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CHANGES IN DEGREE OF SCLEROSIS AS A FUNCTION OF PROPHYLACTIC TREATMENT IN CANCER-PRONE AND CHD-PRONE PROBANDS

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Summary—One-hundred and ninety-two probands were selected on the basis of personality questionnaires as being cancer-prone (100) or CHD-prone (92). They were then randomly divided into a control and a treatment group, the latter receiving a special kind of behaviour therapy attempting to change the personality patterns in the direction of a healthier, more autonomous personality. Follow-up after 10 and 13 years disclosed significantly lower death rates in probands receiving prophylactic treatment than in controls. Of special interest was the degree of sclerosis in the fundus of the eye, rateds on a 3-point scale. This was significantly higher prior to therapy in the CHD-prone group than in the cancer-prone group. Treatment reduced the degree of sclerosis, particularly in the CHD group; lack of treatment was followed by an increase in sclerosis. Similar but less marked changes were found in the cancer-prone group. Clearly psychological treatment affects significantly bodily functions associated with CHD. Other risk factors considered were systolic and diastolic blood pressure, blood cholesterol and blood sugar, all of which, together with personality, influenced the degree of sclerosis observed.

THEORETICAL BACKGROUND

Holistic medicine rejects the Cartesian dichotomy between body and mind, and prefers to think of a body–mind continuum, in the same way that physicists reject the distinction between space and time, and assume the existence of the space–time continuum. There is now good evidence for the involvement of the central nervous system in cancer (von Metzler, 1979; von Metzler & Nitsch, 1986), and evidence has also been adduced to demonstrate the importance of personality variables in cancer and coronary heart disease (Osler, 1910; Rosenman, Brand & Jenkins, 1975; Eysenck, 1985, 1988a, b; Kissen & Eysenck, 1962; Grossarth-Maticek, Eysenck & Vetter, 1988). Equally, it has been shown that interventions through psychological treatment (behaviour therapy) can to some extent prevent cancer and coronary heart disease, e.g. the Recurrent Coronary Prevention Project (Thorensen, Friedman, Gill & Ulmer 1982; Friedman, Thoresen, Gill, Powell, Ulmer, Thompson, Price, Rabin, Breall, Dixon, Levy & Breng, 1984; Gill, Price, Friedman, Thoresen, Powell, Ulmer, Brown & Drew, 1985; Thorensen *et al.*, 1985; Friedman, Thoresen, Gill, Ulmer, Powell, Price, Brown, Thompson, Rabin, Breall, Breng, Levy & Dixon, 1986); The Maudsley Intervention Project (Eysenck, 1988a, b; Eysenck, 1990; Grossarth-Maticek, Eysenck, Vetter & Frentzel-Beyme, 1988); as well as independent studies such as those of Rodin (1984) and studies summarized by Roskies (1987). Some of these studies like those by Lovibond, Birrell and Langeluddecke (1986) and Grossarth-Maticek and Eysenck (1989) have also shown that intervention studies promoting physical health have beneficial effects on blood pressure, aerobic capacity, reduction in serum cholesterol, percentage lymphocytes, and many other physical functions often accompanying disease. The present study aims to extend our knowledge of the effects of psychological intervention studies by demonstrating an effect on the degree of sclerosis in relation to personality, and the effects of a certain type of behaviour therapy on the degree of sclerosis.

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BACKGROUND OF THE PRESENT STUDY

In 1972, two sets of persons underwent detailed investigation in Heidelberg, amounting to 2449 persons in all. These constituted a representative group of 1026 persons, and a stressed group of 1443 persons. Members of the stressed group were nominated as such by members of the representative group. All were assigned to one of four personality types, Type 1 constituting those who were cancer-prone, Type 2 those who were coronary heart disease-prone, Type 3 a mixed group which was relatively healthy, and Type 4 a healthy, autonomous group. (Health, in this connection, means mental health, used as a predictor of physical health.) Details concerning the questionnaires used, and the method of assignment, as well as details concerning the samples in question are given in Grossarth-Maticek *et al.* (1988).

The normal group was selected on a random basis from the electoral register, with age and sex limitations arranged on an *a priori* basis. The stressed group was nominated as being severely stressed psychologically by members of the normal group from friends and relatives they knew well. Probands were assigned to personality types on the basis of an interviewer-administered personality inventory. Cancer-prone individuals (Type 1) were so designated on the basis of such behaviours as suppression of emotional reactions and expressions, and failure to deal appropriately with interpersonal stresses of various kinds, leading to the development of feelings of hopelessness, helplessness and depression. CHD-prone individuals (Type 2) were so designated because of strong feelings of anger, hostility and aggression, together with a failure to deal appropriately with interpersonal stresses. Type 3 was characterized by behaviour alternating between those characteristic of Types 1 and 2, while Type 4 showed appropriate demonstrations of emotion and a capacity to deal effectively with interpersonal stresses. Interviews were carried out by specially trained student investigators; these were blind to the treatment.

The age of the probands in these studies in 1972 was between 30 and 69 years; half were men, half were women. The mean age of the probands was 50 years. A group of 192 persons was selected for an intervention study, and these constitute the sample which forms the basis of this article. Pairs were formed from the members of the stressed group, such that they were similar in age, sex, degree of stress, intensity of cigarette-smoking, blood pressure, blood sugar and cholesterol. Originally, 134 pairs of Type 1 probands and 138 pairs of Type 2 probands had been approached with an offer of psychotherapy; of the former, one or both members refused in 34 cases, of the latter, in 46 cases, thus leaving 100 pairs of Type 1 probands and 92 pairs of Type 2 probands. Care was taken to exclude from the study anyone suffering from heart infarct, cancer, stroke, or any other severe chronic disease; details concerning measures for exclusion have been given elsewhere (Grossarth-Maticek, Bastiaans & Kanazir, 1985). Members of each group were assigned to a control group or to a therapy group on a random basis. We thus have 50 pairs, members of which had been assigned to Type 1, and 46 pairs, members of which had been assigned to Type 2.

From the beginning of 1972 to the end of 1974 several attempts were made to ascertain a number of psychological and medical data. Cholesterol, blood sugar and blood pressure were measured three or four times before the beginning of therapy, the different measures being separated by 1–3 months. The therapy continued for up to 6 months, lasting between 20 and 30 hr for each proband. After therapy was concluded, a further set of measures was instituted, including a minimum of two measures of blood pressure, blood cholesterol and blood sugar. Equally, psychosocial factors were ascertained before the therapy and 6–12 months after its conclusion, in particular the belongingness of probands to one of the types, and the degree to which that type was expressed.

Degree of sclerosis, measured in the fundus of the eye, was undertaken at two points of time. The first ascertainment was at the beginning of 1973, after the probands for the therapy experiment had been selected, and the second at the end of 1974 or the beginning of 1975, usually 2 years after the first measurement. A measurement of sclerosis was undertaken by two specialists in ophthalmology, half the probands being assigned to one or the other on a chance basis. Probands were assigned to one of three groups according to the degree of sclerosis observed: (1) not sclerotic, i.e. not exceeding changes characteristic of age; (2) sclerotic changes of a benign character; (3) sclerotic changes of a malignant character. Assessment was blind as to therapy or type of proband.

Type 3 embraces both types 3 and 4 of the usual four characters defined by opthalmologists. A detailed description of these four stages, as normally defined, is given below, in Table 1 (Gallasch, 1985).

Table 1. Definition of different stages of sclerosis in the fundus of the eye

Stage I (red fundus):

Of red color because of increased blood circulation in retinal vessels, dilation of congested arterioles (arterioles show same width as venules), omega-shaped branching of arterioles of first order or second order, golden reflex of vessels (copper-wire arteries), occasional perivascular stripes, Gunn's phenomenon and Salus crossing, omega-shaped branching of venules, corkscrew-shaped venules around the macula with perimacular localized intraretinal hemorrhages, complicated at rare instances by apoplexia papillae.

Stage II (pale fundus):

Pale fundus becasue of reduced retinal circulation and reduced transparency due to gliosis retinae, stretching and constriction of arterioles (relation of arteriole/venule from 2:3 reduced to 1:4), silvery reflex of vessels (silver-wire arteries), variable calibers of arterioles, in redfree light bloodfilled vessels accompanied by greyish-white stripes (vasosclerosis by fibrous reconstruction and hyalinose), Gunn's phenomenon and parallel Gunn's phenomenon as well as Saluss crossing signs, exsudates, but not further neuroretinal changes.

Stage III (cotton wool foci):

Stripe- and flame-shaped bleedings particularly around the papilla, cotton wool foci, spotted star figure of the macula, oedema of the retina, in extreme cases exsudative ablation of the retina (oedema is difficult to recognize by funduscopy, because of the similar refraction index of the oedema), capillar ecstasias, unclear border of papilla.

Stage IV (cotton wool foci with papillar oedema):

In principle similar to stage III, however with more pronounced swelling of the papilla as well as heavy oedema of the retina and increasing capillar ecstasia. Acute changes are more prominent in stage IV.

Names of the probands had been desposited in independent university departments (Zurich and Karlsruhe) prior to ascertainment of mortality, which was carried out first in 1982 and again in 1986; we will be concerned with the data for the second, 13 year follow-up. Collection of mortality data was carried out by Dr E. Heller, an independent assessor from the Statistical Institute of the University of Karlsruhe. The methods of treatment used will not be discussed in detail in this paper; they have been described in extenso elsewhere (Grossarth-Maticek & Eysenck, 1991). Essentially, an attempt was made to change the emotional suppression and/or anger of the probands towards socially acceptable expression, and to help them to find suitable stress-management techniques which would satisfy their emotional needs and requirements. There were no changes in smoking habits, but jogging and sport participation increased in the therapy groups. In addition advice was given to Type 1 probands to eliminate depressant drugs (e.g. valium), and to Type 2 probands to eliminate stimulant drugs (e.g. caffeine).

RESULTS

Table 2 shows the composition of the various groups according to sex, Table 3 according to age. Crucial to our study is of course the efficacy of the treament in providing a change in the probands' behaviour, feelings, etc. as expressed in the questionnaire. Taking the cancer-prone group first, we find that for the control group there is no significant change in their Type 1 inventory answers from the first application to second application 6–12 months later (9.84 ± 0.47 to 9.76 ± 0.92). For the therapy group there is a change significant at a $P < 0.0001$ (9.78 ± 0.76 to 5.78 ± 2.21). Results for the CHD-prone group, using scores on the Type 2 inventory, are similar. For the control group there is no significant change (9.17 ± 1.00 to 9.57 ± 1.28). For the therapy group there is a change significant at a $P < 0.0001$ level (8.96 ± 1.19 to 4.87 ± 3.04). Thus self-evaluation of the probands discloses no change in the control group, but a very significant diminution in the size of the risk factors measured by the questionnaire. These subjective evaluations of course require validation along more objective lines, i.e. greater degree of survival of therapy as compared with control groups.

Table 2. Male–female composition of samples tested

Group	Not ascertained	Male	Female	Total
Ca-control	0	30	20	50
%	0.00	60.00	40.00	100
CHD-control	0	29	17	46
%	0.00	63.04	36.96	100
Ca-therapy	0	28	22	50
%	0.00	56.00	44.00	100
CND-therapy	1	26	19	46
%	2.17	56.52	41.30	100
Total	1	113	78	192
%	0.5	58.9	40.6	100

Table 3. Age composition of samples tested

Age/group	–39	40–49	50–59	60–69	Total
Ca-control	3	24	18	5	50
%	6.00	48.00	36.00	10.00	100
CHD-control	3	18	18	7	46
%	6.52	39.13	39.13	15.22	100
Ca-therapy	7	15	15	9	50
%	14.00	30.00	38.00	18.00	100
CHD-therapy	3	20	14	9	46
%	6.52	43.48	30.43	19.57	100
Total	16	77	69	30	192
%	8.3	40.1	36.0	15.6	100

Table 4. Effects of behaviour therapy on cancer-prone and CHD-prone groups

Type 1 Cancer-prone	Alive	*Deceased from* Other cause	Cancer	Total
Control group	19	15	16	50
Therapy group	45	5	0	50
Total	64	20	16	100
Type 2 *CHD-prone*				
Control group	17	13	16	46
Therapy group	37	6	3	46
Total	54	19	19	92

Table 5. Degree of sclerosis in probands of Type 1 and Type 2

	Not ascertained	*Sclerosis* 1	2	3	Total
Type 1	1	50	42	7	100
%	1.0	50.0	42.0	7.0	100
Type 2	0	6	52	34	92
%		6.5	56.5	37.0	100
Total	1	56	94	41	192
%	0.5	29.2	49.0	21.3	100

Table 4 shows the effects of prophylactic behaviour therapy on the cancer-prone and the CHD-prone probands respectively. It will be clear that treatment by means of creative novation behaviour therapy (the specific method of behaviour therapy employed) has had a highly significant prophylatic effect, preventing deaths from cancer in probands of Type 1, and death from coronary heart disease in probands of Type 2. In each case there is also an effect of a prophylactic kind on death from other causes. In view of the known unreliability of diagnoses as recorded on death certificates (Eysenck, 1986), the precise allocation of cause of death should not perhaps be taken too seriously but the overall difference in the proportion still alive between control groups and therapy groups does indicate the efficacy of the treatment. Differences are significant beyond the 0.001 level.

Table 5 shows the relationship between sclerosis and personality type at the beginning of the study. It is clear that for the CHD-prone group the rating of 1 on the sclerosis scale is much less frequent, and therefore a rating of 3 much more frequent, than for the cancer-prone group. χ^2 is <0.001. Clearly personality and sclerosis as here measured show a close correspondence.

Table 6 shows the effects of the therapy, giving the rating for the degree of sclerosis before and after therapy (for the therapy group) or the same interval without therapy for the control group. The cancer-prone control group hardly shows any change; the cancer-prone therapy group is in the first instance hardly differentiated from the control group, but shows after therapy a slight shift from a rating of 2 towards a rating of 1. The CHD-prone groups show right at the beginning many fewer ratings of 1, and many more ratings of 3, as compared to the cancer-prone groups. In the CHD-prone control group there is a clear increase in ratings of 3, at the cost of ratings of 2, while in the therapy group there is a smaller number of ratings of 3, and an equal increase in ratings of 1. Figure 1 shows the details of this progression.

Paired sample t-tests were carried out to establish the significance of the difference between pre- and post-treatment scores. For the CHD-prone groups, the *decrease* in sclerosis scores for the treatment group was significant at the 0.018 level; the *increase* in sclerosis scores for the control group was significant at the 0.037 level. For the cancer-prone group, the *decrease* in sclerosis scores for the treatment group was insignificant at the 0.09 level; the *increase* in sclerosis scores for the control group was significant at the 0.031 level. Independent sample t-tests showed a lack of significance pre-treatment difference for the CHD-prone groups ($P = 0.725$), but a high level of significance post-treatment ($P = 0.003$). For the cancer-prone group, the pre-treatment level is also insignificantly different (0.385), but post-treatment levels are significantly different (0.013). Thus

Table 6. Effects of behaviour therapy on degree of sclerosis

	Degree of sclerosis Before				After				
	Not ascertained	1	2	3	Total	Not ascertained	1	2	3	Total
Ca-control	0	24	21	5	50	0	20	21	9	50
%		48.0	42.0	10.0	100		40.0	42.0	18.0	100
Ca-therapy	1	26	21	2	50	1	32	13	4	50
%	2.0	52.0	42.0	4.0	100	2.0	64.0	26.0	8.0	100
CHD-control	0	4	25	17	46	0	6	12	28	46
%		8.7	54.3	37.0	100		13.0	26.1	60.9	100
CHD-therapy	0	2	27	17	46	0	8	28	10	46
%		4.3	58.7	37.0	100		17.4	60.9	21.7	100
Total	1	56	94	41	92	1	66	74	51	192
%	0.5	29.2	49.0	21.3	100	0.5	34.4	38.5	26.6	100

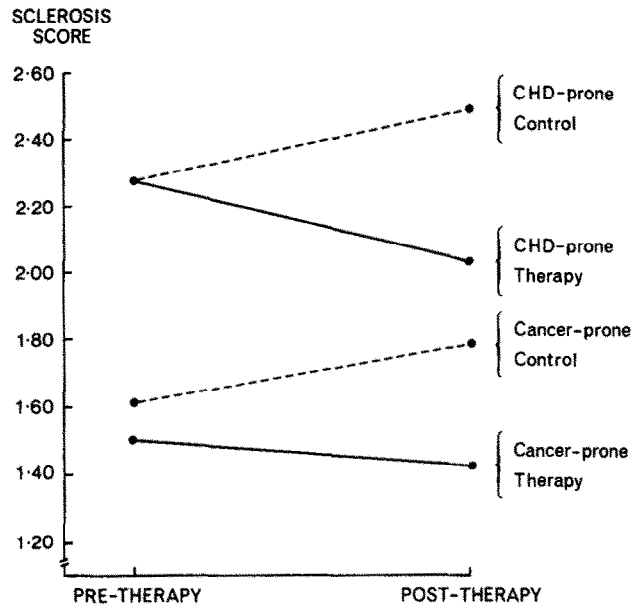


Fig. 1. Effects of therapy–no therapy on sclerosis score of cancer-prone and CHD-prone probands.

treatment significantly affected sclerosis level for both cancer-prone and CHD-prone probands, in comparison with control groups. The initial difference between cancer-prone and CHD-prone groups are significant by independent sample t-tests at the 0.001 level.

The relation between mortality and degree of sclerosis, on the occasion of the second ascertainment, showed a very significant χ^2 with $P < 0.001$. Death from CHD occurred in 0, 6 and 52% respectively of probands having scores of 1, 2 or 3 on the sclerosis scale. A similar increase is found per death from other causes (3, 14 and 35% respectively). For probands dying of cancer, the figures are 21, 6 and 2%, i.e. here higher sclerosis scores do not imply higher death rates. This is not surprising as sclerosis is not usually assumed to be a risk factor for cancer.

Table 7 shows that there is a close correspondence between the values for blood sugar, blood cholesterol, diastolic and systolic blood pressure, and the degree of sclerosis as shown in the fundus of the eye. All these relationships are significant at better than 0.001 by χ^2.

Table 7. Relation between sclerosis and other physical factors

Before therapy or control introduced		Sclerosis 1	2	3	Significance of difference
Blood pressure: systol.	n	56	94	41	
	m	147.1	180.2	207.4	
diastol.	n	56	94	41	
	m	81.1	90.6	100.6	
Blood cholesterol	n	56	94	41	
	m	233.1	301.8	333.8	
Blood sugar	n	55	94	40	
	m	155.5	210.2	206.3	
					All $P < 0.001$
After therapy or control introduced					
Blood pressure: systol.	n	64	74	51	
	m	147.6	167.0	211.7	
diastol.	n	64	74	51	
	m	81.8	87.0	104.3	
Blood cholesterol	n	64	74	51	
	m	238.7	265.8	350.4	
Blood sugar	n	54	73	50	
	m	145.4	185.5	234.3	

Table 8. Path model showing standard regression coefficients and multiple correlations between typology, physical risks factors, and therapy

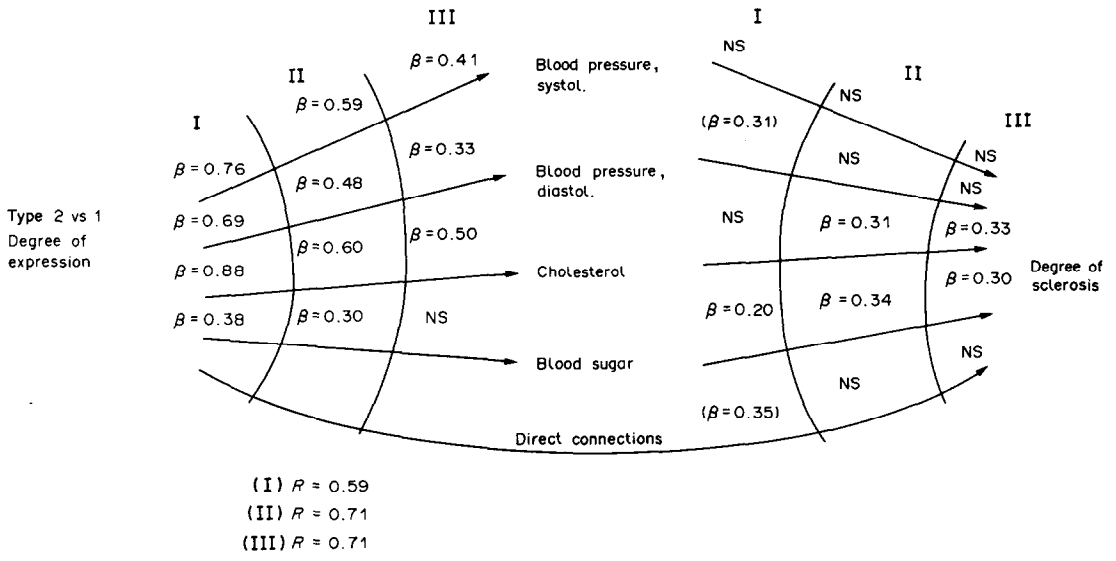
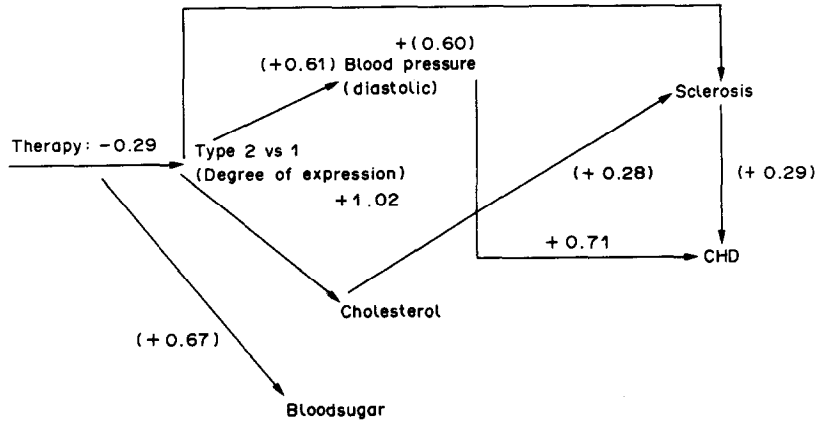


Table 8 shows the connections between degree of sclerosis, the various measures of blood pressure, blood cholesterol, blood sugar and the personality types 2 vs 1. The values for the degree of expression of the personality types were derived on a scale from 1 to 10, depending on the degree to which a person resembled his specific type. The table refers to 189 people, half belonging to the CHD-prone and half to the cancer-prone group, half subjected to therapy and half not. The table shows the standard regression coefficients β, as well as a multiple correlation R, and so far as these are significant at the 1% level; values significant between the 1 and 5% level are given in brackets: (I) stands for values ascertained prior to therapy or announcement that no therapy would be given; (II) refers to measures taken after therapy, or the appropriate announcement that no therapy would be given; (III) refers to change from before to after. In each case, the "before" refers to the mean of the first four measures taken, the "after" to the mean of the remaining measures.

The results show a significant relation, both in the means of the first four measures (before therapy) as also in the remaining measures (after therapy) between the degree of expression of Type 2 and the physical risk factors. Equally, there is a significant relation between the change in expressiveness of Type 2 behaviour, i.e. diminution of Type 2 behaviour after therapy, or spontaneously in the control group, and the lowering of the cholesterol and blood pressure values.

Table 9. Deaths from CHD in Type 2 probands, as related to therapy and physical factors



The table also shows the differential effects, and the relationship between blood pressure, blood sugar and cholesterol values and degree of sclerosis. Here too, we differentiate between the first measure taken, the second measure taken, and the change between the two. Only on the occasion of the first measure is there a direct significant relationship between the degree of expression of Type 2 and the degree of sclerosis. All other relations are determined indirectly through the physical factors of blood pressure, blood sugar and blood cholesterol.

Table 9 refers only to the results of the CHD-prone group, totalling 92 probands. The dependent variable in the table is death from coronary heart disease, 1973–1985, and the table constitute is a hierarchical causal model. Shown are the standard regression coefficients in so far as these are significant at the 1% level, or (in brackets) at the 5% level. All measures are taken after therapy (or a similar duration of time for the control group); the physical factors are means of at least two measures.

The table also shows that a change in the expression of type 2 produces a significant lowering in the values for blood sugar, blood cholesterol, and blood pressure (diastolic), in comparison to the unchanged type values in the control group, and the repeated measures of the medical risk factors. In addition there is a significant effect of the lower cholesterol values on the degree of sclerosis. There is also a significant direct relation between the change in personal behaviour and the degree of sclerosis; this relationship may of course be mediated by variables not here included in our measurements. Diastolic blood pressure, in this causal model, is directly related to death from CHD; there is no significant relationship between personality and systolic blood pressure.

DISCUSSION

The results of this study show a close relationship between personal behaviour (Type 1 and Type 2 personality), the expression of physical risk factors, the degree of sclerosis observed in the fundus of the eye, and death from heart infarct, stroke, and other chronic diseases related to the circulation of the blood. Another important finding is the negative relationship between degree of sclerosis and cancer. Personality, expressed in behaviour, obviously plays an important role, for the degree of sclerosis as well as the production of CHD, but the effects are mainly mediated by physical factors. Creative novation behaviour therapy is apparently in a position to change personal behaviour, and simultaneously to lower the physical risk factors, the degree of sclerosis, and the mortality from stroke and infarct. From the point of view of epidemiology, it would seem to be sensible to make greater use of the hitherto neglected abilities of the ophthalmologist to take a useful part in preventive medicine. Equally, it will be obvious that the use of psychological methods of treatment as a prophylactic measure could be of great value in preventing death from cancer and coronary heart disease in people predisposed to these diseases, i.e. people of Type 1 and Type 2 respectively.

Certain points may require discussion. It may seem improbable that major behaviour patterns, such as those characterizing Types 1 and 2 can be altered by 30 hr of behaviour therapy. The answer must be that there is ample evidence for the effectiveness of behaviour therapy in changing deeply ingrained neurotic behaviours which have proved resistant to all other psychiatric, medical and psychotherapeutic attempts, such as obsessive-compulsive cleaning rituals (Eysenck & Martin, 1987; Rachman & Hodgson, 1980). These methods changed rates of recovery from almost zero for psychoanalysis, electric shocks, and lobotomy to around 90% in three separate, independent studies. Thus there can be little doubt about the effectiveness of behaviour therapy to alter strongly embedded behaviours which are clearly based on a genetic foundation (Eysenck, 1987).

How does behaviour therapy bring about the prophylactic effects observed? We have certain suggestions but no certain knowledge on this point. As far as cancer is concerned, Eysenck (1985b) and Eysenck and Kelley (1987) have developed a theory implicating certain neuropeptides and hormones, such as ACTH, endogenous opioids, and cortisol, the level at which is partly determined by stress, depression and feelings of hopelessness/helpness, and which in turn influence the workings of the immune system. Thus we have a plausible sequence: hopelessness/helplessness → increase in cortisol → immunodefect → growth of cancer cells. It hardly needs saying that this is not as yet a proper theory, but merely a suggestion regarding the direction in which one would look to find some of the intermediaries between behaviour and disease.

As regards CHD, the obvious link seemed to be sclerosis, and this study suggests that behaviour and treatment may indeed affect the occurrence and degree of sclerosis. Again, it is obvious that much remains to be done to clarify the way in which this association is mediated, and what precisely are the factors involved. We are at the beginning, not the end, of research into this complex chain of events. Only interdisciplinary research can solve the problems involved.

It is inevitable in a pioneering study of the kind here reported that any change in behaviour explicitly targeted by the therapy employed would lead to numerous additional changes not so targeted. We tried to analyse some of these; thus there was no change in smoking behaviour in the therapy group as compared with the control group. There were changes in motor behaviour and sport participation, as already mentioned. Restrictions of time and money made it impossible to go as deeply into possible adjunct changes as would have been desirable, and these questions remain to be answered in a replication study. Whatever they might be, they are clearly subsequent to the behaviour therapy which was the major intervention variable explicitly introduced into the study. Failure of many previous intervention studies (e.g. Rose *et al.*, 1982; World Health Organization European Collaborative Group, 1982; Multiple Risks Factor Intervention Trial Research Group, 1982) incorporating many plausible items which might have been activated by our behaviour therapy interventions suggest that the major variable involved was the actual change in Type 1 and Type 2 behaviour documented in the body of this paper.

REFERENCES

Eysenck, H. J. (1985a). Personality, cancer and cardiovascular disease: a causal analysis. *Personality and Individual Differences, 5,* 535–553.

Eysenck, H. J. (1985b). Smoking and health. In Tollison, R. D. (Ed.), *Smoking and society* (pp. 17–88). Lexington: Lexington Books.

Eysenck, H. J. (1987). The role of heredity, environment, and "preparedness" in the genesis of neurosis. In Eysenck, H. J. & Martin, I. (Eds), *Theoretical foundations of behaviour therapy* (pp. 369–402). New York: Plenum Press.

Eysenck, H. J. (1988a). The respective importance of personality, cigarette-smoking and interaction effects for the genesis of cancer and coronary heart disease. *Personality and Individual Differences, 9,* 453–464.

Eysenck, H. J. (1988b). Personality, stress and cancer: prediction and prophylaxis. *British Journal of Medical Psychology, 61,* 57–75.

Eysenck, H. J. (1990). Type A behaviour and coronary heart disease: the third stage. *Journal of Social Behaviour and Personality, 5,* 25–44.

Eysenck, H. J. & Kelley, M. J. (1987). The interaction of neurohormones with Pavlovian A and Pavlovian B conditioning in the causation of nerosis, extinctiveness and incubation of anxiety. In Davey, G. (Ed.), *Cognitive processes and Pavlovian conditioning in humans* (pp. 251–286). New York: Wiley.

Eysenck, H. J. & Martin, I. (1987). *Theoretical foundations of behaviour therapy.* New York: Plenum Press.

Feinstein, A. R. & Wells, C. K. (1974). Cigarette smoking and lung cancer: the problems of "detection bias" in epidemiologic rates of disease. *Transactions of the Association of American Physicians, 87,* 180–185.

Friedman, M. (1987). Effect of modifying Type A behavior after myocardial infarction on recurrence rate. *The Mount Sinai Journal of Medicine, 51,* 47–55.

Friedman, M., Thoresen, C. E., Gill, J. J., Powell, L. H., Ulmer, D., Thompson, L., Price, V., Rabin, D. H., Breall, W. S., Dixon, T., Levy, R. and Breng, E. (1984). Alteration in type A behavior and reduction in cardiac recurrences in postmyocardial infarction patients. *American Heart Journal, 108,* 237–248.

Friedman, M., Thoresen, C. E., Gill, J. J., Ulmer, D., Powell, L. H., Price, V. A., Brown, B., Thompson, L., Rabin, D. D., Breall, W. S., Breng, E., Levy, R. & Dixon, T. (1986). Alteration of Type A behavior and its effect on cardiac recurrences in post myocardial infarction patients: Summary results of the recurrent coronary prevention project. *American Heart Journal, 112,* 653–665.

Gallasch, G. (1985). Funduskopische Befunde bei Hypertonie. In Ganter, D. &: Ritz, E. (Eds). *Lehrbuch der Hypertonie* (pp. 405–414). Stuttgart: Schattauer.

Gill, J. J., Price, V. A., Friedman, M., Thoresen, L. E., Powell, L. N., Ulmer, D., Brown, B. & Drews, F. R. (1985). Reduction in type A behavior in healthy middle-aged American military officers. *American Heart Journal, 110,* 503–514.

Grossarth-Maticek, R. & Eysenck, H. J. (1989). Length of survival and lymphocyte percentage dskain women with mammary cancer as a functional psychotherapy. *Psychological Reports, 65,* 315–321.

Grossarth-Maticek, R. & Eysenck, H. J. (1991). Creative novation behaviour therapy with cancer patients. *Behaviour Research and Therapy.* In press.

Grossarth-Maticek, R., Bastiaans, J. & Kanazir, D. T. (1985). Psychosocial factors as strong predictors of mortality from cancer, ischaemic heart disease and stroke: the Yugoslav prospective study. *Journal of Psychosomatic Research, 29,* 167–176.

Grossarth-Maticek, R., Eysenck, H. J. & Vetter, H. (1988). Personality type, smoking habit and their interaction as predictors of cancer and coronary heart disease. *Personality and Individual Differences, 9,* 479–495.

Grossarth-Maticek, R., Eysenck, H. J., Vetter, H. & Fretzel-Beyme, R. (1988). The Heidelberg Prospective Intervention Study. In Eylenbosch, W. J., Van Larebeke, N. & Depoorter, A. M. (Eds), *Primary prevention of cancer* (pp. 199–211). New York: Raven.

Grossarth-Maticek, R., Eysenck, H. J., Vetter, H. & Schmidt, P. (1988). Psychosocial types and chronic disease: results of the Heidelberg Prospective Psychosomatic Intervention Study. In Mars, S., Spielberger, C. D., Defares, P. B. & Sarasan, I. G., (Eds), *Topics in health psychology* (pp. 53–75). New York: Wiley.

Kissen, D. M. & Eysenck, H. J. (1962). Personality in male lung cancer patients. *Journal of Psychosomatic Research, 6,* 123–127.

Lovibond, S. H., Birrell, P. C. & Langeluddecke, P. (1986) Changing coronary heart disease risk-factor status: the effects of three behavioral programs. *Journal of Behavioral Medicine, 9,* 915–937.

Metzler, A. von (1979). Zur antineoplastischen Wirkung zentralnervos wirksamer Pharmaka auf chemisch induzierte Tumoren der Ratte. *Journal of Cancer Research Clinical Oncology, 95,* 11–18.

Metzler, A. von & Nitsch, C. (1986). Carcinogenesis and the central nervous system. *Cancer Detection and Prevention, 9,* 259–277.

Multiple Risk Factor Intervention Trial Research Group (1982) Multiple risk factor intervention trial. *Journal of the American Medical Association, 248,* 1465–1477.

Osler, W. (1910). The Lumbian lectures on angina pectorus. *The Lancet, 1,* 839–845.

Rachman, S. J. & Hodgson, R. J. (1980). Obsessional compulsions. Englewood Cliffs, N.J.: Prentice–Hall.

Rodin, J. (1984). Managing the stress of aging: The role of control and coping. In: Levine, S. & Urrin, H. (Eds), *Coping and health* (pp. 171–202). New York: Plenum Press.

Rose, G., Hamilton, P., Colwell, L. & Shipley, M. (1982). A randomized controlled trial of anti-smoking advice: 10 year results. *Journal of Epidemiology and Community Health, 36,* 102–108.

Rosenman, R. H., Brand, R. J. & Jenkins, L. D. (1979). Coronary heart disease in the Western Collaborative Group Study: final follow-up experience of $8\frac{1}{2}$ years. *Journal of the American Medical Association, 233,* 872–877.

Roskies, E. (1987). *Stress management for the healthy type A.* New York: Guilford Press.

Thoresen, C. E., Friedman, M., Gill, J. K. & Ulmer, D. H. (1982). The recurrent coronary prevention project. Some preliminary findings. *Acta Medica Scandinavica, (Supplement), 660,* 132–192.

Thoresen, S. E., Friedman, M., Powell, L. H., Gill, J. J. & Ulmer, D. (1985). Altering the type A behavior pattern in post-infarction patients. *Journal of Cardiopulmonary Rehabilitation, 5,* 258–704.

World Health Organization European Collaborative Group (1982). Multifactorial trial in the prevention of coronary heart disease. Part 2: risk factor change at two and four years. *European Heart Journal, 3,* 184–190.