar-arterial oxygen tension difference (normally less than 10 mm. Hg) was increased in all subjects, with a mean value of 35 mm. Hg (range 11 to 53 mm. Hg).

Uniformity of Ventilation.—Alinear nitrogen washout curves were obtained in 11 out of the 18 patients studied (Table II and Fig. 1).

Haemodynamic Measurements.—These are set out in Table II. Right ventricular pressure only was obtained in six subjects and pulmonary artery pressure recorded in the remaining 11 subjects. The mean systolic pressure was 23 mm. Hg (range 15 to 42 mm. Hg). Cardiac output measurements were made in 18 subjects and the mean value was 3.7 l./min. (range 2.0 to 5.5 l./min.).

Effect of Frusemide.—Table III shows that the action of a rapidly acting diuretic was to increase, occasionally considerably, the arterial oxygen tension with the subject breathing room air but to cause no change in the Pa_{O_2} after oxygen

TABLE II.—*Results of Calculated Gas-exchange Data, Ventilation Distribution, and Haemodynamic Measurement*

Subject	V_D/V_T	$A\text{-}apO_2$	$\dot{Q}s/\dot{Q}t$	$\dot{Q}va/\dot{Q}t$	N_2 Clearance	C.O.	P.A. or R.V. Pressure
1	0·39	37	14	22	Alinear	3·9	30/0
2	0·38	28	17	10	,,	3·9	20/0
3	0·38	28	14	14	,,	5·0	24/8
4	0·26	11	13	8	,,		42/22
5	0·50	37	12	20	,,	3·6	27/0
6	0·25	48	19	24	Linear	4·2	23/5*
7	0·41	31	10	14	,,	4·3	
8	0·27	37	13	20	Alinear	2·8	18/0
9	0·40	31	11	12	Linear	5·5	15/–4*
10	0·42	40	15	18		4·0	23/2*
11	0·37	50	20	32		3·5	*
12	0·50	36	20	20		3·5	15/5*
13	0·43	29	17	12		3·1	30/8*
14	0·36	46	13	48		4·8	18/8
15	0·36	43	16	44		3·1	30/8*
16	0·28	42	14	28		4·7	23/5*
17	0·47	16	18	18		2·0	15/0
18	0·39	20	20	26		3·2	21/7
19	0·47	51		68		2·1	25/11
20	0·38	49	22	24	Linear		
21	0·26	33	23	16	Alinear		
22	0·36	25	11	16	Linear		
23	0·40	32	12	18	,,		
24	0·33	35	15	26	Alinear		
25	0·57	38	27	64	,,		
26			22		,,		
27			21		Linear		
28			21		Alinear		
29	0·42	34	35	36			
30	0·31	21	16	20			
31	0·40	30	22	20			
32	0·40	53	24	62			
Mean	0·38	35	18	26		3·7	23 systolic
Range	0·25–0·57	11–53	10–35	8–68		2·0–5·5	15–42

Symbols.—V_D/V_T is physiologic dead space/tidal volume ratio (corrected for apparatus dead space); $A\text{-}apO_2$ is the ideal alveolar–arterial oxygen tension difference in mm. Hg; $\dot{Q}s/\dot{Q}t$ is the percentage venoarterial shunt assuming an arteriovenous oxygen content difference of 5 volumes %; $\dot{Q}va/\dot{Q}t$ is the percentage venous admixture with the same assumed arteriovenous difference; C.O. is the cardiac output in litres per minute. Pressure measurements with a diastolic pressure of 2 mm. Hg or less are right ventricular pressures.

* Haemodynamic measurements made up to 24 hours apart from other measurements.

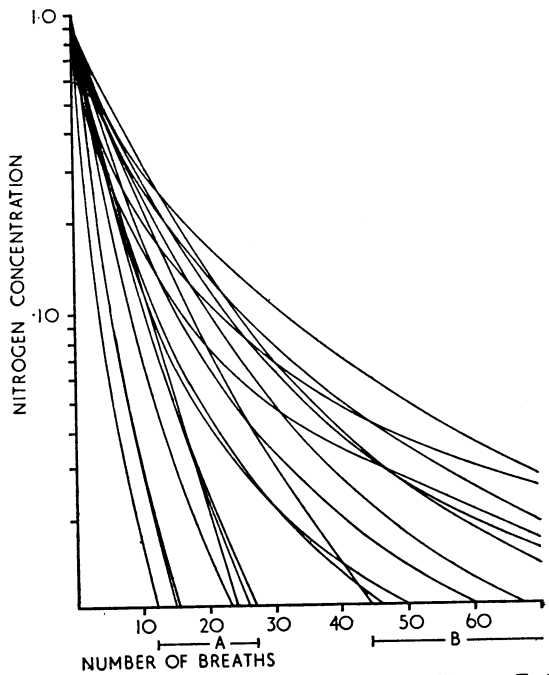

FIG. 1.—Nitrogen-clearance curves in 18 subjects. End-expired nitrogen concentration is plotted on the logarithmic ordinate and the number of breaths on the linear abscissa. Those clearance curves considered linear are grouped as "A" and those considered abnormal as "B."

breathing. Taken as a group, however, these changes are not significant (P=0.10).

TABLE III.—*Mean Results of Arterial Oxygen Measurement in 11 Subjects Before and One Hour After the Administration of 80 mg. of Frusemide Intravenously*

	Breathing Air	Breathing Oxygen
Initially..	62 mm. Hg	415 mm. Hg
After diuretic	67 mm. Hg	410 mm. Hg

$t = 1.7$. $P = 0.10$.

Discussion

Reduction in arterial oxygen tension has been demonstrated in subjects after anaesthesia, surgery, and cardiopulmonary bypass. With the restriction in breathing associated with post-operative pain it is not difficult to see why disturbances of pulmonary function occur in most of these situations. The explanation is not quite so apparent in cases of myocardial infarction.

Our studies show that quite soon after the onset of myocardial infarction there is already considerable reduction in Pa_{O_2}. The studies during oxygen breathing reveal that the majority of patients had a considerable increase in the amount of venoarterial shunting of blood. The venous admixture breathing air is plotted against the venoarterial shunt, both expressed as a percentage of the total blood flow, in Fig. 2, and it is apparent that, though in most cases the venous admixture and alveolar-arterial oxygen tension gradient is largely the result of the venoarterial shunt, in seven patients there were additionally regions of relative hypoventilation. Further evidence of maldistribution of pulmonary ventilation and blood flow is provided by the values for V_D/V_T ratio, which was elevated in 24 out of 29 instances.

The pattern of disturbances we found was one of abnormal venoarterial shunting together with defects in the matching of pulmonary ventilation to pulmonary blood flow. These findings are in agreement with those of McNicol *et al.* (1965), but are unlike those of Valentine *et al.* (1966). These latter workers showed only minor venoarterial shunting in seven patients studied during oxygen breathing but considerable ventilation-perfusion imbalance. The reason for this difference may lie in the pattern of ventilation during the period of oxygen breathing. The venoarterial shunt can be reduced, though not abolished, by increasing transpulmonary pressure above normal during the oxygen-breathing period (personal observations). Disturbances

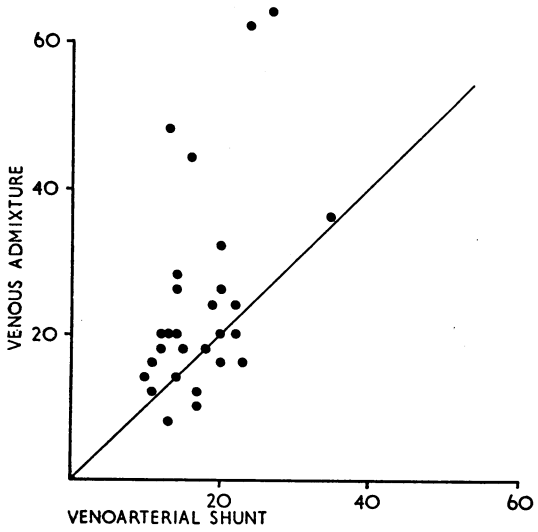

FIG. 2.—Calculated venous admixture and venoarterial shunt expressed as a percentage of total blood flow and assuming an arteriovenous oxygen content difference of 5 volumes %. If the venous admixture was always due to venoarterial shunting alone, then the points would lie along the line of identity.

of ventilation distribution, in the context of myocardial infarction, might be caused by narrowing of airways owing to intrabronchial or peribronchial transudate, alveolar oedema, or alteration in mechanical properties due to congestion of lung vessels associated with a rise in left atrial pressure. A rapidly acting diuretic can improve the Pa_{O_2}, but our data indicate that this is not due to a decrease in the venoarterial shunt. We have no data on the change in nitrogen clearance after diuretic therapy, but it seems that these agents improve the ventilation-perfusion relations in those areas of the lung which are being ventilated. We could not demonstrate any difference in the amount of venoarterial shunting among patients with linear and alinear nitrogen-clearance curves (Fig. 3).

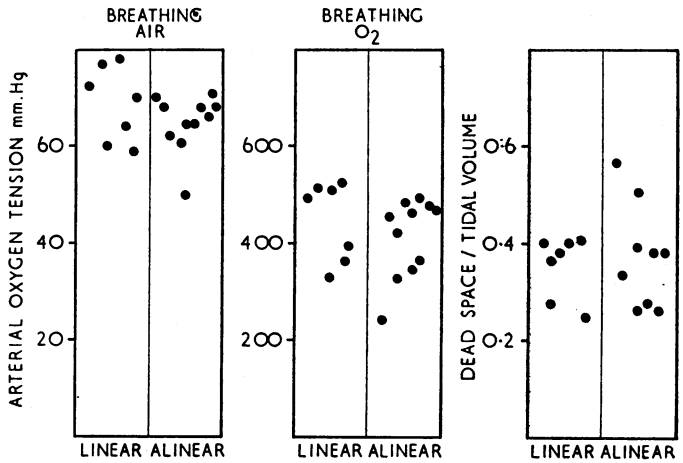

FIG. 3.—Degree of arterial hypoxaemia, venoarterial shunt, and V_D/V_T ratio in patients with linear and alinear nitrogen clearance curves.

Changes in pulmonary blood flow due to myocardial infarction might result from pulmonary hypotension due to an acute reduction in cardiac output or from pulmonary hypertension due to pulmonary venous hypertension with left ventricular failure. Despite a wide range of pulmonary artery pressure and cardiac output in our data we were unable to demonstrate any simple correlation between V_D/V_T ratio and pulmonary haemodynamics such as that shown in other situations (West and Jones, 1965 ; Saunders, 1966 ; Askrog, 1966).

While defects in various aspects of pulmonary function after myocardial infarction are readily demonstrable the precise mechanisms producing them are not. Alterations in pulmonary haemodynamics, airways closure, and alveolar transudation, perhaps due to altered alveolar-capillary permeability characteristics, probably all interact. It remains to be shown that correcting the hypoxaemia which is present in even mild instances of infarction alters the ultimate outcome. There is as yet little evidence that the incidence of arrhythmias may be reduced by oxygen therapy, which fortunately easily raises the Pa_{O_2} to above 100 mm. Hg in all but the most severely ill patients.

Summary

Arterial blood-gas analyses have been made in 33 patients immediately after admission to a coronary care ward after a myocardial infarction.

Reduction in arterial oxygen tension breathing air without abnormality in carbon dioxide tension was an invariable finding. This was shown to be due to an abnormal venoarterial shunt with commonly associated disturbances in the matching of pulmonary ventilation and blood flow.

Diuretics can improve the oxygen tension breathing air but do not alter the amount of venoarterial shunting. Oxygen therapy easily corrects the hypoxaemia.

We wish to thank the honorary medical staff for allowing us access to patients under their care, Dr. B. Walder for his help at

various stages of this study, and Miss Nancy Rogers and Mrs. Anne Watkins, who performed much of the technical analyses. Misses L. Dalby, W. Thoren, and L. Shannon assisted with the bedside haemodynamic measurements.

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Aversion Therapy in Management of 43 Homosexuals

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A wide variety of techniques have been used in the treatment of homosexuality. They include psychotherapy, psychoanalysis, hormones, and several types of aversion therapy. There are relatively few published reports involving more than a small number of patients. To date, only one series of patients treated by aversion therapy has appeared (Freund, 1960). This involved the use of apomorphine as the aversive stimulus. A satisfactory response to treatment was obtained in 25% of all cases, but this was only after patients referred by the courts had been excluded. The same percentage of success was obtained in a series of 100 patients treated by psychoanalytic techniques (Bieber *et al.*, 1962). Follow-up data for this series have not been reported. The two British series which have been published obtained treatment results which were even less satisfactory than those of Freund and of Bieber *et al.*

Curran and Parr (1957) were able to follow up 52 out of their original 100 patients, most of whom received psychotherapy, and in only nine was there a change of preference towards heterosexuality. Woodward (1958), reporting a series of patients treated at the Portman Clinic and referred by the courts, found that out of the 48 who completed treatment without interruption only seven had no homosexual impulse and an increased heterosexual interest and activity. Very little follow-up data are available for Woodward's series. It seems, therefore, that in the published series approximately one-quarter at best of treated homosexual patients make a satisfactory response to treatment in that they display a noticeable change in the direction of their sexual preference and practice towards heterosexuality. Such follow-up data as are available suggest prevention of relapse to be one of the major problems in the treatment of homosexuality.

Method of Study

The present paper is a report on a series of 43 homosexual patients treated by us and our colleagues over a period of three and a quarter years, by means of the technique of anticipatory avoidance learning using an electrical aversive stimulus. The minimum period of follow-up is 12 months. A preliminary report on the technique has appeared elsewhere (Feldman and MacCulloch, 1964) and a detailed description is given in an account (Feldman and MacCulloch, 1965) of the response to treatment of the first 19 patients. A survey of the results of treatment of homosexuality by aversion therapy, together with a critical account of the aversive techniques used to date, has also been presented (Feldman, 1966). A brief account of the technique used by us follows.

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Treatment Technique

The homosexual patient views a slide of a male which is back-projected on to a screen. He is instructed to leave this picture on for as long as he finds it attractive. After the slide has been on the screen for eight seconds the patient receives an electric shock if he has not by then removed it by means of a hand switch (with which he is provided). If he does switch off within the eight-second period he avoids the shock. The circuit is so wired that the patient's attempts to switch off can be delayed by the therapist. A schedule of reinforcement is used so that one-third of all the patient's attempts to switch off are delayed but do eventually remove the male slide within the eight-second period; one-third are non-reinforced—that is, the patient is shocked despite his attempts to switch off—and one-third result in the picture being removed immediately. This mixture of trials has been shown to assist considerably in delaying extinction (relapse). A photograph of a female is introduced and remains on the screen for 10 seconds immediately the male slide leaves the screen, but in order to preserve the principle of unpredictability the female slide is not introduced on every possible occasion. Finally, the patient can press his switch to request the return of the female slide should he wish to do so. Once again his request is not met on every occasion but only randomly.

The whole treatment situation and the various variables referred to above are designed to make the fullest possible use of the extensive knowledge available to us of the psychology of learning (Kimble, 1961). The slides are first set up by the patient in a hierarchy of attractiveness, and we begin with a male slide which is only mildly attractive, working up to one which is very attractive. The opposite is carried out with the female slides, beginning with one which is relatively attractive to the patient and gradually moving along the hierarchy. The aversive stimulus (unconditional stimulus) is provided by a 12-volt make/break induction coil and is controlled by a rheostat. About 24 stimulus presentations are used per session, and each session lasts for about 20 to 25 minutes. On average each patient receives 18 to 20 sessions of treatment. Treatment is continued until either a change of interest occurs or it becomes clear that no change is likely. A number of patients (see below) have discontinued treatment of their own accord.

Recently we have been carrying out a controlled trial of the technique described above, in which it is compared with classical conditioning and psychotherapy. The results of this will be reported later. Both the apparatus and the treatment technique employed have been made somewhat more complicated and advanced so as to increase the degree of control over the situation exercised by the therapist.