PSYCHOSOMATIC FACTORS IN PREMATURE MORTALITY FOLLOWING DEPRESSION

A Prospective mortality study of 685 patients diagnosed as suffering from a depressive illness

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Submitted in partial fulfilment for the requirement for the degree Master of Philosophy at the University of Surrey
The association between depression suicide and unnatural death is well established, but the association between depression and premature death due to natural causes has yet to be unequivocally established.

This thesis sets out to explore whether or not premature mortality is part of the natural history of a depressive illness; to establish the period of highest risk, and to discriminate between death following endogenous and reactive depressive illness.

A cohort was available for study consisting of all depressed patients referred to the psychiatric service in two catchment areas. These patients were followed for 24 years, and with the co-operation of the Office of Population Census and Surveys, copies of the death certificate of those who died were obtained by the researcher. A control population was prepared for statistical analysis using the England and Wales mortality Tables which are published annually.

Statistically significant premature mortality was found throughout the 24 year period from both natural and unnatural causes. Death was found to occur predominantly in the early years after referral and the diagnosis of endogenous depression was found to incur the greater mortality.

The discussion speculated on the most likely mechanisms mediating between depression and death. Possible improvements in the design were discussed and further research highlighted.

This thesis by establishing that premature mortality is part of the natural history of depressive illness, has contributed to scientific knowledge.
## CONTENTS

<table>
<thead>
<tr>
<th>CHAPTER 1</th>
<th>INTRODUCTION</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHAPTER 2</td>
<td>ONE OR TWO DEPRESSIONS?</td>
<td>7</td>
</tr>
<tr>
<td>CHAPTER 3</td>
<td>MORTALITY STUDIES OF DEPRESSION</td>
<td>10</td>
</tr>
<tr>
<td>CHAPTER 4</td>
<td>DRUGS &amp; TREATMENT PRECIPITATING</td>
<td>15</td>
</tr>
<tr>
<td>CHAPTER 5</td>
<td>DEATH FROM UNNATURAL CAUSES &amp; ITS ASSOCIATION WITH DEPRESSION</td>
<td>18</td>
</tr>
<tr>
<td>CHAPTER 6</td>
<td>THE ROLE OF ACCIDENTS IN ASSOCIATION WITH PSYCHOPATHOLOGY</td>
<td>21</td>
</tr>
<tr>
<td>CHAPTER 7</td>
<td>CARDIOVASCULAR DISEASE</td>
<td>22</td>
</tr>
<tr>
<td>CHAPTER 8</td>
<td>NEOPLASMS, DEPRESSION &amp; MORTALITY</td>
<td>28</td>
</tr>
<tr>
<td>CHAPTER 9</td>
<td>MEDIATING MECHANISMS</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Stress</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Social Events as Precipitating Disease</td>
<td>34</td>
</tr>
<tr>
<td></td>
<td>The Milieu Interior &amp; Physiological Adaption</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Physiological and biochemical change in response to emotional stress</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Personality correlates of stress</td>
<td>37</td>
</tr>
<tr>
<td></td>
<td>Psychosomatic disease and mediating mechanisms</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>SUMMARY OF LITERATURE REVIEW</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>HYPOTHESES</td>
<td>42</td>
</tr>
<tr>
<td>CHAPTER 10</td>
<td>METHOD</td>
<td>43</td>
</tr>
<tr>
<td>CHAPTER 11</td>
<td>RESULTS</td>
<td>54</td>
</tr>
<tr>
<td>CHAPTER 12</td>
<td>DISCUSSION</td>
<td>69</td>
</tr>
<tr>
<td>CHAPTER 13</td>
<td>AN INTERPRETATION OF THE RESULTS</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td>PERSONAL POSTSCRIPT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ACKNOWLEDGEMENT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>BIBLIOGRAPHY</td>
<td></td>
</tr>
<tr>
<td></td>
<td>APPENDICES</td>
<td></td>
</tr>
</tbody>
</table>
Introduction

This thesis is concerned with structural change following an emotional illness, depression which is followed by premature death. The pathogenic power of the mind on the body is well established. Wolff (1947) a pioneer in this field, was one of the first to record, following direct observation, how the emotions of his laboratory assistant Tom were accompanied by changes in his stomach mucosa. Other workers like Parkes (1969), have established that emotions are the pre-condition of disease.

The search for aetiological specific factors has been in response to the mechanistic approach to scientific enquiry pervasive in the 19th century, which yielded very little in the way of knowledge showing the exact mechanisms which effectively demonstrate how the mind and body inter-relate to produce structural change.

The medical model of disease causation which was formulated in response to the mechanistic approach has led to a gulf between the mind and body in medicine, favouring the body. For example, there is a direct causal association between the assault to a host by a pathogen and subsequent illness, but an established link between emotions and disease might be considered as pre-conditions of disease and reactions to circumstances, thus alone they cannot be regarded as causal of disease. Therefore determinants are likely to be multifactorial, and listed as constituents of time, course, response, outcome, personality.

Plato (1942) gives the reason why the cure of many diseases was unknown to the physicians of Hellas. He blamed their "disregard of the 'whole' which ought to be studied, for the part can never be well unless the whole is well". This was a holistic concept. Centuries later there is still no firm evidence to show just how the mind and body inter-relate to cause disease.
This thesis aims to provide a little more evidence on the nature of man and his relationship and reactions to his environment, by examining the structural changes and resulting disease which follow a depressive illness, and perhaps lead to death. Society will do everything within its power to circumvent death by natural causes, and it will reject those who reject life within Society, even although that Society may have been the pathogen. The favouring of the body over the mind reflects the views and prejudices of Society. Society accepts little responsibility for those who commit suicide, even showing some contempt; likewise depression is often regarded as a weakness. Yet the fact that Society can prevent a proportion of suicides by indulging in war, and that depression as an illness increases when the prevailing economic climate is in decline, implies a social interaction.

Winokur (1981) states "Awareness and recognition that depression is one of the major scourges of human life is growing steadily. Through improving diagnostic insights, it is becoming clear that 3% to 5%, and maybe even 8%, of the population suffer from this disturbance of mental stability, with an increasing risk of death by suicide."

The literature review will investigate this inter-relationship between a psychological condition, depression and death which is considered a physical condition. It will also consider the predicament of the patient experiencing a depressive illness and the constellation of symptoms involving both mind and body.

If Winokur is correct and depression is an illness of such proportions of human suffering, then clearly if part of the natural history of the disease does include risk of death, greater resources should be made available to minimise the sinister consequences.

AIMS. These are threefold to answer:

1. Is premature mortality part of the natural history of a depressive illness?

2. If so what is the period of highest risk?
3. Can a mortality study throw light on whether or not reactive and endogenous depression are separate entities?

**REVIEW OF THE LITERATURE**

**The Mortality Associated with a Depressive Illness**

All illnesses, including emotional illnesses, have an established natural history. This includes onset of illness, precipitating factors, and whether the onset is sudden or prolonged. It also includes the evolution of symptoms, the likelihood of recurrence, the choice of treatment, and attendant risks associated with the illness. The natural history of depression is well recognised as far as mortality from suicide is concerned, but the mortality following depression from natural deaths has yet to be definitely established. This review will explore the contribution of mortality to the natural history of depression.

The constellation of both psychological and physical symptoms associated with a depressive illness would seem to be associated with reduction of life on a wear and tear basis. Selye (1974) found that stress whether due to strong emotions like depression or extremes of temperature, draws on the adaptive capacity of the body. This mechanism he calls the General Adaptation Syndrome (G.A.S.). Until the work of Selye there was no good evidence of bodily deterioration following stress.

Patients dying from both natural and unnatural causes might possibly have had a depressive illness as an antecedent, but the Registrar of Deaths is only interested in the immediate cause of death. Prior and possibly causal, events such as excessive physical strain or excessive anger, are not part of the required return. It is therefore impossible to argue the case for depression as a cause of death within the existing categorisation of disease, the view being that emotions cannot kill. Resources are often allocated according to the degree to which the illness is life threatening. To this extent the status of a depressive illness is diminished in comparison with a life threatening illness like cancer. This difficulty can be traced back to the philosophical atmosphere prevalent during the
nineteenth century which encouraged research showing direct causal associations. In this scientific climate research flourished which involved physical illness, but neglected the multifactorial associations between mind and body.

The ambivalent nature of the depressive illness, having, as it does, a foot in both the mind and the body camps, causes difficulties for the patient, as well as the doctor and the researcher in their search for hard facts. What is therefore the nature of a depressive illness?

The Ambivalent Nature of Depression

Physical symptoms and psychological signs are used as part of the diagnostic criteria in defining a depressive illness, (Hamilton (1960) and Beck (1961)).

Depression is an illness characterised by a prevailing mood of depression, pessimism, apathy, lack of self esteem, exhaustion, impaired concentration, self neglect, guilt, loss of interest and suicidal tendency. Anxiety, paranoid, phobic and obsessional symptoms are often part of a depressive illness. Sleep patterns are disturbed. So much for the psychological aspects, what about the physical symptoms?

The division between psychological and physical symptoms is arbitrary but can also be helpful in making the diagnosis. Some physical symptoms are consequences of psychological symptoms: appetite may become either excessive or diminished; sexual function is usually disturbed, with frigidity in women and impotence in men. Women frequently suffer from amenorrhoea, or menorrhagia. Retardation, slowing of movement, or clumsiness leading to accidents, also occur in depression.

Physical symptoms either appear de nova, or alternatively they might be exacerbations of pre-existing symptoms. New symptoms in the absence of physical signs may affect any part of the patient's body in a depressive illness. If the depressed patient already suffers from a condition causing pain, then
depression will make the pain worse. The individuality of the patient will also effect the patient in an idiosynchratic way, depending on his personality and previous circumstances. Some patients take their symptoms to the doctor, while others do not.

Brown (1975) for instance, has shown that many depressed patients remain untreated in the community. This might be caused by the mental state prevalent in the illness and also by the confusing ambivalent nature of a depressive illness. Many patients fear stigma, they would prefer to be labelled with a tangible illness, rather than with an ill-defined psychological one.

The doctor too is likely to prefer, and is usually better able, to recognise and treat physical complaints, rather than the underlying psychological causes. In this atmosphere the patient and doctor may collude, and concentrate on physical symptoms which the doctor proceeds to treat.

The either/or orientation towards organic or functional medicine leads the doctor to adopt a stance which rarely fuses the two. The researcher also has difficulties.

**Comparability between Studies**

The research worker has the difficult task of forming testable and repeatable hypotheses which will contribute towards a greater understanding of the mechanisms which mediate between mind and body in sickness and in health.

The principal aim of this review is to seek evidence of a relationship between depression and premature death, and if so, whether there are direct or indirect causal associations. Comparability between studies is difficult, methodology is rarely congruous. Differences occurs between clinical studies with rigorous selection procedure and whole population surveys. Patients treated in hospital are usually more severely depressed than those treated as out-patients.

Length of follow-up effects the results causing an uneven distribution of unnatural deaths. Barraclough (1974) demonstrated that unnatural deaths occur predominantly in the first months following discharge from hospital. Short term
follow-up studies are also likely to include an excess of causes with depression secondary to undiscovered physical disease. Allowance must also be made for the fact that results obtained from retrospective studies are less reliable than those from prospective studies. Sex, age, social class and ethnic differences also make for difficulty when comparisons are made.

All these factors must be considered when comparing the results from different studies and when designing research to test hypotheses. Finally, results may be confounded by the continuing controversy as to whether depression is one illness or two.
CHAPTER 2

One or Two Depressions?

Controversy exists over whether there are two types of depression or whether the two apparent types are at different ends of the same continuum. The popular view is of a dichotomy of depression, with neurotic depression following precipitating causes, and endogenous depression, being an illness that appears for no apparent reason in patients with well balanced premorbid personalities. Endogenous illness is considered to be caused by some internal metabolic imbalance, this process then distorts mood and often reality, so that endogenous depression is called a psychosis. In neurotic depression there is no distortion of reality. Unipolar is the name often given to those patients who have recurrent attacks of depression only; while bipolar patients suffer both depression and mania. Lader (1981) feels there is more emphasis on physical symptoms in patients suffering from bipolar depression.

Depression frequently appears in association with organic illness while patients can also be classified as having primarily a personality disorder together with secondary depression.

There are no established laboratory tests which help the psychiatrist to formulate a diagnosis. Psychiatry, unlike other branches of medicine, depends on clinical skills which include studying the course of the illness, social and family background, and premorbid personality. The psychiatrist relies on his personal judgement, usually during a face to face interview.

There are two official principal methods of classification in use. One is the 9th revision of the International Classification of Diseases of the World Health Organisation, (ICD). This is used in most countries with the exception of America. In America the 3rd edition of the Diagnostic and Statistical Manual (DSM III) of the American Psychiatric Association is used to define and classify disease.
The ICD classification depends largely on the experience of the examiner and allows some leeway in making a decision, whereas DSM-III provides systematic and operational criteria defining the clinical picture, into which all patients with a particular diagnosis must fit.

The criteria for a primary major depression (DSM 111) excludes that superimposed on bereavement (death of close relative or friend).

This illustrates the difference that classification could make in research performed in the United States of America compared with that in countries using the broader classification of ICD.

Hirschfield et al (1980) recommended some caution in using the term 'situational' or 'reactional' depression to denote a discrete type of depression. They found no evidence to support the validity of a distinct subtype of depression on the basis of precipitating events. They did find that major depressives generally experienced more stress prior to the onset of depression when compared with controls. The group which they termed 'situational' depression did not have abnormal personalities, and their symptomatology and clinical course were not strikingly dissimilar from major depression.

Paykel et al (1971) set out to test the distinction between endogenous and neurotic depression and to verify if they form distinct groups, or whether they are best regarded on a continuous dimension with no clear cut boundaries. Low life event scores and low neuroticism were associated significantly but weakly with symptoms described as typical of endogenous depression. The authors cite other findings and concluded that the endogenous/neurotic distribution is a continuum with many gradations and no clear cut-off points.

Copeland (1984) established that there is no distinctive clinical picture associated with either diagnosis, and there were no important differences on any measure of outcome at follow-up after 5 years.
Hirschfield, Paykel and Copeland all concluded that there is no distinct clinical picture associated with reactive and endogenous depression. Lader (1981) suggests severity of depression is perhaps a more important distinction. This factor also determines whether patients are treated by their general practitioner, or by a psychiatrist.

There are other studies which favour a depressive dichotomy. Cortisol suppression has been associated with the neurotic/endogenous dichotomy of depression. Cortisol, a hormone which comes from the adrenal gland, is controlled by the pituitary gland, which in turn is regulated by that part of the brain called the hypothalamus.

In depressed patients elevated levels of cortisol were found in the blood and urine when compared with controls. It is possible to suppress the cortisol secretion in the normal person by giving a drug called dexamethasone, but in the most seriously ill patients with endogenous depression suppression does not occur. Such a response is not seen in reactive or neurotic depressed patients. Because of these factors it is difficult to ignore the endogenous/neurotic dichotomy which is extensively used by psychiatrists.

What remains lacking in the depression controversy is comparable outcome studies. Mortality is an outcome which is easy to measure, but prospective long-term mortality studies using specific criteria are rarely directly comparable, as the next chapter shows.
Mortality Studies of Depression

The last chapter highlighted difficulties which make comparison between studies problematical. The next step must be to review mortality studies to find out whether (1) Depressive illness is associated with premature death. (2) To determine the causes of death.

Scientific advancement leads to changes in emphasis, studies conducted several decades ago reflect the treatment practices current at that time. Drugs and other treatments considered safe are often later found to have harmful effects. Trends such as hospitalisation vs. community based treatment may also effect mortality. For these and other reasons the selection of a controlled population on which to base probability calculations needs careful consideration.

Norton and Whalley (1984) set out to examine the mortality of patients treated with Lithium. At first sight this study appeared comprehensive, but on closer scrutiny the flaws appeared, probably due to the retrospective design used. The authors searched Public and Health Service records of all the 791 depressed patients who had received lithium for at least two months in a 10 year period. They then traced 751 patients, of whom 33 patients had died, 7 remained un traced. The expected mortality was 11.66. Excess mortality was attributed either to suicide or to cardiovascular disease. This study confirms excess mortality, and highlights suicide as the most frequent cause of death in the younger age group. Cardiovascular disease was the major cause of death in the older age group, but 9 of the 14 patients who died from cardiovascular disease already had clinical abnormalities of the cardiovascular system before the introduction of the lithium.

This work suggests that both a depressive illness and cardiovascular disease were associated with death in the older patients. The method shows that the authors used case records and conducted a retrospective study, both of which factors throw limitations on the results obtained.
If lithium had the suggested causal association, then the quantity of the drug should be an important factor, but the authors appeared to have neglected this, they did not compute total dosage and even included those patients who had only been prescribed the drug for a two month period. They did compare records of serum lithium levels and found no difference between those patients who died and controls. Presumably the older and more chronic patients would have received the drug over a prolonged period without necessarily incurring a high concentration of lithium at any one time.

**Lewis** did pioneering work back in (1934). He studied the culminating structural effect of stress in a manic-depressive illness in relation to prognosis. He quotes Strecker and his co-workers who compared 50 recovered and 50 unrecovered cases of manic depressive psychosis in patients admitted to a mental hospital during a four year period. The unrecovered group were found to have significantly more cardiovascular and renal disease. Strecker's work is in agreement with Norton and Whalley (1984), i.e. that unrecovered patients were older and had cardiovascular disease.

The findings of **Selye** (1974) are important here; he found cardiovascular disease and renal disease in stressed animals in stage 3 of the General Adaptation syndrome. This will be discussed on page 33.

**Norton and Whalley** (1984) associate death with lithium. The Lewis study in 1934 also found excess deaths in a cohort of depressed patients. Cardiovascular deaths were in excess in both studies. Neither study considered premature death to be due to the stress of suffering from repeated attacks of the illness over a prolonged period. The findings of Selye were not available in 1936 and the 1984 study failed to consider this hypothesis.

The evidence is still inconclusive as other authors like **Larson and Sjörgen** (1954) and **Fremming** (1951) found no increased mortality associated with a depressive illness. Nor did the recent American study by **Martin et.al** (1985). The latter authors claim that their study design permits confident evaluation of mortality. As the study was conducted on less ill patients (outpatients), the results cannot be extrapolated to include all patients.
Severity is associated with depth of depression and associated symptoms and is therefore most likely to include those patients most at risk from premature death. Norton and Whalley confirm this and also highlight the diagnostic differences.

Patients in the Martin et al. (1985) U.S.A. study, with a preponderance of physical symptoms, were associated with the label Briquet’s Syndrome, a diagnosis with connotations of hysteria. The United Kingdom more readily accepts depressed patients as having co-existing physical symptoms, the view being that the psychological illness will activate symptoms due to central nervous system arousal. In this way some, though not all, depressed patients will somatise their depression, showing a number of physical signs. Use of DSM III classification as previously discussed might have excluded some patients who would have been included by using the broader criteria of classification of the ICD.9.

It is interesting to speculate at this point whether treatment practices have any bearing on differences in formulating a diagnosis. When assigning a diagnosis, the diagnostician will be influenced by the treatment and management available. Eclectic treatment allows a more varied programme of intervention.

Tsuang and Woolson (1978) examined mortality over 30-40 years in patients suffering from schizophrenia, mania and depression. They considered all diagnostic groups had raised death rates in the first 10 years of follow-up; but when suicide and accidental deaths were excluded there was no significant excess of deaths in males with mania and females with depression.

Tracing, as Sims (1973) found, is an important variable. He showed that the death rate manifested in the easily traced patients is substantially lower than in those patients traced with more difficulty.

Age - A study where the mean age is low (such as Tsuang with a mean age of 44 years) is likely to contain a higher percentage of unnatural deaths; a cohort with a higher mean age would expect more deaths from natural causation, and this is what was found. The Martin study does not provide data on age enabling this to be considered.
Kay (1966) throws some light on the subject of the elderly with functional illness. In a four year follow-up of 297 subjects over the age of 65, 98 subjects were originally regarded as functionally ill mainly with anxiety and depression. The mortality at follow-up of the functionally ill was found to be significantly higher than the age-specific death rates for England and Wales.

Only one case of suicide was recorded. Kay concludes that the association between physical illness and functional disorder in old age is real and cannot be explained in terms of hypochondriasis or depression.

Kerr et al (1969) in a well designed study included a physical examination of all patients and followed 56 depressed patients for 4 years. The small number of patients followed up makes direct comparison difficult, but the method used and detailed prospective design are particularly impressive. Of the depressed male patients, 7 died from physical disease: one chronic bronchitis, one coronary thrombosis, and 5 from carcinoma. One patient committed suicide.

The two female deaths were due to cerebral thrombosis and congestive heart failure respectively. Using the exact Poisson probability test to determine the significance of the differences between observed and expected deaths, a significantly raised mortality rate was found in the total male depressive group.

Of the 28 males admitted with a depressive illness, 5 died from carcinoma, a statistically significant finding. The initial physical examination failed to reveal the presence of physical disease, yet the malignancy must have been present at that time, as all the deaths from cancer occurred soon after admission to hospital. (mean survival 1.28 years) In contrast to the patients who died from carcinoma, physical disease was evident at the time of psychiatric admission in those patients who died from other causes.; Chronic physical illness preceded the onset of persistent depressive symptoms in those patients in whom marked pre-occupation with somatic symptoms was prominent. The importance of the work by Kerr et al will be discussed again in relation to death certification.
Most mortality studies are based on death certificates. As the cause of death is seldom confirmed by an autopsy, which only occurs in 10% of deaths, studies using autopsy reports are particularly important. Enzell (1984) examined the death rate for persons in Stockholm born in 1905, who died during the years 1971-9.

This is an important study because autopsies were performed on between 70 and 80% of deaths occurring during the period. An excess mortality was found, due to cardiovascular disease and neoplasms. Neoplasms, it seems, go undetected in studies which are unable to confirm the cause of death by using autopsies. In studies which fail to establish the cause of death, undiscovered neoplasms might well have been responsible for the excess mortality found.

The mortality associated with a depressive illness and the actual cause of death is central to this thesis. There is no disputing death, but the certifiable cause of death is open to some dispute. Cameron and McGoogan (1981) found that "statistics from death certificates are so inaccurate that they are unsuitable for use in research planning." The major cause of death was confirmed by autopsy in only 61% of cases.

Autopsy proved cerebrovascular disease and infection to be particularly liable to inaccuracies of diagnosis. Furthermore, diagnostic accuracy bore an inverse relationship with the age of the patient and with time spent in hospital. Hospital records were found by the authors to contain many inaccuracies.

Thus it seems that the only reliable sources of information on cause of death are those studies where autopsies were performed, such as the studies of Enzell (1984) and Kerr (1969).
CHAPTER 4

Drugs and Treatments Precipitating Premature Mortality

This chapter will consider the part treatment plays in reducing mortality, or perhaps even accentuating mortality. Depressed patients who are referred to a psychiatrist are likely to be suffering from a severe illness needing intensive treatment, including high dosages of antidepressant drugs. Reactions to the Tricyclic and Monamine Oxidase Inhibiting antidepressant drugs which were commonly used, are frequent and may range from the mildly irritating to the life threatening. Lader (1981) reported that cardiac conduction is altered in patients receiving tricyclic drugs. The pharmacological mechanisms seem complex and they include anticholinergic blockage of vagal nerve endings, a direct effect on the myocardium, and heightened sensitivity of the heart to circulating catecholamines. The more serious defects recorded include complete heart-block, bradycardia, tachycardia, ventricular extrasystoles, atrial and ventricular arrhythmias.

Norton and Whalley (1984) presented evidence of increased mortality in a lithium treated population. We have already discussed their methodology, the conclusions drawn did not convincingly support their opinions. If the authors were nevertheless correct in attributing excess mortality to lithium, then the 2.83-fold greater than expected mortality compared with a normal population deserves consideration: of course if does so from whatever cause. This study suggests that deaths from cardiovascular disease among lithium-treated populations "maybe somewhat more likely in those patients with more severe psychiatric illness." Deaths from suicide and cardiovascular disease were increased. As previously discussed, however, increased mortality was found in depressed patients before the use of lithium and tricyclic drugs.

A further consideration is that some patients could have had pre-existing cardiovascular disease which drugs could then exacerbate. A further danger is the use of the prescribed drugs in an overdose. Mortality tables show that, as the use of coal-gas diminished, the use of tricyclic drugs and antidepressants drugs for suicide rose, corresponding with the increased prescribing practices.
Electro-convulsive treatment has been practiced for some 50 years. Electrodes are placed on the patient's temples and an electrical current is passed between them, causing a convulsion. The exact mechanism which brings about improvement is still unknown. This form of treatment is only contra-indicated in patients with severe cardiac, respiratory, or skeletal conditions.

Avery and Winokur (1976) followed 519 depressed patients for a period of one to three years and noted that patients treated with Electro-convulsive therapy had a lower mortality rate in the follow-up period than those patients who either had no drug treatment or inadequate drug treatment. The authors examined those patients who had adequate drug treatment and electro-convulsive treatment. "There was a striking decrease in mortality in both these groups as opposed to the patients who were treated with inadequate doses of medication, ward management, or non-specific psychological management". Heart attacks were considerably fewer in the group who were offered adequate treatment (either adequate drugs or E.C.T.)

Avery and Winokur (1976) showed severely depressed hospitalised untreated patients, to have a higher mortality rate than those patients who received adequate treatment. The older patients in particular were most at risk of receiving inadequate treatment and as a consequence experienced a higher mortality. As would be expected, suicide and myocardial infarction contributed to the high death rate, in patients who were inadequately treated.

Huston (1948) is in agreement, because in the late 1940's he found that Electro-Convulsive Treatment actually prevented mortality when it was given to depressed patients, compared with the untreated depressed control patients.

In conclusion, the mortality associated with depression appears to be influenced more by lack of sufficient treatment than by any harmful effects of the treatment; and this is particularly relevant in the short term where the risk of suicide is greatest. However in the long-term, prolonged use of drugs may contribute to premature death from natural causes.
The observation that adequate treatment should reduce the mortality found in depressives is good evidence that the depressive process includes mortality as part of the natural history.

The next chapter will examine the mortality associated with unnatural death.
Death From Unnatural Causes and its association with Depression

Suicide

Suicide is defined as the act of taking one's own life voluntarily and intentionally. It has a well established association with depression. As suggested in the introduction suicide statistics implicate a sociological phenomenon. Additional factors reinforce this viewpoint.

The suicide rate rose in the 1930's at the time of the Depression and fell in both World Wars. The current rate for England and Wales is about 1 in 1,000 of the adult population per year. Urban areas have higher suicide rates than rural districts, and suicide is more common in the upper than in the lower social classes; also abolition of the death penalty coincided with fewer suicide deaths by hanging.

Social isolation and lack of social support is also associated with suicide. Recently researchers have found increased deaths from suicide in the unemployed. Breakdown of relationships or loss, as forms of life stress, are often given as precipitating factors. In the elderly physical illness and pain are found to be the main contributory factors. These factors altogether suggest an underlying psychosocial association.

Between 1963 and 1974 the United Kingdom suicide rate dropped by approximately one third. The drop was ascribed to improved recognition and care of suicidal patients, particularly by general practitioners. Since 1974 there has been a minor increase in suicide and this is a cause of concern.

The sexes behave differently. Although suicide is twice as common in men as in women, the latter take overdoses or make other suicidal attempts much more frequently. The female rate is highest in the sixth decade of life, whereas in men it continues to rise to the eighth and ninth decade. This might fit in with the observation made, that women cope with widowhood better than bereaved men.
Follow-up studies reviewed by Miles (1977) indicate that approximately 15% of depressives and 10% of alcoholics eventually commit suicide. In the prevention of suicide to diagnose the underlying depression is vital, as without proper diagnosis treatment is likely to be inadequate or absent, as was suggested in the last chapter.

The fact that many patients consult a doctor in the month preceding suicide suggests that depression goes unnoticed. Barraclough et al (1974) found that two thirds of a hundred consecutive suicides had visited their family doctor in the month before death. This finding suggests that the depressed patients recognised that they were sick and needed help. It appears that either the patients failed to convey the severity of their illness to the doctor, or the doctor failed to recognise the condition of the patient.

64 of the 100 were diagnosed retrospectively as suffering from depression, but only 19 were receiving antidepressants, and in most of these the type and dose were inappropriate.

The weakness of Barrachough et al's study is that like most suicide studies it was retrospective, but even well designed prospective research will not include all psychopathology as many suicides remain undetected.

This is in keeping with the findings of Brown et al (1975) that depression which is serious enough to warrant treatment is common in the community in patients who do not receive treatment. Such covert morbidity concurrently never becomes a statistic.

Tsuang and Woolson (1978) found that suicide and accidental death contributed greatly to mortality in affective disorder. In their study, however, if suicide and accidental deaths were excluded excess mortality disappeared for males with mania and for males and females with depression. They found that the increased mortality of affective illness was associated with unnatural deaths.
Work on hormone levels by Bunny et al. (quoted by Winokur 1981) shows that striking elevations in excretion levels of adrenal hormone were found in the urine of serious suicidal patients prior to the suicide. This test might be useful in separating the suicidal patients from the non-suicidal patients.

Holding and Barraclough (1977) investigated accidental deaths and found 60% to be associated with mental illness. Barraclough lists symptoms recorded during the four weeks before suicide. The depressed suicides resembled an unselected sample of depressives, but they appeared to be more severely depressed when assessed on symptoms. It is interesting to note that abnormal personality was a feature of the depressives who committed suicide. This may be due to the patients response to being ill, or more likely the suicide might be one of the consequences of possessing an abnormal personality. A history of attempted suicide was also found by Barraclough to occur 8 times more frequently in such personalities. They also found that in their population the single and widowed were overrepresented. A high proportion of married suicides who were either separated or living unhappily with their spouses committed suicide. This is confirmed by Berkman and Syme (1979) who found that isolation led to mortality. (To be discussed later).

The verdict of accidental death is categorised under unnatural death; the association between suicide and accidental death is not always easy for the coroner to establish.
CHAPTER 6

The Role of Accidents in Association with Psychopathology

The natural history of a depressive illness has a well established association with suicide but the association with accidental death is less well defined; no doubt this is because fatal accidents, like suicides, are difficult to assess retrospectively.

Hinkle and Wolff (1957) found that those people who had the greater number of psychological disturbances of mood also had the greater number of accidents. The work of the following authors suggests that psychological disturbance was a factor in accidental deaths; whether this could be further associated with a depressive illness is another possible explanation for the increased mortality associated with unnatural deaths and depression.

Holding and Barraclough (1977) showed, following an examination of 110 coroners records of accidental deaths, sixty percent to be classified as mentally ill before they died. Depression, drug dependence and alcoholism accounted for over three-quarters of the diagnoses. These authors concluded that deaths given accidental verdicts should be included in the study of the mortality of the mentally ill.

The work of these authors suggests that a verdict of accidental death could have been brought in some cases which were really suicide. The next chapter will review the association between natural causes of death following a depressive illness.
Cardiovascular disease

The studies which have found an excessive death rate have highlighted causes of death following a depressive illness as suicide and cardiovascular disease, and to a lesser extent neoplasms.

The close connection between the heart and the emotions has been inferred in English literature throughout its history. Poetry, the supreme English art, expresses the constancy of human values and emotions with such phrases as "death due to a broken heart." The term heart-ache implies that feelings may provoke pain in the heart. This chapter will review research and look for evidence of direct and indirect causal associations.

Swift (1744) exemplifies this when he said "My female friends whose tender hearts have better learned to act their parts". On a purely physiological basis the effect of the emotions on the heart is understandable according to both Bishop and Reichert (1971) and to Wolf and Wolff (1946).

Parkes (1969) associated death following bereavement with cardiovascular deaths. He found 77 deaths due to coronary thrombosis in widowers occurring in the first six months of bereavement, where only 46 deaths were expected from the control population.

Appels and Mulder (1984) give some support to the hypothesis that depression may both precede and follow a myocardial infarct. In view of Selyes work, it is interesting that these authors make particular mention that exhaustion and depression precede myocardial infarction.

The present author's unpublished study of post infarction depression failed to support the hypothesis that depression postdates infarction.
Cameron and McGoogan (1981) advised some caution in using death certificates when individual categories of death were being studied. In the cardiovascular category they found that coronary thrombosis was frequently incorrectly diagnosed, but was falsely included in the death certification return as often as it was incorrectly excluded from the return to the Registrar. This demonstrates a weakness in studies based on death certificates. Studies which have used autopses like Enzell (1984) have nevertheless found excess mortality due to cardiovascular disease and to neoplasms.

Coronary heart disease is the leading cause of death in Britain and has been rising for the last 40 years. Of course not all those who die from heart disease are depressed, but in previous chapters an association between a depressive illness and cardiovascular disease was repeatedly found by authors studying mortality and depression. Wolf and Wolff (1947) studying the physiology of the heart, discuss the capacity of the healthy heart. They emphasise the need to study not the heart in isolation, but to include the circulatory system and the interaction between life situations causing minor stress, and the effect these stresses have on emotions: "The undamaged heart has a capacity to meet strenuous efforts far beyond those of the usual daily activities. The ability to tolerate strenuous effort cannot be interpreted solely as an expression of myocardial effectiveness but rather as a manifestation of the total circulatory function, which in turn is intimately related to the life situation of the individual, his attitudes towards the latter, and his feelings".

The contribution of the study by Wolf and Wolff is that the reactions of individuals in and to their everyday environment are relevant to disease. This opinion was formed by following over a one year period, on a day to day basis, the cardiovascular and respiratory function of healthy human subjects.

Emphasis was placed on the persistent low grade stresses and strains which are part of every day living.
Breathlessness, palpitations, heart pain, giddiness and fatigue were found to occur in response to emotions generated by adverse life circumstances. Feelings of anxiety, guilt, rage, frustrations, fear and resentment were found to provoke costly demands on the work of the heart. It was observed however that individuals differed in their response to life situations and thus in the intensity and duration of cardiovascular and respiratory responses. All of this suggests that the individual manifests a variety of ways of dealing with his environment which may either involve or spare his cardiovascular and respiratory functions. This variability would depend on cognitive and individual differences and on personality makeup.

Many authors reinforce the important role of psychological factors in cardiovascular disease by studying the same problem from different directions. They all agree that stress causes emotional reactions which are costly in terms of the performance of the heart and respiratory system. The reciprocal interplay between emotions and physiology has been reviewed, but it is still not clear how psycho-pathology causes tissue damage leading to structural death. The alternative must also be considered, that structural damage is the genesis of psychopathology.

Davies (1970) studied a particular style of behaviour in which "unventilated affect takes its toll of the appropriate physiological system." The studies of Brod (1970) showed how all components of the cardiovascular system are responsive to relatively minor stress confirming that there is an increase in peripheral vascular resistance during psychological stress which in turn decreases during exercise. They advance the hypothesis that peripheral resistance increases when contained stress is a substitute for action.
Friedman and Rosenman (1959) produced the concept of 'Type A' coronary prone behaviour and they identified this particular behaviour as sustained aggression, competitiveness, and a chronic sense of time urgency. 'Type A' are further described as impatient, constantly alert, and intensely committed to vocational goals. The authors hypothesised that coronary risk would vary with the intensity of this behaviour.

Friedman and Rosenman proposed a Sisyphus pattern of behaviour, "striving without a sense of satisfaction or fulfilment like the legendary Greek giant". The authors reported a 10 year prospective study of 65 patients who had suffered from myocardial infarction and 65 controls. There was excess mortality in the patients who were positive in the Type 'A' behaviour questionnaire.

Although the emphasis in this research was on personality, it was reported that depression correlated with the mortality rate. The two deaths by suicide in the group were not predicted. The almost incidental findings by Friedman and Rosenman, are in keeping with the work so far reviewed. They not only makes the association between cardiovascular disease, personality, behaviour and depressive illness, but goes some way in showing the mediating mechanisms involved in structural deterioration. Some authors, it must be remembered, have disputed the work of these authors.

One postulation could be that although stress is an integral part of the maturation process, the ability to discriminate between, or adapt to, a stressor depends on personality.

One likely hypothesis might be that peripheral resistance increases when contained stress is a substitute for action. It has long been felt that suppressed anger contributes to raised blood pressure. Groen (1957) described the dramatic fall in blood pressure associated with a leucotomy. He cites a patient who developed malignant hypertension, the prognosis being rapid death. After a prefrontal leucotomy, there was complete recession of hypertension.
Hypertension due to stress or tension, can be reversed by using behavioural treatments such as relaxation or bio-feedback techniques. The results are not as good as the early literature suggested, because reduction is not sustained without continued behaviour therapy. From this it also follows that if a prolonged pattern of behaviour leads to structural arterial change, then this is no longer amenable to treatment aimed at reversing the psycho-physiological mechanism.

Davies (1969), in a well designed study investigated the relationship between specific personality dimensions and blood pressure. He used male factory workers aged from 45-54 as subjects. He used males, not only because they were available but also because of the twin study findings of Mathers et al (1961). They studied blood pressure, heart rate, and the electrocardiogram in twin adults, and produced evidence that environmental factors influence the blood pressure more in men than in women. The subjects were then divided into groups of high, average, and low blood pressure.

A significant positive correlation was confirmed between the level of blood pressure, body weight, arm circumference, a square body build and a family history of cardiovascular disease. A significant negative relationship, independent of these factors was found with a history of neurotic traits in childhood, current neurotic symptoms, and the neuroticism scale of the Eysenck Personality Inventory.

If these findings are correct they imply that neuroticism protects one from raised blood pressure. Davis (1970) found no relationship between the diastolic blood pressure, extraversion and the lie scale of the E.P.I. Those subjects, however, who were rated high in the neuroticism scale and who regarded themselves as prone to anxiety, were noted to have lower diastolic blood pressure readings than those who did not display such features.

This interesting finding, when considered with the findings of Hinkle and Wolff (1957) which are discussed later, suggests that differing personalities have different coping strategies. The various authors discussed have consistently found that the reactivity of the heart, tested in laboratory situations, is subject to emotional influence. Depression, an emotional illness, has also been found to have strong associations with death due to cardiovascular disease.
Eastwood and Trevelyan (1971) studied the problem from a different direction. They conducted an epidemiological study via a screening programme in a group practice.

They designed their study to examine the relationship between physical and psychiatric morbidity, they examined multiple disease aetiology and multiple responses by man to agents threatening health.

Their findings confirmed the relationship between stress, as measured by psychiatric disturbance, and presumed coronary heart disease. Eastwood and Trevelyan postulated that the psychiatric illness is the stress. This highlights the difficulty caused by the different definitions of the word stress.

Two points are relevant here; firstly, the strong emotional links between the mind and the heart via the physiological response of the body resulting from mental turmoil. Secondly, interpretation of the findings seems not to include the effect perception has on an individual’s response to stress. Adjustment depends on learning coping behaviour via personality. A type “A” person would experience some difficulty if told to avoid strong emotional involvement, if Davis (1970) is correct when he says Type “A” individuals attach emotions to their ideas and goals.

Summary

This chapter has demonstrated the importance of psychological factors in cardiovascular disease. It has looked at the reaction of the cardiovascular system, by monitoring its reactivity to stress, and from the other direction by looking at depression when it is associated with cardiovascular disease. There seems little dispute that emotions have a powerful influence on physiological reactivity.

The pathological mechanisms involved have been discussed, but until the underlying mechanisms are found, little can be achieved in the important work of prevention.

Neoplasms have already been found in association with depression and the next chapter will discuss this further.
CHAPTER 8

Neoplasms Depression and Mortality

So far in this review the overall mortality has been discussed in association with depression. This was followed by discussion of the two subdivisions of death: natural and unnatural death. The preceding chapter examined one of the main causes of death associated with a depressive illness, i.e. cardiovascular disease. The role of neoplasms in relation to psychological and physical morbidity is a subject of current interest.

Malignant disease has been found in some studies to be preceded by a depressive illness antedating the discovery of malignancy. Kerr et al (1969) merits special consideration because, although the authors had the problem of finding a comparable control group, a post mortem was performed on most of the subjects. Studying the relationship between premature death and affective disorders, they found deaths from carcinoma among male patients with depression significantly more frequently than expected.

The authors considered that the depressive illness appeared to bear no specific relationship to the site of the tumour. Although numbers are small, this study is rigorous in design and therefore the findings are particularly relevant to this study. The patients examined had no physical disease apparent at initial assessment, apart from one patient who had moderate hypertension and two patients where routine sedimentation rates were abnormal i.e. 30-34 mm./hr. these two patients subsequently died of cancer. Considering that the mean time between hospital admission and death was only 1.4 years, the probability is that these patients were diagnosed as suffering from depression and that the cancer had remained undetected and pre-existed the depression. Cameron and McGoogan (1981) also found that neoplasms often go unnoticed.
The patients who subsequently died of cancer had responded rapidly to antidepressant measures, although "the reason for their excellent immediate response to anti-depressant measures lasting some weeks or even months remains obscure". The explanation might be that the patients were denying the physical symptoms and deceiving their doctors by focusing on the depression. This behaviour might actually have reduced the life of these patients, because attention was diverted towards treating the emotional illness causing the physical illness to be neglected.

The authors used autopsy reports and found tumours which often go undetected, so that any mortality study examining causes of death needs to consider the unreliability of death certificates. The presence of a tumour detected or undetected need not be related to the cause of death.

Hagnell (1966) also reported a higher than expected incidence of cancer in women with "substable" personalities and suggested that personality could predispose to a depressive illness, and a depressive illness could lead to cancer.

Brown (1975), found a preponderance of modern evidence suggesting that malignant disease is, in some cases, preceded by a depressive illness of an apparently endogenous kind, antedating the discovery of the malignancy. Clinical observations pointed strongly to a non-metastatic causal connection between cancer (including occult cancer) and functional depressive illness on the one hand, and structural brain damage on the other. Brown proposes that some cases may be caused by immunological interference with the activity of serotonin, one of the neurotransmitters thought to be involved in depression.

Denial, which is a defence mechanism has also been implicated by Greene (1956) in leukaemia and lymphoma. Similarly Bahson and Bahson (1966) studied cancers of various sites in a small number of males and females, and reported that denial and repression implicit in the concept of poor outlet for emotional discharge, were present.
Schmale and Iker (1966) designed a most interesting study to test the hypothesis that the presence of cancer can be predicted on the basis of psychological criteria, defined as high hopelessness potential, and revealed by the subject's reaction to life events. An interview to predict the presence or absence of cancer was significantly correct. There is clearly a relationship between functional illness and organic destruction, i.e., between neoplasms, personality, behaviour, depression and death; the nature of this relationship is as yet unknown.

Enzell (1984) during a nine year period investigated the mortality of depression in the elderly and found excess mortality due to cardiovascular disease and to neoplasms. This study was well designed, it was prospective, and autopsies were performed. One weakness was that the cohort was elderly and therefore comparison with a younger cohort cannot be made.

The literature gives support for an association between personality and emotion and depression with death due to cancer. However, only in those studies where autopsies are included in the investigation, is depression followed by death due to cancer, defined. Neoplasms may have been a predisposing factor in the depressive illness, but not always the actual cause of death.
So far in this review, the studies which have found premature mortality have suggested that there is an association between an emotional illness and death. The principle cause of death has been suicide and cardiovascular disease, and to a lesser extent neoplasms. Unnatural death has an accepted association following a depressive illness, but the mediating mechanisms between depression and natural death are difficult to confirm. The research reviewed so far has shown that personality and behaviour provoke adverse emotions that trigger physiological responses, which in turn might be responsible for disease and death. The next step must be to use the evidence provided by research studies, and examine the most likely route from depression to death.
Mediating Mechanisms

Stress

We have read earlier of the associations between various diseases and emotions, but the mediating mechanisms are not clear.

*Eastwood and Trevelyan* suggested that the psychiatric disturbance resulted from the stress generated by coronary heart disease. *Wolf and Wolff* and *Taggart* measured the physiological effect on the cardiovascular system caused by day to day stress. Other authors like *Selye* and *Groen* studied the structural changes which occurs as a result of stress. Finally *Davis, Friedman* and *Rosenman* related heart disease to personality and to individual coping behavioural response. All of this demonstrates that emotional illness is associated with death due to natural causes, which occurs principally by cardiovascular disease and to a lesser extent by neoplasm.

Stress related disease is a concept which has only recently been adopted by the medical profession, though disorders such as gastric ulcers, psychogenic asthma, or dermatoses have long been regarded as psychosomatic disorders.

The word "stress", was originally borrowed from the physical world and is there defined as "force or pressure producing change". *Selye* (1974) defines stress as the biological response to any type of demand made upon the body, and not a component of the environment.

*Haward* (1960) revealed that the word stress is used in different ways: "sometimes it is the stimulus as implied by the phrase stress-evoked behaviour, at other times it maybe the response, as when reference is made to stress inducing stimuli, or it can be used as a combination of both. An example of this is when investigators claim that stress can be defined only in the terms of the behaviour it elicits." This illustrates the elusive identity of stress.
Selye (1974) a Venetian endocrinologist used rats as his experimental animals and wrote his first book on stress in 1950. He said that "From the point of view of its stress producing, or stressor activity, it is immaterial whether the agent or situation faced is pleasant or unpleasant; all that counts is the intensity of the demand for readjustment or adaptation".

Essentially different stressors, heat, drugs, sorrow or joy, could provoke an identical biochemical reaction in the body. Selye further points out that it can be demonstrated by objective quantitative biochemical determination that certain reactions are non-specific and common to all types of exposure to a stressor. Selye's General adaptation syndrome consisted of a three part pattern of responses over a period of time:

1. The alarm reaction. This corresponds to the fight or flight response which includes autonomic physiological activity.

2. The stage of resistance. Here the stressed animal's function returns to normal, and its threshold to further stimuli rises. If stress continues the third and final stage may occur.

3. The stage of exhaustion. At this stage the symptoms of alarm reaction reappear and the animal dies shortly afterwards.

Death according to Selye is caused when the animal's adaptation ability has been exhausted. If the animal is dissected at this stage it has enlarged adrenal glands, the spleen releases more red blood corpuscles and the blood clots more quickly. The second feature found by Selye was that the lymphatic nodes and thymus glands had atrophied, and the stomach was covered in ulcers. The mechanism which mediates adrenal enlargement is the autonomic nerves, they directly stimulate the adrenal glands to release epinephrine and norepinephrine. It is now believed that epinephrine is associated with fear, while norepinephrine is associated with rage. The release of these hormones further reinforces the autonomic nervous response by increasing the heart beat and blood pressure. These physiological consequences of stress will be discussed in the next chapter.
Perhaps Wolff summarises the situation by saying "Mans attempt to adapt to life situations which do not fulfil his needs, which frustrate his aspirations, or which place heavy and conflicting demands upon him are very often associated with an increased susceptibility to all forms of illness".

**Social Events as Precipitating Disease.**

Dohrenwend (1974) summarising the work of many eminent researchers who support the hypothesis that stressful life events play a part in the etiology of various somatic and psychiatric disorders says, "there is considerable disagreement among researchers, as to the nature of this role."

Holmes and Masuda (1974) (quoting from Dohrenwend) similarly postulated "that life change events, by evoking adaptive efforts by the human organism that are faulty in kind and duration, lower bodily resistance and enhance the probability of disease occurrence." In contrast, Hinkle and Wolf (1957) emphasised the primary role of predisposing factors and the secondary role of life events, with respect to certain types of illness.

It appears that looking for causal mechanism in terms of stressful life events is inconclusive. Most studies concentrate on those who present themselves as patients, a selective and biased minority. Life events are very subjective measures. Bereavement may be devastating to one person enjoying a close relationship, but a happy release to another suffering an unhappy marriage, yet it is always listed as a stress factor.

This does not contradict Selye's thesis, for he reports that positive and negative experiences can be stress producing, and it is the intensity of adaptation which counts.
The Milieu Intérieur and Physiological Adaptation

Stress when external to man in the environment yet influences the constancy of the milieu interior.

Claude Bernard the French physiologist early in the nineteenth century recognised that the 'milieu intérieur' of a living organism must remain constant despite changes in the external environment. He realised that it is the fixity of the milieu intérieur which is the condition of free and independent life. Numerous physiological states must be maintained within narrow limits to keep the 'milieu intérieur' stable. Stress response begins in the hypothalamus. Its functions include regulation of growth and sexuality, it also helps stimulate such emotions as fear, rage, and pleasure. The hypothalamus works to control the autonomic nervous system and activates the pituitary gland which in turn releases hormones into the bloodstream.

There is some modern evidence which suggests that people who feel responsible and in control of their lives react medically in a different way from those whose locus of control is external and who feel that other people regulate their lives. Perhaps an example of this is provided by the findings of Brown (1975) and his work on vulnerability factors.

Physiological and Biochemical Changes in Response to emotional Stress

Under this heading will be discussed the position of the depressed patient in terms of how feelings of pessimism and hopelessness may influence the body.

As long ago as (1939) Cannon discussed the mechanisms whereby signals and symbols produced by conditioned noxious stimuli, alter neuroendocrine secretion levels in the body and have a direct effect on the autoimmune system. This effect acts to undermine the host resistance and furthermore shows why, in spite of the fact that we all have the same internal apparatus, the individual response alters according to the way one interpretes signs and symbols.
Homeostasis depends mainly upon two types of reaction, syntoxic (together) and catatoxic (against). Either of these biochemical reactions can lead the body to mobilise and pacify, or incite and fight.

Selye (1974) discusses how syntoxic stimuli act as tissue tranquilizers creating a state of passive tolerance; whereas the catatoxic agent causes chemical changes mainly by producing destructive enzymes which actively attack the disease or pathogen. Syntoxic hormones are the corticoids such as anti-inflammatory cortisone. These reactions have evolved during the course of evolution, living beings having learned to defend themselves against all kinds of assaults, whether arising in the body or coming from the environment.

Emotional illness produces damage through exaggerated emotional responses, whereas the direct pathogen causes harm irrespective of the body’s reactions. An individual may thus combat disease either by passive tolerance, or by active combat. There is some evidence to suggest that personality can determine vulnerability towards certain diseases. Fighting spirit as a predictor of a favourable outcome in response to cancer is one such association. The following authors give some insight into physiological reactions.

The various biochemical reactions are observed in illness, McClure et al (1966) found high plasma cortisol levels in depression due to an increased response of the adrenal cortex.

Raab et al (1966) investigated the mechanism by which emotional factors produce coronary insufficiency, due to an increased oxygen demand by the myocardium, with catecholamines and corticosteroids acting as mediators.

Funkenstein et al (1954) emphasised that adrenaline release would be associated with anxious emotional state, whereas noradrenaline release would be associated with an aggressive emotional state.
Schlachter (1957) studied volunteers and found 72% to have a predominantly adrenaline response to acute fear, and 35% predominantly a noradrenaline response to pain. These authors thus give evidence to support the view that emotional factors trigger biological responses which might trigger physical disease.

Cassel (1976) speaking as an epidemiologist amalgamated the work of Selye and others that psychosocial processes enhance susceptibility to all disease. By causing a psycho-social connection between the internal state of homeostasis and the environment.

Henry (1969) examined colonies of animals. In the process of establishing their dominance they show a sympathetic adrenal medullary response with persistent elevated blood pressure.

The animals forced into subordination, however, showed more of the pituitary adrenal cortical response pattern, a pattern more consistent with depression and hopelessness. As the human species have the same internal structure, it would seem logical to expect a comparable response to environmental conditions. However, man by virtue of individual differences due to personality differs by not responding in a stereotyped manner, being free to exert control and manipulate his environment. In man it is the mind which has to change in order to live in harmony with the environment. This will become clear in the next section which considers personality.

Personality Correlates of stress

Hinkle and Wolf (1957) found that emotionally insulated stress resistant subjects, who had certain personality traits in common, were usually flexible in their attachments to other people, groups and to goals.
They readily shifted to other relationships when established ones were disrupted. Many displayed a clear awareness of their own psychological limitations. If such a person saw it as his lot in life to work at an undemanding job, to live alone, to fail to get ahead, he felt no need to be unhappy about it, or to rebel. This work suggested that the healthiest members of the sample often showed little psychological reaction to events or situations which caused profound reactions in other members of the group.

Eysenck (1969) in his book "Personality Structure and Measurement", indicates certain ways in which individual differences may account for excitation and inhibition in response to external stimuli. This work can be related to the feedback mechanism. Introverts are characterised by a reticular formation, the activating part of which has a relatively low threshold of arousal, while the recruiting part has a relatively high threshold.

Conversely extroverts have a relatively high threshold of arousal and a recruiting or synchronizing part, with a low threshold of arousal. Under identical conditions, therefore, cortical arousal will be more marked in introverts.

Eysenck (1969) has also indicated certain ways in which individual differences in excitation and inhibition may be instrumental in mediating neurotic and clinical behaviour. He argues that neurotic symptoms such as phobias, anxieties, obsessional and compulsive behaviour patterns, reactive depression and so forth, are essentially autonomic responses, or skeletal reactions made as a consequence of conditioned autonomic responses. The argument from individual differences in conditioning ability is only one link between the law of excitation and inhibition on the one hand, and neurosis and crime on the other.

This review supports more of the theory that personality determines how man shapes his environment to suit his needs, rather than the other way round. The present author Evans (1980) found that stress correlated with the personality dimension psychoticism. It is generally thought that stress is generated within society, which in turn generates strain in the individual, but high psychoticism scoring patients were found to generate their own stress.
The hostile attitudes of patients scoring high on psychoticism and their lack of empathy and need for arousal, supplants concern for others or for the consequence of their actions.

Psychosomatic Disease and Mediating Mechanisms

If the model of disease causation is used in its most general form, which is that disease occurs as the interaction between a host and a pathogen, then it follows that the degree both of pathogenicity and of host resistance are important factors. However, further factors excluded from the medical model, which act to change the relationship between the host and the pathogenic agent, justify consideration.

Patients with a variety of diseases have been noted to have little contact with their inner mental life in terms of fantasies and feelings. Authors like Berkman and Syme (1979) suggest that circumstances like isolation may have pervasive health consequences via their capacity to influence host resistance and affect vulnerability to disease in general.

The findings of Berkman and Syme show that people who lack social contact and community ties are more likely to die than those with more extensive contacts. Death during the 9 year follow-up was due to four principal causes; ischaemic heart disease, cancer, cerebrovascular accidents and circulatory disease. These authors conclude that the isolation was an indirect factor of death, but an important consideration for this thesis is, why were these patients isolated? Personality and the propensity to live in isolation, might be likely to relate to isolation and therefore to death.

In a similar vein the study of Hinkle and Wolff (1957) suggests that there is a move from a state of health to a general state of illness.

They found a clustering between the occurrence of bodily illness and a further similar relationship between illness and accidents. Those people who experienced the greater number of illnesses, showed an increased susceptibility to illness in general.
The important inference from this study is that the illness is a state of the total organism and that when a human moves from a state of health into a state of illness, the illness is likely to be manifested by a variety of syndromes appearing concurrently or consecutively, their nature being dependent upon the various factors acting upon the organism at that time.

This is a valuable and well designed study and the findings demonstrate the importance of viewing illness from the holistic viewpoint.

So far in this exploration time has been a component of the genesis of disease. The maturation of the individual is a prerequisite for the cognitive understanding of signs and symbols and these in turn influence host resistance. The following well-known anecdote illustrates how pervasive and influential culture can be and how also can indoctrination. "A young man on a journey lodged in a friend's house for the night, the friend had prepared for their breakfast wild hen, a food strictly banned by a rule that must be invariably observed. The young fellow demanded whether it was indeed a wild hen, and when the host answered "no" he ate of it heartily, and proceeded on his way.

A few years later when the two met again, the old friend asked the younger man if he would eat wild hen. He answered that he had been solemnly charged by a wizard not to eat that food. Thereupon the host began to laugh and asked him why he had refused it now after eating it at his table before.

On hearing this news his friend immediately began to tremble, so great was he possessed by fear, that in less than 24 hours he was dead."

This case summarises rather well the impact of psychosocial stresses. The biological and physiological process evoked was interaction with adrenaline, rather than noradrenaline release.
SUMMARY OF THE LITERATURE REVIEW

The literature review began by exploring the nature of a depressive illness, revealing the large numbers within a population which can reasonably be expected to suffer from the illness at any one time. Furthermore it revealed that symptoms involve both the mind and body, making the illness difficult for sufferers, the doctors treating them and for the researcher investigating.

The controversy regarding diagnoses was discussed and the difference in classification used. Is a depressive illness one or two illnesses?

Mortality as part of the natural history of a depressive illness has been established as far as unnatural death is concerned. However, the mortality from natural causes following a depressive illness remains unclear.

Death following a depressive illness was linked to the circulatory system and to a lesser extent to neoplastic deaths. Mechanisms mediating between depression and death were explored, but many questions remained and no easy explanation became apparent.

It is left to the hypotheses of this study to throw more light on the natural history of a depressive illness.

Depression is bestridden with many bridges and joined by many tributories in its tortuous journey, and its end appears to be lost in a sea of confusion.
HYPOTHESES

1. Depression is associated with premature death.

2. Excess mortality will be most prominent in the early years after referral.

3. There will be a differential mortality between the reactive and endogenous depressives.
CHAPTER 10

Method

It was now necessary to plan a method that would accurately test the hypotheses that will require the researcher to;

1. Select a group of accurately diagnosed depressed patients.
2. Following them for a pre-determined period.
3. Tracing them to calculate the numbers dead.
4. To determine the causes of death, and to compare the causes of death in the population under test with the normal population who will act as the control population. From the gross population data, eg. the Registrar Generals returns compute the 'expected' data and to calculate significance levels.

A cohort was available that had been systematically selected 24 years previously. The study was designed to follow a cohort of depressed patients referred to a psychiatrist. The aim of the study was to examine the mortality rates in the cohort using indirect standardisation, with all England and Wales as the standard population. No attempt was made to adjust for local differences, as the Office of Populations Censuses and Surveys showed no significant differences in the mortality rates. Death from all causes and some specific causal groups needed to be examined. Comparison by sex and by type of depression and change during the period of study (1960-84) was made.

Since patients were referred in 1960 - 61, some patients were not in the study for any of 1960. This was allowed for by scaling down the deaths in the statistical programs which calculate the expected numbers of deaths. Referrals were made at a fairly even rate over the 15 month period during which the cohort was assembled.
The Cohort

The original data was collected by Sainsbury and Grad (1966) as part of an evaluation of community care. The Chichester Psychiatric Service was one of the pioneers of community care, Carse et al (1958). In 1960, in order to evaluate community care, a comparative study was commenced between the Community service in Chichester and District, and in the nearby hospital based service in the Salisbury District. Sainsbury and Grad collected standardised data on all the 1413 referrals to the Psychiatrists from the population of these two census districts over a period of 15 months. They describe the method, the population, and the interview schedule used. The referral rates can be seen in table 1.

Kreitman et al (1961) conducted a reliability study on the diagnoses.

There was thus data on 685 depressed patients available, which had been systematically collected by independent psychiatrists and was consequently unprejudiced. One of the valuable features of the cohort was that it was based on referrals not on admissions. The two areas selected had a miniscule number of private patients as there were no psychiatrists in private practice; consequently the study examined the total referrals.

The 1413 referrals (see M1) included 480 diagnosed as endogenous depression, and 205 as Neurotic depressives.

Table M.1
Population

<table>
<thead>
<tr>
<th>Population</th>
<th>All Referrals</th>
<th>Cohort of Depressives</th>
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</thead>
<tbody>
<tr>
<td>Endogenous</td>
<td>480</td>
<td>480</td>
</tr>
<tr>
<td>Neurotic</td>
<td>205</td>
<td>205</td>
</tr>
<tr>
<td>Other Diagnoses</td>
<td>728</td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1413</td>
<td>685</td>
</tr>
</tbody>
</table>
Diagnosis

A strength of the research design was that it was a total sample of patients diagnosed as depressives by consultant psychiatrists. Separation into endogenous and reactive depression was made at that time by senior psychiatrists, who assigned each patient to a diagnostic category.

Further, there is reason to believe that the criteria for diagnosing depression used by non-research psychiatrists has not changed significantly since 1960. To this extent the cohort is representative of the large majority of English Regional Consultant Psychiatrist-diagnosed cases of depression.

Statistical Methods

The Registrar General of England and Wales uses indirect standardisation to compare annual mortality rates in different regions. The age-sex specific death rate of the total population is used as standard; it is compared with the number of deaths which actually occur in a cohort. This comparison is expressed as the Standard Mortality Rate (S.M.R.). It is the product of:

\[
\frac{\text{Number of Deaths which occur}}{\text{Expected number of deaths}} = \text{S.M.R.}
\]

The chi square test was used to test significance between the observed and the expected frequency, where frequencies exceed 5. The Poisson test was used if the frequency is less than 5. The Z test measured comparisons between males and females. In the cohort it was necessary to know the numbers of dead and the cause of death. In order to satisfy this requirement, details of each of the 685 patients not known to be still alive was sent to the Office of Population and Censuses and Surveys. Returns from this Office included a copy of the death certificate giving the cause and date of death. The cut off point of the study was 30.6.84.
Coding Using I.C.D Numbers

International agreement on the coding of disease is one of the most influential activities of the World Health Organisation. During the 24 years of the present work different classifications had been in operation. The original patients dying in 1960 were classified using the 7th coding whereas the code in operation in 1986 is the 9th coding. Accordingly every cause of death had to be reclassified according to the 9th classification. This was a time consuming activity but essential for the accuracy of the research. Every cause of death listed in the data was checked by a medical consultant. In some cases it was necessary to re-allocate the death code to a different category. All the control population were classified to the 9th classification.

Preparation of Statistics

Details of each patient were converted into binary numbers and put onto computer sheets in preparation for the statistical analysis.

The aim was to search for all the 685 in the cohort, and then to record details of those patients who had died during the 24 years. Patients were counted alive only if they personally replied to letters, or if their family doctor certified that he had seen them subsequent to the close of the enquiry, or if the National Health Service Register showed they were still alive on the index day.

Selection of the Control Group

Normative data from the entire population of England and Wales is collected and analysed by the Office of Populations Censuses and Surveys (O.P.C.S.) at St. Catherines House in London, using the National Health Service Central Register to obtain the actual deaths in the total population of England and Wales. For the purposes of the study contact was made with O.P.C.S., the death tables for the twenty four years were purchased and from these the following tables were produced.
1. The National death rate per million by age and sex for all causes of death.

2. The National death rate for each year of the study.

3. The National death rate per million by age and sex for the principal causes of death; All remaining deaths were listed as 'other' deaths.
The National Health Service Central Register (N.H.S.C.R.)

The N.H.S.C.R. was set up to help the local Family Practitioner Committees (F.P.C.) carry out their registration work effectively by maintaining a central register of all N.H.S. patients in England and Wales. Each patient is identified by a number, name, sex, and date of birth, and a symbol which denotes the area in which the person is currently on a N.H.S. doctors list. Removal from the list due to death and embarkation is also routinely noted against an individual's name. The N.H.S.C.R. can thus be used as a tracing device for follow-up studies since, once the person's N.H.S.C.R. entry has been traced, the F.P.C. for the area in which the person is currently on a N.H.S. doctors' list will be identified. Researchers can then write direct to the relevant F.P.C. administrator, asking him to pass on a separate letter or questionnaire to the person's current doctor.

The researcher made application to the N.H.S.C.R. with the submission of a protocol. The merits of the project and the potential value of the research together with the demands it will place on the O.P.C.S. are all factors considered before the N.H.S.C.R. will agree on payment of appropriate fees, to assist with the research. Once the protocol has been accepted the next step is to supply essential information.

Information has to be supplied on index cards; quality, size of cards, and design are all important for ease of handling. The cards are retained until a notifiable event such as death has occurred, when they are returned to the researcher.

Every patient had duplicate research cards on which was recorded the information required by N.H.S.C.R. One card was retained and the second card was sent to the central register. Full information read:

1. Research number.
2. The patient's full name.
3. The patient's date of birth.
4. The last known address.
5. If dead date of death.

Every card with adequate information was then sent to the register. The research number indicated the diagnosis and the hospital of origin of the patient. The N.H.S.C.R. then tagged the cards of patients found to be alive and on death or embarkation, the researcher was notified. If patients were dead, the card was returned with a copy of the death certificate. This provided the date of death, the cause of death, and the I.C.D. classification.

The third group were the missing group. Sims (1973) demonstrated how important it was to trace as many of the missing as possible. At one stage the missing were a formidable proportion. They were also the group where information was inadequate for NHSCR to attempt tracing. These demanded further investigation by the researcher.

The cohort was first collated in 1960 by Sainsbury and Grad, 24 years later the follow-up proved a difficult task. The present author started by scrutinising the hospital records of Graylingwell and the Old Manor, the two hospitals where the original data was collated. This was not very fruitful, as death was usually only recorded if the patient had died in the hospital. Leafing through the notes revealed that many patients failed to keep their appointments.

Some notes had been stored some distance from the hospitals and could not be found. This was an unsatisfactory method of tracing. However, in a few cases essential information was gleaned.

Gathering and preparing the statistics for analysis was time-consuming, for the data had been gathered 24 years previously and during that time many changes had taken place. The advance in computer technology is an example. The original data had been put onto punch cards and the output in volume was considerable. Two computers had been used. Changes had also been made in the classification of disease and it was necessary to check each cause of death. The missing were a cause of concern but a halt had to be drawn for practical purposes, when exhaustive searching became unproductive. Social change and the mobility of the population inevitably played some part in the difficulty found in tracing patients. In the end of the 685 patients in the cohort 74 (10.8%) were untraced.
Computer Analysis

A program was written to analyse the results obtained from the search using Fortran. The advice and help here of the Assistant statistician to the Wessex Regional Hospital Authority is gratefully acknowledged.

Patient Data Programs

DATA 857B-TR was used to file data for subjects who died during the study. The format of the record was as follows:

- CC1/3 Subject Identification number.
- CC4/1 Sex (1 = male, 2 = female).
- CC5/6 Date of Birth.
- CC11/6 Date of Death.
- CC17/4 4-digit ICD9 code of principal cause of death (for codes 800-999 the E codes are given in this column).
  NB. ICD9 for all patients.
- CC21/4 Nature of injury code, for when the code in CC17/4 is between 800 and 999. Otherwise blank.
- CC25/1 Types of depression (1 = Engodenous, 2 = Neurotic or reactive depression).
- CC26/1 Centre of treatment.

DATA 857A-TR contains data for subjects who are still alive. The format is the same as for DATA 857B-TR, except that CC11/4 is blank.

DATA 857C-TR contains records for patients who are as yet untraced. The amount of information varies but is never more than that given in data 857A-TR.

DATA 857A-TR and DATA 857B-TR were merged to give DATA 857-TR. The data in DATA 857-TR was put into suitable summary form using two programmes. These were altered slightly for different requirements but their fundamental purpose remained the same, namely:
RQ857A-CR calculates the number of persons (by sex and age group) alive in the study at the thirtieth of June each year up to and including 1984, the last year of the analysis. (Thus anyone dying after June 1984 is regarded as alive for the purpose of the analysis). The files produced using this program are as follows:

RQ857A-MT (1) Number of persons alive, sex within year, (age across record).

RQ857A3-MT (1) Number of persons alive, sex within year, within type of depression, age across record.

RQ857A4-MT (1) Number of persons alive, sex within year within centre of treatment, age across record.

**England and Wales Mortality Rates**

England and Wales mortality rates for selected years (1963, 69, 74, 79, 83) were taken from standard publications for the following cause groups:

<table>
<thead>
<tr>
<th>Cause Group</th>
<th>ICD7</th>
<th>ICD9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neoplasms</td>
<td>140-239</td>
<td>140-239</td>
</tr>
<tr>
<td>Hypertensive Disease</td>
<td>440-447</td>
<td>401-405</td>
</tr>
<tr>
<td>Ischaemic Heart Disease</td>
<td>420</td>
<td>410-414</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>330-334</td>
<td>430-438</td>
</tr>
<tr>
<td>Respiratory Disease</td>
<td>470-527</td>
<td>460-519</td>
</tr>
<tr>
<td>Accidents</td>
<td>E800-935</td>
<td>E800-E925</td>
</tr>
<tr>
<td>Suicides &amp; Undetermined</td>
<td>E970-E979</td>
<td>E950-E9599; E980-98?</td>
</tr>
<tr>
<td>All causes</td>
<td>011-99</td>
<td>011-999</td>
</tr>
</tbody>
</table>

The data for these eight cause groups were put into the card-reader file EWMORT857-TR, sorted sex within year within cause group, age group across record. The Fortran program Fortran was run on this to calculate 'other causes' rates as a residual. These were written to EWMORT2857-TR which was then merged back into EWMORT857-TR, immediately before the 'all causes' figures.
A series of Fortran programmes used EWMORT857-TR to calculate expected numbers of deaths in the cohort and then compare these with the numbers actually observed (using SMR's and CHI-square tests). The programmes listed below all calculated the expected numbers for each year, which were then summed within broader time spans. From the years 1960-66, England and Wales rates for 1963 were used; for 67-71, rates for 1969; for 72-76, rates for 1974; for 77-81, rates for 1979; for 82-84, rates for 1983. In all but one case the figures were also summed within these periods, the exception being FORT8572-CR, where the years 60-67 were grouped, then 68-71. The programs are as follows:

FORT8571-CR  figures for all persons.
FORT8572-CR  figures for all persons.
FORT8575-CR  Males and females separately, plus a Z test for comparing the male and female SMR's.
FORT8576-CR  Endogenous and Neurotic depressives separately.

The tape files used by these programs are given in their steering lines. It was decided to calculated expected deaths for all causes for single years, using England and Wales mortality rates for each year. This national data was put into EWACM857-TR, sorted sex within year, age group across record.

It should be noted, however, that data for 1960 and 1962 was not available. The programme FORT8578-CR calculates the expected numbers etc., and uses rates for 1961 for the years 1960-62.

The programme FORT857A-CR ran on RQ857A-MT 9i) and RQ857B-MT (i) to produce RQ857A-TR and RQ857B-TR, card-reader versions of the tape format files (for copying onto floppy disk).

Naming of files:

The programme FORT857n-CR (n = i, ..... 8) have compiled versions PROG857n, and output files (when appropriate) FORT857n-LP. The programmes are run by the macors RTX-857n.
Balance and confounding

It seemed quite possible that spurious differences between two categories of a variable could arise due to confounding in the cohort eg. a spurious difference could be observed between males and females if the proportions of neurotic depressives for one sex was very different from that for the other. Account of the various subgroups of interest was therefore produced using the programme RQ857C-CR without put in RQ857C-LP.

This showed that the sexes were reasonably well balanced with regard to type of depression.

Coding of Deaths

The deaths in the earlier part of the study were recoded by a medical specialists from I.C.D. 7 and 8 to I.C.D. 9. The General Registry Office had already recoded the control group to I.C.D. 9. This procedure allowed more accurate comparisons. It was without undue difficulty except in the case of cardiovascular disease. Here the I.C.D. 7 categories of death Nos 410-421-422, were different (ie. encompassed a somewhat differing range of pathology) from I.C.D. 8 in 1969 categories 410-414. (The I.C.D. 8 changed little into I.C.D. 9). The effect of this was that had the 1960 - 1968 years been analysed with both cohort and controls using I.C.D. 7 then more cohort than control deaths would have moved from "other causes" to cardiovascular and demonstrated a cardiovascular excess in depressives for the early years.
Results

The first hypothesis proposed that a cohort of depressed patients will experience greater mortality than the general population.

Hypothesis I was upheld for the 24 year period of investigation, the overall mortality exceeded expectation when compared with the general population and reached statistical significance at the 1% level.

Table 1 shows statistical significance levels and the standard mortality rates by cause and year of death for all causes throughout the 24 year period.

<table>
<thead>
<tr>
<th>Year Group</th>
<th>Neoplasms</th>
<th>Hypertensive Disease</th>
<th>Ischemic Heart Dis.</th>
<th>Cerebrov. Disease</th>
<th>Respiratory Disease</th>
<th>Accidents</th>
<th>Suicide + Undet.</th>
<th>Other Causes</th>
<th>All Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960-66</td>
<td></td>
<td></td>
<td></td>
<td>204.7*</td>
<td>251.0**</td>
<td>343.0**</td>
<td>947.4**</td>
<td>241.2**</td>
<td>211.1**</td>
</tr>
<tr>
<td>1967-71</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>826.8*</td>
<td></td>
<td></td>
<td>164.5*</td>
<td></td>
</tr>
<tr>
<td>1972-76</td>
<td>599.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1977-81</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1982-84</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1960-84</td>
<td></td>
<td></td>
<td></td>
<td>142.4*</td>
<td>634.1**</td>
<td>369.3**</td>
<td>185.0**</td>
<td>139.6**</td>
<td></td>
</tr>
</tbody>
</table>

* significant at 5% level
** significant at 1% level

Histograms were produced where black represents the cohort and the shaded columns represent the general population.
The scale of the graphs used in this chapter has been altered on the vertical axis. **Graph 1** shows the mortality profile of the population at risk throughout the 24 years. Compared with the control population, the cohort was incomplete in year one as this was the referral period. The actual number of deaths throughout the 24 years was 302 whereas the expected number was 216. There were 288 still alive and 75 missing patients. The graph shows a sudden fall in the number of deaths in the third year of follow-up. The fourth year of follow-up shows a rise which subsides to that of the general population by the 11th year.

**Comparision between Observed and Expected Mortality in a Cohort of Depressed Patients throughout 24 years.**

**Graph 1**

![](image)

**Table 2** shows that the incidence of death in the cohort reached statistical significance when compared with the general population in each of the first 9 years with the exception of one. The years reaching the highest significance levels are those immediately after referral. In 1961 the first full year of the study 31 patients died, when in the general population only 8.3 deaths were expected. These important findings need dissecting in an attempt to search for the causes of the mortality. We shall first examine mortality in greater detail by cause and by sex.
The Statistical Significance between the Control Population and the Patients under test during the first 9 years

TABLE 2

<table>
<thead>
<tr>
<th>Year to Death</th>
<th>Obs</th>
<th>Exp</th>
<th>Chi 2</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1960</td>
<td>15</td>
<td>4.0</td>
<td>30.24</td>
<td>.001</td>
</tr>
<tr>
<td>1961</td>
<td>31</td>
<td>8.3</td>
<td>62.46</td>
<td>.001</td>
</tr>
<tr>
<td>1962</td>
<td>10</td>
<td>9.1</td>
<td>0.08</td>
<td>N.S</td>
</tr>
<tr>
<td>1963</td>
<td>17</td>
<td>9.0</td>
<td>7.23</td>
<td>.01</td>
</tr>
<tr>
<td>1964</td>
<td>15</td>
<td>8.4</td>
<td>5.14</td>
<td>.02</td>
</tr>
<tr>
<td>1965</td>
<td>17</td>
<td>8.0</td>
<td>9.96</td>
<td>.01</td>
</tr>
<tr>
<td>1966</td>
<td>15</td>
<td>7.8</td>
<td>6.53</td>
<td>.02</td>
</tr>
<tr>
<td>1967</td>
<td>14</td>
<td>7.6</td>
<td>5.49</td>
<td>.02</td>
</tr>
<tr>
<td>1968</td>
<td>14</td>
<td>7.6</td>
<td>5.30</td>
<td>.05</td>
</tr>
<tr>
<td>TOTAL</td>
<td>148</td>
<td>69.8</td>
<td>132.43</td>
<td>.001</td>
</tr>
</tbody>
</table>

Histograms 2-8 on subsequent pages show the mortality profile by unnatural and natural deaths.

Unnatural Deaths

Table 1 (Page 56) shows that unnatural death occurred predominantly in the first 10 years of the study, (27 deaths occurred whereas only 6.2 were expected). Graph 2 shows the mortality from suicide and undetermined deaths. Death in this category occurred predominantly in the immediate post-referral period which is the expected finding. There were no suicides in the depressed male patients but 16 deaths from suicide in the female patients where 2.8 were expected. (Table 3, page 65).
Suicide

There were no male Suicide and Undetermined Deaths

Graph 2

Accidental Death

Accidental deaths are statistically significant at the 1% level but only in the female population. Table 1 shows that accidental death occurred prominently in the first 10 years.

Graph 3 shows a comparison of accidental death between the patients suffering a depressive illness and the general population.

Accidental Death

Graph 3
Death from Natural Causes

We will now examine the differences in mortality due to natural causes of death between the sample studied and the general population.

Deaths from "Other Causes"

Graphs 4 shows the 'other cause' category which contained all deaths other than those in the defined categories. Table 3, (Page 64) shows a large part of the mortality came within this category. Males show 33 deaths, whereas only 14.9 were expected. There were 50 female deaths with 30 expected from "other causes".

In the first 6 years, 'other causes' reached the 1% level of statistical significance, then dropped to the 5% level in the next 5 years. Table 1 (page 56).

Graph 4

Respiratory Disease

Graphs 5 shows death from respiratory disease to be a considerable mortality factor for both the male and female population, in the early post referral period.
Table 1 (page 56) shows respiratory disease to be a statistically significant cause of mortality at the 1% level, in the first 6 years of the study.

**Males** Table 3 (Page 65) shows that 22 males died from a respiratory cause, 14.3 were expected. The excess deaths were only significant at the 5% level (table 4) page 65. **Females:** (Table 5, page 64) shows respiratory disease to be statistically significant at the 1% level. 21 females died, whereas 15.8 were expected. Respiratory disease was a significant cause of death but confined to the first 6 years of the follow-up, as is shown by Graph 5.

**Neoplasms**

Graph 6 shows that in the first 16 years neoplasms followed the trend of the general population, then rose above the general population but only at the 5% level in the female population table 5, page 64.
Hypertension is not a cause of significant excess mortality for either sex but does show slight discrimination between the types of depression, Table 7, page 70).

Ischaemic heart disease Table 1, page 54 shows no statistically significant mortality from ischaemic heart disease. This was an unexpected finding as the literature review did in many studies demonstrate an association between mortality and depression.
Cerebrovascular Disease

Table 1, page 54 shows Cerebrovascular disease to be statistically significant at the 5% level in the early years of this study. Table 4 for males (page 63) shows a statistically significant difference in the incidence of death from Cerebrovascular Disease at the 1% level. The mortality occurs largely in the first 6 years (as is demonstrated in graph 9). Table 5 (page 64) shows no statistically significant mortality from this cause in the female cohort.
Comparison of cause of death by sex

TABLE 3

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obs</td>
<td>Exp</td>
</tr>
<tr>
<td>Neoplasms</td>
<td>18.0</td>
<td>19.6</td>
</tr>
<tr>
<td>Hypertensive</td>
<td>2.0</td>
<td>1.4</td>
</tr>
<tr>
<td>Isc Ht Disease</td>
<td>31.0</td>
<td>24.9</td>
</tr>
<tr>
<td>Cer Vas Dis</td>
<td>13.0</td>
<td>9.4</td>
</tr>
<tr>
<td>Resp Dis</td>
<td>22.0</td>
<td>14.3</td>
</tr>
<tr>
<td>Accidents</td>
<td>3.0</td>
<td>0.7</td>
</tr>
<tr>
<td>Suicide</td>
<td>0.0</td>
<td>1.6</td>
</tr>
<tr>
<td>Other Causes</td>
<td>33.0</td>
<td>14.9</td>
</tr>
<tr>
<td>All Causes</td>
<td>122.0</td>
<td>86.8</td>
</tr>
</tbody>
</table>

Death by Natural Causes for Males and Females

**Males**

The mean age at referral for males was 58.13 years. Males formed 32.26% of the cohort. Throughout the 24 year period (Table 1, page 54) males demonstrated an excess death rate from "all causes" which reached statistical significance at the 1% level. But the surprising finding was that there was no excess mortality from unnatural causes.

Cerebrovascular disease, respiratory disease, 'other causes' and deaths from 'all causes', all contributed to the statistically significant mortality in males for the first 6 years after referral. For the entire 24 years, 'other causes' and 'all causes' reach statistical significance. Death from all causes in the males totalled 122 whereas 86.8 were expected (Table 3).
## Death of Males Only

### TABLE 4

<table>
<thead>
<tr>
<th>Year Group</th>
<th>Neoplasms</th>
<th>Hypertensive Disease</th>
<th>Ischaemic Heart Dis.</th>
<th>Cerebrov. Disease</th>
<th>Respiratory Disease</th>
<th>Accidents</th>
<th>Suicide + Undel.</th>
<th>Other Causes</th>
<th>All Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-66</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>67-71</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>72-76</td>
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<td></td>
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<tr>
<td>77-81</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>82-84</td>
<td></td>
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<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>80-84</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* = significant at 5% level  
** = significant at 1% level

---

### Females

The female cohort formed 67.737% of the population, at a mean age of 51.19 years they were younger than the males. Respiratory disease, accidents, undetermined deaths and suicide discriminated between the female patients and females in the general population at the 1% level. Both sexes demonstrate statistically significant mortality in the first 6 years at the 1% level. In the following 5 years there was a female excess but only significant at the 5% level, and that only for accidents and 'other causes'.

---

63
Death of Females Only

TABLE 5

<table>
<thead>
<tr>
<th>Year Group</th>
<th>Neoplasms</th>
<th>Hypertensive Disease</th>
<th>Ischemic Heart Dis</th>
<th>Cerebrov. Disease</th>
<th>Respiratory Disease</th>
<th>Accidents</th>
<th>Suicide + Undet.</th>
<th>Other Causes</th>
<th>All Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-66</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>291.8**</td>
<td></td>
<td>1189.7**</td>
<td></td>
<td>219.7**</td>
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* significant at 5% level
** significant at 1% level

Summary of Hypothesis 1

The findings in this research are interesting, and the important finding is that there is a statistically significant difference in the incidence of death between the patients studied and the general population. The results show that causes of death which suggest an association between depression and death do not occur equally in both sexes.

The most significant finding is the magnitude of both unnatural and natural deaths in the early years of the study. An unexpected finding is that statistically significant death from suicides, undetermined deaths, and accidental deaths occur only in the females. The causes of excess natural death are cerebrovascular disease, respiratory disease and 'other causes'.

It is interesting to observe the profile of mortality throughout the 24 years. Premature mortality is shown in Table 1 (Page 54) to extend throughout at the 1% level of significance for Accidents, Suicide and undetermined deaths, 'other causes' and 'all causes', but only at the 5% level for respiratory disease.
Hypothesis 2

Excess mortality will be most prominent in the early years after referral.

Statistically significant deaths occurred within the first 6 years of the study, from unnatural deaths, accidents, suicide and undetermined deaths, 'other causes': cerebrovascular and respiratory disease.

Table 2 (Page 56) shows that the difference in the incidence of death between the patients and the general population is highly statistically significant in the first 6 years of the study. From both unnatural and natural deaths between 1960 and 1966, 120 deaths were found, only 54.6 expected, more than double the death rate expected in the general population. 1960 shows that there were 15 observed deaths where only 4 were expected, the significance being P>.001. In 1961, 31 deaths were observed and only 8.3 were expected, again an equally significant result. In 1962 the difference in the incidence of death in the patients compared with the general population was not statistically significant, but this is largely explained by the relative absence of suicides and undetermined deaths which inflated the results immediately after referral.

Conclusion

Hypothesis 2 is confirmed, the early years were associated with the highest levels of statistically significant deaths.

Hypothesis 3

Hypothesis 3 - There will be a differential mortality rate between patients diagnosed as having a reactive depressive illness and those diagnosed as having an endogenous depressive illness.
Patients with Reactive Depression

The mean age at referral of the patients with a reactive depression was 44.40 years compared with 58 for the endogenous depressives. The reactive-depressed patients were smaller in number, consisting of 205 or 29% of the total cohort. They were selected and diagnosed as having a reactive depressive illness from all referrals in the catchment area. Table 6 shows that patients with this depression do not appear to be at significant risk of death over the 24 year period.

The 205 in the reactive depressed cohort, however, demonstrated statistically significant excess mortality in unnatural deaths, at the 5% level during the 7 to 11 year period of follow-up. Accidents were weakly significant throughout the 24 year period. Thus in the sample studied, patients with a reactive depression were not strongly associated with premature mortality from unnatural death and showed no evidence of excess mortality from natural causes.

<table>
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<tr>
<th>Year Group</th>
<th>Neoplasm</th>
<th>Hypertensive Disease</th>
<th>Ischemic Heart Dis.</th>
<th>Cerebrov. Disease</th>
<th>Respiratory Disease</th>
<th>Accidents</th>
<th>Suicide + Undet.</th>
<th>Other Causes</th>
<th>All Causes</th>
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* significant at 5% level
** significant at 1% level
Endogenous Depressives

### TABLE 7

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<th>Cerebrov. Disease</th>
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</table>

* significant at 5% level
** significant at 1% level

Table 7 shows that in the first 6 years after referral, the 480 endogenous depressive patients suffered very significant mortality at the 1% level from cerebrovascular disease, respiratory disease, accidents, suicide and undetermined deaths, other causes, and 'all causes'. 12 years after referral hypertensive disease became associated with excess mortality at the 5% level of significance.

Throughout the 24 years respiratory disease, accidents, suicide and undetermined death 'other causes' and 'all causes', were all associated with excess mortality at the 1% level of significance in the group diagnosed as suffering from endogenous depression.

**Conclusion**

Mortality in this cohort is shown to discriminate between the neurotic and endogenous diagnosis of depression. Hypothesis 3 is upheld. Further research needs to be carried out to see which patients within this diagnostic category are most at risk. The findings suggest that endogenous depression, the more serious of the two diagnoses, is associated with increased mortality from both natural and unnatural causes. The weak association between unnatural deaths and neurotic depression is inconclusive.
SUMMARY OF THE RESULTS

In this large unselected cohort comprising all depressed patients referred to the psychiatrists in 1960, all hypotheses were confirmed. The overall premature mortality predicted was confirmed suggesting that premature mortality should be considered as part of the natural history of a depressive illness.

The patients diagnosed as endogenous depressed were shown to be at greatest risk of dying prematurely. The early years after referral proved to be the most hazardous.

The sexes behaved differently, the statistically significant mortality in the male cohort was confirmed. It was mainly due to death from natural causes occurring predominantly in the early post referral years. Whereas the statistically significant death in the female cohort included both natural and unnatural death.

The review of the literature produced evidence of an association between death due to cardiovascular disease and depression but the results here do not support this association.

These results are interesting and have important implications for all those concerned with the diagnosis and treatment of depression. The next step must be to discuss the findings both in the context of this study and in their relevance to the future.
CHAPTER 12

Discussion

Introduction

The review of the literature showed that a depressive illness is one of the major scourges of human life, it has been estimated that as many as 8% of the population (Page 2) may suffer this disturbance of mental stability at any one time. The review also showed that whereas there is a causal link between a depressive illness and premature mortality with respect to unnatural deaths, there is no accepted causal association between depressive illness and death from natural causes.

The literature review further highlighted the controversy as to whether there is one type of depressive illness or two. Hypotheses were formulated and a method designed to test these areas of uncertainty (see Page 42). The next step must be to consider the reliability of the method to accurately test the hypotheses and to question whether the results were prejudiced in any way.

The starting point for the Method of this research was a M.R.C. prospective study (Sainsbury and Grad (1966)), comparing a hospital based with a community based psychiatric service. The base line was 1960.

The method was meticulous in the criteria laid down for inclusion in the population under test (page 43). Senior psychiatrists collected standardised data from all referrals from a total population of two census areas. It is important to observe that patients were at that time assigned a diagnosis. A reliability study was conducted which showed an acceptable level of concordance between the psychiatrists making the diagnosis. From this total sample of psychiatric referrals all (bar none) cases with the diagnosis of depression were extracted for the present research. There is thus no reason to believe that the selection process prejudiced the Results in any way.
Three principal methodological problems were discovered during the research:

(a) In Depression

1. Psychiatric diagnosis has problems of reliability only somewhat mitigated by the reliability study on Page 44.

2. The controversy which existed throughout the 24 years about whether there are one or two types of depression.

(b) In Death

3. Problems (see Page 15) arise about the validity of death certification.

There can be no disputing death so there seems no reason to conclude that the overall mortality (Table 1, Page 54) was a spurious result.

At this point there are two identifiable events common to the test population: 1. A diagnosis of depression and 2. death. It would be easy to make the assumption that these two events are causally associated but this would be dangerous because a statistically significant association is not necessarily a causal association. In other words the factors which mediate between depression and death need careful consideration.

Overall Mortality

The overall mortality included unnatural and natural deaths, excess deaths extended over the 24 year period at the 1% level of statistical significance when compared with the general population. As the patients were all referred to a psychiatrist, the implication is that both the psychological and physical symptoms were pronounced.

Table 1 (page 54) shows the diseases which were a statistically significant cause of death in depressed patients. The table shows that depressed patients die from both natural and unnatural causes. Thus this work is at variance with Tsuang and Woolson (Page 12) who found an association between death from unnatural (but not from natural) causes and depressive illness.
Graph 1 (Page 55) shows the profile of the test population compared with that expected in the general population, it demonstrates graphically the toll of death in the early years.

The actual number of deaths throughout the 24 years was 302 whereas the expected number was only 216. This figure, though alarming in itself, is considered to be a conservative figure because it is likely that there were a significant number of deaths amongst the 74 patients who remained untraced (Sims Page 12).

The association between suicide and depression is widely believed but depression has no accepted association with premature mortality from natural causes. The present work demonstrated clearly how premature mortality was due to both natural and unnatural causes. Those responsible for the treatment of such patients should now be aware of the risk of early death from natural disease associated with the diagnosis of depression.

It is possible that many patients are treated and discharged as improved or recovered when in fact this might be far from the reality: table 1 (Page 54) shows that the time of greatest risk for these depressed patients was in the years immediately after referral. Table 2 (Page 56) shows that 148 deaths occurred in the first nine years, when only 66 deaths were expected in the control population.

Statistically significant causes of premature death (Page 54) were: cerebrovascular disease; respiratory disease; accidents; suicide and undetermined deaths; and "other causes". With the exception of cerebrovascular disease all these diseases remained a statistically significant cause of premature mortality throughout the 24 year study period.

The results thus suggest that depression was either secondary to a physical illness or alternatively, that if depression was the primary diagnosis then physical illness was present at referral but remained undetected.

A third conjecture could be that a depressive illness and physical illness occurred concurrently the one exacerbating the other.
Reactive Depression

Table 6 (Page 70) shows patients with reactive depression have no statistically significant premature mortality from natural death, but over the 24 years accidental death is associated with premature mortality at the 5% level of significance.

It thus appears that a depressive illness labelled as reactive (which is usually associated with an unstable personality) might protect the patient in some way from mortality due to natural causes, but death from unnatural causes remains a risk for patients with this diagnosis.

Endogenous Depression

Table 7 (Page 67) shows that the diagnosis of endogenous depression is particularly associated with premature mortality from: cerebrovascular disease; respiratory disease; accidents; suicide and undetermined death; "other causes" and "all causes" at the 1% level of significant in the first 6 years of the follow-up. With the exception of cerebrovascular disease, these diseases relate statistically significantly to death throughout the 24 year period. Table 7 shows a similar profile to that of Table 1 (page 54) demonstrating that it is endogenous depressives that contribute largely to all excess mortality.

This is not a surprising finding as endogenous depression has been associated more with physical illness than has reactive depression (see Page 8). Patients with endogenous depression appear to be susceptible to cumulative physical and mental effects causing structural deterioration.

Sex and Mortality

Tables 3, 4 and 5 (Pages 62, 63 and 64) compare death between the sexes. Table 3 shows that male deaths totalled 122 when 87 were expected from the general population. The males are shown to suffer premature mortality from natural causes only. This is a surprising finding as males are popularly associated more with traumatic aggressive causes of death than are females. This will be discussed on Page 73. Cerebrovascular disease, "other causes" and "all causes", were associated with early mortality in the male patients at the 1% level of significance,
(respiratory disease at the 5% level) in the first six years. "Other cause" and "all causes" of premature mortality occurred throughout the 24 years at the 1% level.

Table 3 also shows 181 female deaths occurred whereas 130.3 were expected. Table 5 shows that in the females, diseases causing premature mortality in the first 6 years at the 1% level were: respiratory disease; accidents; suicide and undetermined deaths; "other causes" and "all causes", throughout the 24 year period. All these diseases with the exception of respiratory disease also occurred in the female cohort at the 1% level of significance. An important sex difference in suicide is discussed later.

SPECIFIC CAUSES OF MORTALITY

Unnatural Death

Death certificates were shown on Page 14 to be an unreliable source of information, so some caution must be exercised where using death certificates, unless an autopsy report confirms the cause of death. Nevertheless the data is the best information available. Table 1 (Page 54) defines the diseases causing premature mortality and shows that death occurred predominantly soon after referral. Graph 1 (Page 55) gives the mortality profile of the population tested compared with the control population. Throughout the first 6 years the toll of death was statistically significantly greater than that expected in the general population.

Suicide

Suicide is the only recognised psychiatric cause of death. Approximately 15% of depressives and 10% of alcoholics eventually commit suicide. It ranks among the 10 most frequent causes of death in most industrial countries. The suicide rate is about the same now as it was at the beginning of the century. It rose in the 1930's at the time of the depression and fell in both world wars. It is interesting to note here that suicide is strongly associated with emotional depression and increases during times of economic depression. This suggests that suicide has a social relationship. Currently about 1 in 10,000 of the general adult population die by suicide per year.
Table 5 (Page 64) reveals suicide to be an early cause of mortality in females and to remain in significant excess throughout the 24 year study period. Table 6 (Page 66) shows only in the seventh year after referral do patients with the diagnosis reactive depression have this cause of death over represented. Patients with endogenous depression Table 7 (Page 67) are at risk during the first 6 years after referral and throughout the 24 year period of follow-up at the 1% level of statistical significance.

The finding of the male/female ratio in this research is not in agreement with other authors suggesting that the results here may be based on a sampling error. The literature does not adequately discuss the problem of the sex distribution of psychiatrist suicides but the authors own view is that men tend to keep their problems to themselves and those men who take their own lives do not become patients of the Psychiatrist.

Mortality and morbidity statistics support this view. At every age males die more frequently than do females, yet of the vast majority of NHS clinics females exceed male attendences. Indeed mental health services provide twice as many female as male beds.

In this cohort all the suicides (Table 3, Page 62), numbering 16, occurred in the female cohort. Since all the depressed patients received treatment, it appears that treatment was successful in the men but less so in preventing suicide in the women; why? Did the female patients who committed suicide have insufficient treatment, or are female patients more difficult to assess and treat?

What subjective thought can we put forward in answer to this unusual finding? Women out number men as patients referred to the psychiatrist and this might have caused competition for hospital beds, resulting in the premature discharge of women patients.

It is also possible that with preponderance of male psychiatrists 24 years ago they showed less concern for the female patients, particularly the ageing patients. 24 years ago men were often the sole breadwinners, they therefore had a higher status than the females and the psychiatrist might have showed more concern for them.
Another factor might have been that women usually have homes to run, and they dislike forfeiting their household and maternal responsibilities; they therefore are more anxious than men to return home. This could have caused them to return home too soon, even discharging themselves. Deaths from Suicide did occur predominantly soon after discharge, which reinforces this hypothesis.

One final explanation might be associated with the particular personality of the female suicides; 'abnormal personality' was found to be associated with the suicide patients in the Barraclough et al study. In a cohort of psychiatric suicides a higher predominance of abnormal personalities could be expected. Suicide is a particularly aggressive act and is nationally more associated with men; perhaps those women with more 'aggressive' personalities, are selectively admitted by the psychiatrist.

It would be particularly interesting to conduct a study on all hospitalized patients to compare their personality profiles and scores of aggression. It is predicted that the female suicides would score higher on aggression and higher than the mean score for psychoticism using the Eysenck Personality Questionnaire.

The difficulty would be in gathering a large amount of data for only a small number of suicides.

Physical illness was found in 20.0% of the suicides investigated by Seager and Flood in Bristol. 14 patients out of the 325 in their cohort were found to have severe physical illness which would have been likely to cause natural death within 6 months of the suicide. It is a weakness of the present study that physical examinations were not performed, and consequently there is no data available to ascertain the presence of physical illness in the women patients who took their own lives.

**Accidents**

Table 1 (Page 54) shows that accidents were associated with premature mortality both in the first 6 years and over 24 years at the 1% level of statistical significance. Tables 4 and 5 (Pages 63 and 64) shows that excess mortality arises from female but not from male, patients. This is a surprising finding as males normally predominate in accident statistics. The present research thus suggests that the
intervention of depression reverses the normal male/female finding.

Table 6 and 7 (Page 66, 67) demonstrate that depressives labelled reactive have excess deaths by accident at the 5% level, those labelled endogenous at the 1% level.

The cause of accidents needs consideration, for accidents can be intentional or unintentionally caused by accident proneness, a factor associated with personality and extraversion.

Accidental death can also be disguised as suicide. The coroner will bring a verdict of undetermined death if there is any doubt about the cause of death.

Holding and Barraclough (see Page 21) emphasised the importance of considering accidental deaths when the mortality of mental illness is studied. They found that of the 110 accidental deaths which were investigated, they diagnosed 60% as mentally ill. Suicide investigators find there is bias on the part of doctors and coroners in particular to construe sudden death as accidental where doubt exists, in order to save relatives unnecessary grief, guilt or embarrassment. So it is possible that a significant number of the accidents could in fact have been suicides.

Neoplasms

There were 46 deaths from neoplasms against 48.1, expected Table 3 (Page 62). Table 5 (Page 64) shows that the only time when neoplastic death became significant was 12 years after referral when the female patients suffered premature death at the 5% level of statistical significance. Perhaps this weak association is only to be expected in the light of the findings of various authors (Pages 29-31). Physical examinations were not part of the criteria for inclusion into the study population. The literature review has already established that neoplasms go undetected in cohorts without physical examinations as part of the initial assessment. Furthermore neoplasms remain undetected by studies which do not confirm the cause of death by autopsy. It is therefore not surprising that the findings in this cohort did not confirm the association between depression and neoplasm.
Hypertension

Table 1 (Page 54) shows no statistical significance in death from hypertensive
disease. Table 3 (Page 62) shows that there were 8 deaths from this cause
whereas 4 were expected. But Table 7 (Page 67) shows the patients with
endogenous depression suffered premature mortality from hypertensive disease
12 years after referral at the 5% level of significance. Some workers have
suggested that certain physiological responses normally associated with affective
states may persist when the appropriate emotion is no longer outwardly apparent.
This may go some way to explain the latency period between first referral and
death from this cause.

It is particularly interesting that the deaths from hypertensive disease occurred in
the patients suffering from endogenous depression. One explanation could be that
endogenous depression, the more serious disease, has something to do with lack
of movement over the 12 years which could cause an increase in weight which
would tend to push up the blood pressure, with increased deposition of cholesterol
and other deposits in the blood vessels. Hypertension is well know to precipitate
strokes so death attributed to strokes could have hypertension as the true
precipitating cause.

Davies (Page 26) found that there is a psychosomatic component in the
aetiology of high blood pressure. Henry (see Page 83) provides some support
for this hypothesis, and he found that social support can be a protective factor. In
one animal experiment he produced persistent hypertension in mice by
developing experimental territorial conflict, but hypertension only occurred when
the mice were strangers.

Individuals who cannot express their feelings adequately directly or indirectly by
means of neurotic symptoms may develop high blood-pressure. If this is true the
neurotic patients might actually protect themselves from high blood pressure.
This is interesting, as in this cohort only the endogenous depressives were weakly
associated with hypertension.
Ischaemic Heart Disease

Contrary to expectation ischaemic disease here (Table 1, Page 54) is not associated with premature mortality. The review (Page 22) indicated that a depressive illness was associated with mortality via the cardiovascular system, but this study reports no such association. During the 24 year period the I.C.D. coding (Pages 7, 53) was changed 3 times from the 7th to the 8th and 9th. To allow more valid comparisons with the control population it was necessary to change the coding on the death certificates to the 9th classification.

Cerebrovascular Disease (Strokes).

Table 1 shows that in the first 6 years this is a cause of excess death in depressed patients at the 5% level of significance. Table 4 however, (Page 63) shows that stroke is a statistically significant cause of death in the male patients in the first 6 years at the 1% level.

There is no such association for females (Table 5, page 64), thus the sexes here follow different paths leading to premature mortality.

Table 7 (Page 67) demonstrates that the patients with endogenous depression suffer premature mortality from strokes at the 1% level of statistical significance during the first 6 years of follow-up. Reactive patients showed no excess death from this cause.

Early death suggests that cerebrovascular disease was present at the time of referral. Another possibility is that depression is secondary to strokes. Computerised Tomography (C.T.) would be helpful in such cases.

Cameron and McGoogan (page 14) found both over and under diagnosis of cerebrovascular disease. The authors suggest that a stroke is often little more than a convenient label.

The most common problem of differential diagnosis is distinguishing cerebrovascular from cardiovascular death. Thus it is possible that a proportion
of deaths were recorded as death due to stroke, but which should have appeared in the cardiovascular category or vice versa.

**Respiratory Disease**

Respiratory disease is shown to be a frequent cause of death particularly in the immediate post referral period for both the male and female population, (Table 1, Page 54). It occurs at the 1% level of statistical significance and also throughout the 24 years at the 5% level. There were excess deaths in depression from respiratory disease in the first 6 years Table 1 (Page 54). Table 4 (Page 63) and Table 5 (Page 67) demonstrate that males suffered excess death at the 5% (but females at 1%) level of significance. Premature mortality from respiratory disease was a cause of death in those patients diagnosed with endogenous depression at the 1% level during the first 6 years of follow-up and throughout the 24 years, this was not so in neurotic depressives.

Psychiatric hospitals nowadays are one of the few places where smoking is still widespread, and 24 years ago they contained many patients who smoked heavily. Excess death from respiratory causes was confined to the endogenous depressives, particularly the females. It is also possible that some of these deaths were due to tuberculosis.

Depression is often associated with motor and sensory retardation; lack of motivation to exercise, lack of fresh air. All these factors provide the right climate for chest infections. Some of these patients are also likely to have suffered from self neglect and malnourishment which further enhances the likelihood of respiratory disease.

Another hypothesis might be that stress modifies the response of the immune system. In many diseases the influence of stress and other emotional factors on the immune system may prove to be of fundamental importance in both increasing susceptibility to disease and adding stress during the course of the disease. Such non specific stimuli have been shown to alter the respiratory tract mucosa of mice, which can lead to activation of a latent viral pneumonia.
Endogenous depression which is the more serious illness, would certainly require more adaption by the patient than the patient with reactive depression. Baker (1983) gives some support for this hypothesis.

Thus infections, particularly respiratory infections, would be expected in a depressed cohort. According to Cameron and McGoogan respiratory causes of death are particularly likely to be misdiagnosed. Gruver and Freiz (1957) in a survey of more than 1000 autopsies found that infections, particularly pneumonia and meningitis, were the most frequently overlooked diagnoses. In this cohort respiratory disease might therefore have even been underestimated.

**Other causes**

Table 1, Page 54 shows that the remaining causes of death were over represented at the 1% level of statistical significance in the first 6 years and over the whole period at the 5% level.

According to findings of Cameron and McGoogan (see Page 14 and 23), it might be expected that the specific categories grouped together in 'Other Causes' may carry therapeutic indications and obscure important clinical distinction. If the stress hypothesis is correct, then 'other causes' could be hiding important diseases of the organ systems of the body which are then excluded from detailed analysis.

**Factors of Mortality**

All the patients in the cohort were referred to a psychiatrist indicating that they all had depression of sufficient severity for the family doctor to refer to the specialist. The period of greatest risk for early deaths, particularly for the patients diagnosed with endogenous depression, was soon after referral. Depression when severe is an intolerable burden with physical psychological and social disruption, the implication of having a depressive illness is wide reaching with financial, social status and other, including bodily, consequences. The G.A.S. (Page 33) does explain the latter showing how structural deterioration follows such a stressful illness. The suggestion being that the mind ravages the body causing physical deterioration. Such severity would not only explain the deaths due to natural
causes but also the deaths due to unnatural causes which occurred; one can imagine patients who are battling with problems and confusion relieving their stress by taking their own lives.

Severity

Severity implies disruption to both the internal homeostasis of the patients, and to their external environment. The internal homeostasis in a depressive illness is frequently accompanied by fairly profound changes in the physiological internal milieu. Disruption of relationships and difficulties with socialisation and the maintaining of standards in the home and at work, would be severe in comparison with a milder depressive illness. Thus severity implies stress and the assumption must be that depression activates the general adaption syndrome discussed in the literature review.

Stress

Selye's stress hypothesis (Page 33) goes some way in providing a bridge between depression and bodily deterioration. Stress triggers progressive stages of the General Adaptation Syndrome, and in this way physiological exhaustion in the final stage 3 leads to irrevocable structural deterioration and death.

Selye's hypothesis is non-specific as regards to causes of stress; any demand for adaptation evokes the same stress response, whether it be an inner personal conflict or problems in the external environment like heat and cold. Stress in the form of a life event like bereavement precipitating illness is discussed by Hirschfield (1980) who found that those patients with severe depression had more stress prior to the illness. A depressive illness itself also causes demands for adjustment. Stigmatisation, estrangement from society, a lowering of self esteem, are just a few examples of stresses which will effect the patient in idiosyncratic ways and make further demands for adjustment on the body. Such adjustment takes place on an ever changing stage, with an ever changing role in a depressive illness.

People react to the social environment as they perceives it and in the case of the patient who becomes depressed, perception and reality can become confused.
and distorted. There is a large body of opinion which promotes the idea that change in the lives of people can cause depression, bereavement being one such example. Holmes and Rahe's (1967) formulated an index of social events, including bereavement, which can cause mental illness.

The postulation in this thesis is that depression causes stress by placing unreasonable demands on the host. There is no available information about precipitating stress in this sample of patients compared with the control population. The assumption nevertheless must be that, by virtue of the demands made for adjustment during the cause of the illness, stress was considerable and could have led to structural deterioration and death.

**Personality**

The cohort were divided into two groups; a group diagnosed as neurotic, and a group diagnosed as endogenous. A factor which identifies one from the other is pre-morbid personality. The neurotic group is generally thought to include those patients with poor pre-morbid personalities, who act out their lives, externalising conflict, and experience difficulties in interpersonal relationships. The endogenous group have more stable premorbid personalities. The present author found that personality could also be related to stressful life events (Evans 1981), that is, by virtue of personality we create lifestyles to which we then react. In other words man reacts to the environment he creates.

In this cohort the reactive neurotic group did not suffer a mortality rate comparable to the endogenous group. One cause of the differential mortality might be that the neurotic depressives protect themselves as their ability to blow off steam, their reactivity, acts as a safety valve. The endogenous group usually become ill in the absence of explicit causal events. The severity of symptoms in this group is generally thought to be greater. They thus differ from the reactive group, having no point of reference on which to conceptualise their illness.

**The individual brings about his own destruction**

This hypothesis has been suggested by the number of deaths which occurred so soon after referral, and suggests that a sub-section of depressed patients might
deteriorate both psychologically and physically relentlessly to death irrespective of intervention. This might relate too either a genetically determined condition, or an unconscious form of self destruction.

The ability to die following suggestion has been found in association with voodoo death. Such influences might demonstrate a self destructive mechanism in man. If man can bring about his own demise, perhaps it is more than just a 'giving' up syndrome; it is a more definite, if unconscious effort to promote death.

If this is so, then to prevent death such mechanisms must be understood, so that treatment can play an effective role. To take this hypothesis a step further, it is interesting that although committing suicide is the conscious equivalent of self-destruction, the consistency of the proportions of a given population taking their own lives does suggest a form of scapegoating by the societies in which they are domiciled. This mechanism appears to have been changed during times when a country is at war. Treatment seems to have had little affect on the consistency of suicide statistics.

**Hospital Conditions**

Conditions in hospital may have contributed to mortality, in an indirect way. 24 years ago hospitals were much more forbidding than they are today; indeed they were rather frightening places. Henry's (1969) findings in animal experiments showed that being placed in captivity evokes a depressive reaction. If this reaction is similar in people, then to be placed in a locked ward with strangers and with little privacy could have reinforced estrangement and stigmatisation.

Patients 24 years ago entering psychiatric hospitals gave up a large degree of individual freedom. The stigmatisation associated with hospitalization reinforced the losing of self-esteem so central to a depressive illness, both in the eyes of the patient and most probably in those of relatives, friends and everyone around them.

Life after hospitalisation for some patients could have been more intolerable than before.
Diseases and infections like T.B were rife in large hospitals. A number of respiratory deaths could have been caused by tuberculosis. All these factors could have amalgamated to be additional factors likely to cause increased mortality.

Considerable changes have taken place over the years. So it is possible that these changes, plus changes in drugs and treatments, would now effect the outcome of depressed patients in a different direction.

Treatment

Not very much is known about the variables of treatment which were prescribed for this cohort. Avery has found along with Barraclough et al that insufficient treatment leads to mortality. On the other hand harmful treatments could also lead to increased mortality.

Tricyclic drugs were widely used, together with Electro Convulsive treatment, 24 years ago. Tricyclic drugs are associated with cardiac irregularities, but the paucity of cardiovascular deaths does not support this causal association. E.C.T. again is associated with reducing mortality, not producing it. The results therefore suggest these patients had insufficient treatment, as was found by Barraclough (Page 19), but there is a paucity of first hand evidence on which to base these conclusions. So what are the other factors which could have caused increased mortality?

One should not consider depression in isolation; as previously discussed, a depressive illness includes the amalgamation of many factors causing a complexity of interaction. What is abundantly clear is the difficulty which this causes for the patient. Those involved in planning and executing treatment need to recognise the demands made on patients enduring this illness. It would seem important to restrict further demands on the patient to minimise the need for adjustment.

The literature review discussed the inaccuracies of death certification. Classification of deaths changed three times during the 24 years, and as explained on page 53, particularly affected the classification of coronary thrombosis. It is also
important to recognise that if autopsies had been performed, these would probably have altered the recorded natural causes of death. Neoplasms are particularly liable to be misdiagnosed, but 16 years after referral they make an appearance as a cause of death. It would be interesting to ascertain whether autopsies were performed, or if a change took place at that time.

**Conclusion**

Examination of excess mortality has provoked the need to discuss mortality as a reflection of morbidity. Various multiple factors influencing the patients with a depressive illness have been put forward.

Types of death were examined to see if causal mechanisms could be detected. In view of the unreliability of death certificates, some healthy scepticism about the use of the data is necessary. The two categories of death, natural and unnatural deaths, were seen as two pathways to the same destiny, and in the author's view personality may be an important arbitrator.

The sheer magnitude of the mortality found to follow a depressive illness (302 found to have died when a non depressed population would have only produced 216 deaths i.e. 86 "unnecessary deaths") is of great concern and a very important finding. It demonstrates that premature mortality is part of the natural history of a depressive illness and that the conferring of this diagnosis implies an adverse prognosis of more serious dimensions than is popularly believed.

These findings support a hypothesis which favours a holistic rather than a dualistic relationship between mind and body. Life is a function of the human organism involving mind and body. The two cannot be separated, and no psychic experience can ever take place without a simultaneous change in somatic function. Patients consequently require treatment which takes into consideration physical, psychological and social aspects; to provide one and neglect the other two is to neglect the nature of man and the nature of a depressive illness.
An Interpretation of the Results

Each hypothesis listed was confirmed;

1. A depressive illness was found to be associated with premature death.
2. Excess mortality did occur predominately in the early years of the study.
3. The diagnosis reactive and endogenous depression did confer a differing outcome with regard to morbidity and mortality.

All these factors add to the information concerning the natural history of a depressive illness. The review of the literature highlighted the surprising paucity of knowledge concerning the mechanisms which mediate between a depressive illness and premature death.

Circumstances which might reduce Morbidity

Due to pressure from patients on the waiting list, it is understandable that once acute symptoms subside the Consultant responsible discharges patients; he is unaware that a proportion who appear to have recovered still die prematurely. This is one reason why studies such as this that follow patients well beyond discharge, should be encouraged.

Treatment certainly failed to help some patients as the results demonstrate. Those patients dying prematurely had perhaps not benefitted from treatment within the psychiatric speciality though presumably they were appropriately referred.

A further tentative explanation concerns diagnosis: depression could be secondary to an undiscovered cause such as physical illness that has remained undetected. This hypotheses is suggested by the number of deaths which occurred so soon after referral. It could be that once a patient is referred to a particular speciality a differential diagnosis involving other specialists is less likely to be considered and the patient will more likely receive treatment only in the speciality to which they were referred.
In many patients physical and psychological illness may appear concurrently but our system of medical care copes inadequately with people whose concurrent illness fits into more than one speciality.

The excess mortality period extending as it did over a 24 year period is suggestive of a build-up of deterioration perhaps provoked by repeated attacks of depression culminating in premature mortality: the method unfortunately does not investigate patient health subsequent to referral.

It is also possible that these patients would have suffered less mortality had they not taken on the status of a psychiatric patient. Did this added stigma reinforce the feelings of hopelessness and further undermine their lack of self esteem which in turn increases in social isolation and leads to a substantial decrease in status?

Could there be a genetic association with the implication that mental and physical well-being are interrelated and the breakdown of both is a programmed event and beyond the intervention of treatments which prolong life.

**Conclusion**

It would appear that doctors and others have underrated the physical effects of depression. This is perhaps not surprising as the medical experts in depression (Psychiatrists) have been those doctors who have moved to the specialisation furthest from a study of bodily disease. We have also shown that depressives diagnosed as endogenous are more prone to premature mortality than are reactive depressives. Also that the early years after referral account for more of the extra mortality.

Treatment of the mind seems to achieve little for some patients. This could be because their therapists treat symptoms not whole people and lose interest once symptoms subside. One reason might be that doctors trained initially to treat the body expect the mind to heal in the same way.

Further research is now needed to find out how the mortality associated with a depressive illness which we have demonstrated can be avoided.
Studies such as this should assist those treating mental patients to be more aware of the long term outcome. i.e., that depression is associated with increased mortality not only through unnatural death but for natural disease as well.

To summarise possible causal explanations for the mortality effects following a depressive illness:

1. Psychiatric doctors may tend to neglect somatic disease.

2. Some patients with a depressive illness present with bodily and mental illness and the former is missed or neglected.

3. Bodily illness may cause depression with only the latter being presented and treated.

4. Doctors treat symptoms and not people. The advent of a scientific approach to medicine may lead to training emphasizing the physical nature of the human organism to the neglect of the psychological and spiritual aspects. In consequence physicians trained prior to the contemporary interest in holistic medicine are more liable to take a mechanistic view of the problems of these patients.

5. The stress of a depressive illness could cause somatic deterioration via the G.A.S. and endocrine system.

6. Depressive illness and physical illness occur concurrently the one exacerbating the other.

7. The final suggested causal explanation is the one favoured by the author. It is that a depressive illness ravishes the body causing structural deterioration. This promotes bodily illness leading to premature death. In the authors view items 1-6 are all relevant but the 'best fit' explanation is no. 7 it explains the interaction of mind and body: a psychosomatic hypothesis.
This thesis is all about the human organism in disease and death. Death is a physical event caused by structural failure.

The patients I have studied all had psychological disease and many died prematurely. The mechanisms which were involved remain obscure although I have proposed hypotheses to suggest what they might be.

I have worked with patients suffering from physical disease who despite treatment remained physically ill and with patients with a psychological disease where physical symptoms were presented and remained the focal point of treatment. Disease, has a role in society, and the related behaviour of individually diseased people has interested me throughout my career.

Most westernised Countries spend large sums of money treating and caring for the diseased in an attempt to put off death; nevertheless a proportion will consiously take their own lives. What is not usually debated is if man can consciously, or more likely unconsciously, accelerate bodily deterioration causing disease and death. After my clinical experience and by completing this work, it is my personal belief that this is the case.

The gulf in medicine between mind and body has thwarted progress historically; this thesis has highlighted the inadequacy of adopting such a stance. The work of Hinkle and Wolff, Querido and Selye all give some support to disease being a condition which needs to be considered from a holistic viewpoint.

If in the future disease could be seen in both a social and individual context, underlying mechanisms, rather than symptoms, might become understood. This could then facilitate appropriate treatment and so improve the cost effectiveness of the national resources devoted to health care.
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Human Gastric Function.
An Experimental Study of a Man and his Stomach.
Personality and stress

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(Received 3 June 1985)

Summary—Commercial airline pilots were investigated to determine the relationship between stress, personality and life events in a normal, i.e. non-clinical population. Pilots were asked to complete the Eysenck Personality Questionnaire, the Social Adjustment Rating Scale and a specially devised Occupational Stress Inventory. The results obtained support the hypotheses that personality factors rather than the environment play a causal role in the generation of a stress reaction within individuals.

INTRODUCTION

This article is concerned with the interaction of personality and stress. Stress is viewed by society as having only a negative influence on its members, causing sometimes a stress-induced illness. Stress-induced change leading to benefit rather than illness is a long-term concept and as such is neglected. Society takes responsibility for the generation of stress, which is then imposed on the individual, and thus the implication is that stress comes from without not from within. The present author (Evans, 1981) obtained results which implied that stress is generated in part at least by the individual by virtue of his personality. This study was conducted on unselected psychiatric patients attending a psychiatric day unit, and showed how stress precipitated the illness. High scores on a life-event scale (Holmes and Rahe, 1967) correlated significantly with high scores on P (Eysenck and Eysenck, 1975). It was hypothesized that it was personality in addition to environment which played a causal role in the generation of a stress reaction within individuals. The next step taken was to examine a healthy coping cohort, and to see if the personality and stress hypothesis still held. Aviation pilots were chosen. The mean age of the 43 pilots was 42.9 ± 10.2 yr. The pilot possesses certain qualities, which probably operate to play a selective part in his choice of career. Commercial pilots are a self-selected as well as a chosen professional group, and as such one would expect them to have certain personality characteristics in common. Early aviators were associated with feats of daring and courage, and the present-day aviator still has to experience the first solo flight, accept command responsibility and the possibility of dealing with emergencies. Selye (1974) showed that physiological stress is evoked irrespective of whether the exposure is exhilarating or frightening. The stress response is non-specific, physiological stress.

METHOD

Commercial pilots have to attend a mandatory medical examination every 6 months and failure to pass the examination means withdrawal of their licence to fly. The pilot attends an aviation specialist who is responsible for testing the pilots. Commercial pilots were selected because they form a homogeneous group for sex, intelligence, maturity and responsibility and from the point of view of this study it was important that they were not a sick population. An approach was made to the Institute of Aviation Medicine who proved to be extremely helpful and introduced the author to a large private practice in London specializing in aviation medicine. The Director showed considerable interest and was willing to allow the author to question the unselected pilots attending for examination.

Medical screening is a highly emotive subject to a pilot. His livelihood depends on maintaining health to a required standard. It was therefore to be expected that high degrees of dissimulation would occur. Hence it was necessary to allay these reasonable fears by reassuring the pilots in the initial instructions as to the complete anonymity of the study. Dissimulating conditions can be discovered by correlating the L score with the N score of the EPQ. Michaelis and Eysenck (1971), found that when conditions provided high degree of motivation to dissimulate, N and L correlated approx. 0.4 or above. Where conditions provided low motivation to dissimulate, the correlation between N and L was low.

From what is already known the presence of a high P score might mitigate against pilot safety: some correlates of P, i.e. lack of vigilance and attention set, abnormality of perceptual judgement and impulsivity would be negatively related to the skills needed by pilots. It was therefore considered particularly interesting to see if there is an abnormal degree of P in the population to be studied. An Occupational Stress Questionnaire (OSQ) was designed especially for this study and is given in the Appendix.

Procedure

As each pilot attended for the medical examination, he was asked if he would be willing to take part in an investigation, and was given an envelope containing the following questionnaires:

1. The Eysenck Personality Questionnaire (EPQ, Eysenck and Eysenck, 1975).
2. The Social Adjustment Rating Scale (SARS, Holmes and Rahe, 1967).
3. An Occupational Stress Questionnaire (OSQ, especially designed for this project).

The pilots were supplied with a stamped and addressed envelope. Included also was a letter explaining the nature of the study and requesting their help. The data was then collected and analysed to test the hypotheses.
Please place a cross on the following lines to indicate in your judgement the amount of stress reaction you experience due to or in the undermentioned situations, for example:

<table>
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<tr>
<th>0%</th>
<th>Take off</th>
<th>100%</th>
<th>Very considerable stress</th>
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<tbody>
<tr>
<td>No stress at all</td>
<td></td>
<td>Very considerable stress</td>
<td></td>
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**Flying:**

1. Monotony of Mission
2. Limited Visibility
3. Instrument Flying
4. Seating Comfort
5. Aircraft Vibration
6. Night Flying
7. Stacking
8. Landing
9. Take-off
10. Aircraft Reliability
11. Seat-belts
12. Field of View
13. Cabin Lighting
14. Aircraft Instruments
15. Navigation Instruments
16. Avionics (Radios)
17. Interest in Mission
18. Glare
19. Adequacy of Ground Support
20. Hunger and Thirst
21. Noise
22. Temperature Regulation
23. Economic Cutbacks Which Affect Safety etc.
24. Administration; Paperwork
25. Meteorological Checks
26. Taxiing
27. Personnel Relationships
28. Social Involvement
29. Recreational Outlet
30. Morale
31. Command Relationships
32. Medical Checks
33. Type Testing
34. Sleep
35. Lag
36. Fatigue; Job Overload
37. Thwarted Ambition
38. Emergency

Please list any additional stresses:
STRESS AND PSYCHOTICISM

Wendy Evans
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(Received 5 May 1980)

Summary—The EPQ, a stress questionnaire, and a bodily symptom questionnaire were completed by 21 female and 12 male psychiatric patients. The P score correlated with a high stress score, and certain stress items differentiated extreme high and low P scorers. In addition, high P scorers were found to have a tendency to increase, rather than decrease some of their bodily symptoms after treatment. A different approach to treatment for high P scorers is suggested.

INTRODUCTION

The importance of personality in the determination of disease is rarely recognised outside the realm of psychology, and psychiatry. Even within psychiatry criticism can be levelled at the blanket approach to treatment, without due regard to the part individual personality dimensions play in the way an individual reacts to stress. There is evidence, that disease can reflect personality; for example Sainsbury (1960) found that patients attending clinics at a general hospital, showed significant differences in personality variables: patients receiving treatment for warts were found to be significantly more neurotic, and more extraverted than controls, reflecting a hysterical pattern, whereas cases of prolapse, reflected the dysthymic personality (high neuroticism, low extraversion). The fracture clinic was particularly interesting; the mean extraversion score was significantly high, while the mean neuroticism score was low. Thus it was reasonable for Sainsbury (1960) to conclude, that the existence of certain personality dimensions may make one accident prone (see also Shaw and Sichel, 1971).

A relatively new dimension of personality, the psychoticism, or tough-mindedness dimension, may also be relevant (Eysenck and Eysenck, 1975). This dimension is quite independent of extraversion and neuroticism and it is believed that genetic factors contribute more to individual differences, than do environmental factors. High 'P' scorers as described by Eysenck are: solitary individuals, not caring for people, often troublesome, not fitting in anywhere, lacking in feeling and empathy, insensitive, hostile, aggressive and impersonal sexually. Criminals and psychotics have high P scores, while the psychiatric disorders which typify the above behaviour patterns are: drug addicts, alcoholics, schizoid, psychopathic and behaviour disorders.

It is generally thought that stress is generated within society, which in turn generates strain in the individual, and that different personality types differ in their vulnerability to stress. What might be extremely stressful to one might not be so to another. Another way of looking at stress is to hypothesize that certain individuals, such as those scoring high on P, actually generate their own stress. Their life-style eventually catches up with them. They are surrounded by the results of their own behaviour and their need for arousal. They act with some disregard for danger, as their impulsivity supplants concern for the consequences of their actions, to themselves or to others.

An opportunity arose to test this hypothesis, while the author was exploring the relationship of bodily symptoms to psychological adjustment, in a psychiatric day hospital.

PROCEDURE

Permission was obtained to invite each new day-patient at a small psychiatric day hospital, to participate in the inquiry. All admissions to the day hospital between October 1978 and May 1979 were approached, with the exception of a group of ten...
patients who were admitted during a time when for personal reasons, the author was not available.

The day hospital where this study took place, does not adhere to any one particular method of treatment. It maintains a somewhat eclectic approach, but with a psychotherapeutic bias. On admission, the patient becomes a member of a group, which operates to closely resemble a family. This facilitates depth of feeling, sharing, developing loyalties, and if necessary inflicting sanctions, on those within its influence. A treatment programme is planned, in which all the members of the group participate. Thus, in this treatment setting, all are accountable for their own behaviour, with overall accountability to the psychiatrist in charge.

Every new patient, on the second day at the Psychiatric Day Hospital, was asked if he would take part in a study. The patient was then given three questionnaires.

(1) The Eysenck Personality Questionnaire (1975).
(2) The Holmes-Rahe Life Event Score (1967). This provides a social adjustment rating scale (S.A.R.S.), which indicates stress due to life events, one year prior to admission. A score of 200 or more indicates vulnerability to mental illness.
(3) Bodily Symptom Questionnaire. This questionnaire was developed especially for this study by the author. It aims to measure a number of symptoms, the majority of which are due to autonomic arousal.

The overall sample comprised 21 females and 12 males whose ages ranged from 20–70 yr. The sexes were analysed separately, because the mean P score for normal males is higher than for normal females. In some calculations in the tables there are less than the full sample, because some patients failed to complete all questionnaires.

RESULTS

Table 1 shows that a relationship exists between P and stress in both the males and females significant at the 0.05 > p < 0.02 level.

In order to further examine the relationship the samples were divided into extreme high P, and low P scorers.

Table 2 shows the comparison of the 14 high P scorers with the 11 low P scorers. The differences in stress scores are highly significant.

The 43 items which were weighted in the S.A.R.S. and designed to measure stress, were then scrutinized to find which items were most typical and most often endorsed in the high P group. When the 12 items selected (Table 3) were scored for the two extreme groups, males and females together, the correlation with the P score was found to be 0.634. It would then appear that these 12 items from the S.A.R.S. indicate the type of stress likely to be found in the high P group.

Of additional interest is the question of bodily symptoms. Both the high and low P groups showed high levels of autonomic arousal, as measured by the bodily symptom questionnaire. There was, however, an important difference; whereas the low P group showed a positive response to treatment at follow-up there being fewer bodily symptoms
Table 2.

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<tr>
<th></th>
<th>Female</th>
<th>Male</th>
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<tr>
<td></td>
<td>P</td>
<td>E</td>
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<tr>
<td>Low P (8)</td>
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<tr>
<td>Mean</td>
<td>0.12</td>
<td>5.6</td>
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<tr>
<td>S.D.</td>
<td>0.3</td>
<td>4.6</td>
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<tr>
<td>High P (7)</td>
<td>Mean</td>
<td>7.2</td>
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<tr>
<td>S.D.</td>
<td>2.0</td>
<td>5.11</td>
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P = Toughminded score.
N = Neuroticism.
E = Extroversion/Introversion score.
L = Lie score.

than on admission, this was not so with some of the high P scorers who collected extra bodily symptoms. A correlation between P and extra bodily symptoms resulted in \( r = 0.342 \).

In Table 2 it will be seen that those patients in the low P category are also exceptionally high on L, particularly the females. This might be worth investigating further in a subsequent study, because one possible effect of this could be that dissimulators (who score high on L and exceptionally low on N) would claim fewer symptoms both before and after treatment than they really possess. This argument could also account for the very considerable difference between the stress scores of high and low P scorers.

**DISCUSSION**

A positive relationship has been demonstrated between the P factor and stress, it must now be considered whether this is likely to be causal or coincidental. Does for example, the presence of stress lead to high P or vice versa? Of particular interest in this connection were the 12 items of additional stress identifiable within the high P group. Having isolated these items it was then not difficult to see how the particular traits of high P scorers mentioned in the introduction, can give rise to the type of stress most prevalent in that group.

Change in sleeping, eating, sexual difficulties, change in living conditions, trouble with in-laws, reflect the lack of harmony within the home, and interpersonal relationships. Perhaps most fundamental to a harmonious life is to feel deeply, foresee the consequence of our actions and have the ability to empathize. Business adjustment, change in financial state, change in responsibility, trouble with the boss, violation of the law, indicate the type of stress outside the home to which high P scorers are particularly vulnerable.

Mowbray et al. (1961) found psychiatric patients were referred not on the basis of clinical diagnosis, but because of abnormalities of conduct, social problems or inappropriate responses to medical attention. Approximately a third of the whole sample in this study came within the high P criteria which would correspond to the referral characteristics of Mowbray.

Table 3.

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<tr>
<td>1. Divorce</td>
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<td>2. Sex difficulties</td>
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<td>3. Business adjustment</td>
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<tr>
<td>4. Change in financial state</td>
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<tr>
<td>5. Change in responsibility at work</td>
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<tr>
<td>6. Trouble with in-laws</td>
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<tr>
<td>7. Change in living conditions</td>
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<tr>
<td>8. Trouble with the boss</td>
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<tr>
<td>9. Change in sleeping habits</td>
</tr>
<tr>
<td>10. Change in eating habits</td>
</tr>
<tr>
<td>11. Christmas</td>
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The bodily symptom questionnaire revealed a high level of symptoms associated with autonomic arousal, in both groups. There was, however, an important difference: whereas the overall group showed a positive response to treatment in the bodily symptoms at follow-up, i.e. there were fewer symptoms than on admission, this was not so with the high P scorers, who appeared to have collected extra bodily symptoms during treatment. This suggested that high P scorers do not benefit from a treatment regime which relies heavily on group work. It is possible that the solitary non-feeling P scorer has no point of reference from which to draw, in order to benefit from the strong feelings generated within a group. He may even feel increased isolation. This raises the question 'Should these patients receive treatment alongside patients whose problems are of different complexity?' The evidence would seem to suggest, that at the very least, the treatment team should be aware of the implications. Treatment of those with high P scores might perhaps utilize a more educative approach, whereby behavioural methods are employed to enforce the notion that stress is the result of misapplied behaviour. Thus, personality and attitudes to health must be recognised as potentially important determinants of treatment outcome.

Acknowledgements—My sincere thanks to Dr S. B. G. Eysenck for her help and encouragement, to Dr I. G. Thomson and to staff and patients of the Frank James Day Unit, East Cowes.

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