# "AN EXPLORATION OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STRESSORS AND THE IMMUNE RESPONSE IN HUMANS"

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# ABSTRACT


The traditional biomedical paradigm upon which contemporary Western Medicine is based has been found to be increasingly inadequate to explain a wide range of research findings, both physiological and behavioural, which suggest that rather than being separate entities, 'Mind' and 'Body' are on a continuum and there are bi-directional links between the Central Nervous System and the Immune System. What is emerging is a new paradigm which emphasises the rather complex interactions between social, psychological and biological factors which has become known as "psychoneuroimmunology (PNI)".

The present study reviewed the literature supporting the PNI paradigm and aimed to test empirically the hypothesis that psychosocial variables can influence the workings of the immune system. The measure of immune response used was the subjects' blood antibody titre response to a course of Hepatitis B vaccinations (dependent variable) and a comprehensive range of psychosocial variables were used as the independent variables.

The results indicated that 'hyper-reactivity' (the interaction of anxiety and somatic symptoms of stress) was associated, with raised blood antibody levels, whereas 'hypo-reactivity' (the interaction of depression and emotional exhaustion) was associated with lowered blood antibody levels. The results of a stepwise multiple regression analysis found that these two interactions together with 'perceived control' (manageability subscale of the Sense of Coherence Questionnaire) jointly predicted 26% of the variance in blood antibody titre scores. Independently, 'hypo-reactivity accounted for 11%, hyper-reactivity 8% and perceived control 7% of the variance accordingly ($p<0.0005$). Hypo-reactivity was also found to be predictive of sickness absence over a one year period, accounting for 6.5% of the variance in sickness absence ($p<0.05$). The results also suggest that Personality and Coping Style act as moderating variables between life events and emotional distress.

A 'two stage' model of the relationship between psychosocial stress and the immune response to Hepatitis B vaccine is proposed, which emphasises 'perceived controllability over life events' as a central factor in the type and severity of emotional distress experienced and ultimately effects on the immune system.

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In particular, I would like to thank my wife, Kathy, who has spent many long and lonely evenings sitting on her own downstairs whilst I have been upstairs working in the study.

# DECLARATION

**I, Martin Roy Bamber, declare that this Thesis is all my own work and has not been submitted in candidature for any other degree, diploma or professional qualification.**

Martin Roy Bamber

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# INTRODUCTION

## THE HISTORICAL PERSPECTIVE

The notion that Mind and Body are separate entities can be traced back to the early Greeks (Friedlander 1989). This view point reached its zenith with the writings of Descartes in 1619 (Hall 1989). This perspective became known as 'Cartesian Dualism'. Modern Western Medicine has subscribed overwhelmingly to the notion of 'dualism' and to a large degree has aided its fortification and acceptance, through its rigid adherence to the 'Biomedical paradigm' of health and disease (Friedson 1970; Johnson 1972; Kennedy 1981).

Stereotypically the biomedical model adopts a very mechanistic view of human beings. A person is considered healthy when their machinery is in perfect working order. If there is a malfunction in the machine, then by tinkering around with individual pieces (organs), the machine (the human being) can be repaired. Ill-health is seen as a breakdown in this machinery and causes of ill-health are seen to lie within the individual at the cellular, biochemical and organic level. The 'Mind' half of the dualistic paradigm has on the whole been neglected (Friedlander 1989).

The concept of 'dualism' has not however gone totally uncriticised. In fact, Aristotle was one of the first to hypothesise a connection between physical health and mood (Hall 1989). Also, Sir William Osler, widely accepted as the father of modern medicine stated that:

> "it is as important to know what is going on in a man's head as what is going on in his chest when predicting the outcome of pulmonary tuberculosis" (Solomon 1985).

Broadly speaking however, the biomedical paradigm does not subscribe to the possibility that a person's state of mind can play a causal role in the aetiology of disease. Yet, there is a wealth of historical evidence based upon cultural beliefs and folklore which describes phenomena that cannot be readily explained within the framework of the biomedical paradigm.

The literature is full of historical accounts of 'supposedly' medical remedies which on closer analysis have been found to contain no specific organic effect for the condition being treated and yet which have been demonstrated to, have a therapeutic 'effect' for the individual being treated (Shapiro 1959). Houston (1938) reported that not one treatment with a physical basis can be found in all the writings of Hippocrates!

A catalogue of bizarre, dangerous and often fatal 'treatments' have been used to cure illness throughout history. Preparations containing faeces, urine, eunuch fat, vipers, worms and all manner of insects, metals, pearls, precious stones, coral and religious relics have in all seriousness formed the basis of medications at some time in history (Totman 1979).

'Faith healing' treatments have existed in most parts of the world since classical times, whereby healing has been assumed to come about by some invisible process through the medium of touching, stroking, exorcism and spiritual purging. The bible accredits over fifty miracle cures to the work of Jesus and some of them explicitly related to organic conditions. Such treatments have usually been found to be most effective when carried out by someone of high status (e.g. a witch doctor), or if not high status, certainly someone who is feared (Totman 1979).

Accounts of exorcism, voodoo, witchcraft, faith healing, miracle cures and witch doctors are often dismissed in today's high technology and sophisticated society as being mere folklore, born out of ignorance amongst uneducated and more primitive cultures throughout history. However, it would be very arrogant of us to dismiss such practices in their totality since, what is clear is that they have stood the test of time (unlike some modern medical practices) and people have benefited from them. It would perhaps be more sensible and scientific to try and understand what aspects of such remedies are actually therapeutic, than to simply assert that they are all nonsense. This does not mean however that folklore can be used as a substitute for rigorous scientific investigation.

What all these historical accounts appear to share is not any direct organic effect resulting from the medical remedies described but the "belief" that the remedy will be effective. Having this belief in the remedy does influence something at a physiological level. Such a conclusion that Mind and Body may interact in this way poses a direct challenge to the dualistic paradigm upon which Western Medicine is based.

Perhaps the most dramatic demonstration that beliefs have the power to influence physiology is provided by what has become known as the placebo effect. Shapiro (1978) defined the placebo effect as:

> "Any therapy or that component of any therapy, that is deliberately used for its non-specific, psychological psychophysiological effect, or that is used for its presumed effect on a patient, symptom or illness but which unknown to the patient or therapist is without specific activity for the condition being treated".

The placebo effect has been demonstrated in pain relief (Beecher 1955; 1962) and a number of other conditions including headaches, migraine, sea sickness, insomnia, psychoses, neuroses, cerebral infarction, multiple sclerosis, epilepsy, Parkinsonism, alcoholism, asthma, hay fever, colds, coughs, angina, arthritis, gastro-intestinal disorders, constipation, skin diseases and menopausal disturbances (Haas, Fink and Hartfelder 1963) and hypertension (Ader and Cohen 1985).

Dunlop, Henderson and Inch (1952) reported that about one third of British prescriptions written in 1952 could be considered to be in the 'placebo' category. A particularly graphic example of the placebo effect is provided by Fielding et al (1983) in the following study: The researchers told a group of patients they could expect hairloss from chemotherapy about to be administered. Thirty percent of these patients then unknowingly receive placebos instead of chemotherapy and suffered hair loss even though they had taken pills contained no medication!

In conclusion, what most historical accounts of effective medical cures have in common, whether they be miracle cures, faith healing or one of a whole range of bizarre and often dangerous concoctions described by Totman (1979) is not a direct effect on the organic condition itself but an indirect action through the 'placebo effect'. The placebo effect demonstrates that the power of suggestions, beliefs and expectations in the 'Mind' are able to influence the 'Body' at a biochemical level, such that what one believes can become a biological reality (Cousins 1989). This phenomenon has been acknowledged by the behavioural sciences, which for many years have been aware of the role of psychological factors in the aetiology of certain somatic complaints. This is highlighted in the field of psychosomatic medicine.

## TOWARDS A NEW PARADIGM

Generally , the traditional biomedical paradigm cannot really accommodate deviations from the dualistic notion of Mind and Body and the idea that psychological factors might play a causal role in the aetiology of disease does not sit comfortably alongside it. What is really needed is a new paradigm which can accommodate the findings described in the introduction. Recent research is beginning to provide this.

It is only over the past 15 years or so that a more holistic approach to the study of Mind-Body interactions has been adopted. Molecular biologists, immunologists, neurologists and behavioural scientists have begun to explore more fully the role of the much neglected half of the dualistic paradigm - the 'Mind', in the aetiology of disease. What is emerging is a much more complex picture of the interactions between social, psychological and biological factors in the aetiology, course and treatment, not of just those traditionally thought of as psychosomatic but all diseases (Jemmott and Locke 1984; Reiser 1984), than had ever been contemplated by the rather simplistic conceptualisations of the biomedical paradigm. The abandonment of the autonomous biomedical model is now not in question (Jennings 1985). It is perhaps more the extent of the abandonment which is most in question (Fletcher 1991). Even the traditional psychosomatic model of medicine is now seen as incomplete, since it originates from the notion that certain diseases are caused solely by psychological as opposed to organic factors, rather than an integration of the two (Martin 1987).

It is becoming apparent that the Mind and Body are on a continuum and parts of a critical interacting network, not discrete, separate and autonomously functioning units. A new paradigm of health and illness is emerging which breaks down the artificial constructs of the biomedical model and the separation between Mind and Body. A new and extremely complex window into the psychological and behavioural factors which influence the course and onset of diseases is emerging (Locke and Colligan 1986). This new perspective has generally become known as 'psychoneuroimmunology' (PNI) - a term coined by Ader (1981; 1987). Pelletier and Herzing (1988) have proposed a new commonly accepted definition of PNI as:-

> "The study of the intricate interactions of consciousness (psycho) brain and central nervous system (neuro) and the body's defence against external infection and aberrant cell division (immunology)".

There is a wealth of evidence which supports the PNI hypothesis that there are links between Mind and Body and that these links are bi-directional. According to Tecoma and Huey (1985) and many other PNI theorists, one of the psychological variables most commonly studied is that of 'stress'. Also, with respect to disease aetiology, the variable most commonly studied and presented in the literature on PNI is that of immune functioning! It is no coincidence therefore, that the present study focuses upon the variables of stress and immune functioning in its review of the literature. Since most of the studies reviewed address some aspect of stress and/or the immune response, it could be appropriate at this point to provide a brief overview of both stress and immunity that would be comprehensible to the non-psychologist and non-immunologist respectively. This will hopefully equip the reader with a basic knowledge, which will enable them to more fully appreciate the evidence being presented.

## AN OVERVIEW OF STRESS

### Defining Stress

McGrath (1970) has identified four conceptually useful categories of stress research:-

1. Stress as an 'external force exerting pressure on an object'. The reaction of the object is regarded as strain. This is essentially an 'engineering' definition of stress.

2. 'Stress as a 'response'. This describes stress as a response or class of responses which indicate that the organism has been under stress.' This approach is typified by the work of Selye` (1956; 1974) who suggested that stress is a non-specific response of the body to demands made upon it. Selye` described this as the 'General adaptation Syndrome'. Such an approach concentrates mainly upon the physiological level of functioning.

3. The 'situation-based' definition, whereby stressed is caused by events or characteristics of the environment. This approach is most closely typified by the life events research (Holmes and Rahe 1967; Glass and Singer 1972; Grosser et al 1964).

The three conceptual categories mentioned above are incomplete in that they would predict that stressful conditions would produce dependable effects and this is clearly not the case (Lazarus and Eriksen 1952). In addition the situation-based definition does not take into account factors within the individual which modify their susceptibility to environmental events, such as the 'personal meaning' of events to the individual (Lazarus 1993). Cognitive appraisal and coping resources are central to understanding the concept of stress (Lazarus 1993).

4. Stress as an 'interaction between the individual and the environment' (McGrath 1970; Monat and Lazarus 1977; Cox and Mackay 1978; Lazarus and Folkman 1984; Lazarus 1993). Monat and Lazarus (1977) argue that stress results from the individual's appraisal that coping resources available to him/her are less than he/she needs to cope with a threatening situation. They also view coping as a process involving ongoing efforts involving thoughts and actions aimed at attempting to change external conditions. Lazarus (1991b; 1991c) argues that appraisal and coping act as powerful mediators between the environment and emotional outcomes.

A good definition of stress according to Lazarus (1993) must consider four concepts, namely a causal external or internal agent, an evaluation (or appraisal), coping processes and the complex pattern of effects on the psychology and physiology of the individual. In this sense the definition of psychological stress as an interaction between the individual and the environment is the most complete one, as outlined in McGrath's (1970) fourth category. Lazarus and Folkman (1984) define psychological stress as:-

> "A particular relationship between the person and the environment that is appraised by the person as taxing or exceeding his or her resources and endangering his or her well-being".

This definition is a good one because it incorporates environmental demands, subjective internal demands and the adaptive resources of the individual.

The terms 'stress', 'stressor' and 'strain' are often used interchangeably in a rather haphazard way and yet they refer to conceptually distinct aspects of stress. Beehr and O'Hara (1987) describe 'stress' as a general term which refer to stressors and strains jointly. They define a 'stressor' as an environmental characteristic (external stimulus) or a thought (internal stimulus) which causes an adverse reaction in the individual.

This adverse reaction which is evoked is known as 'strain', which has both psychological and physiological consequences.

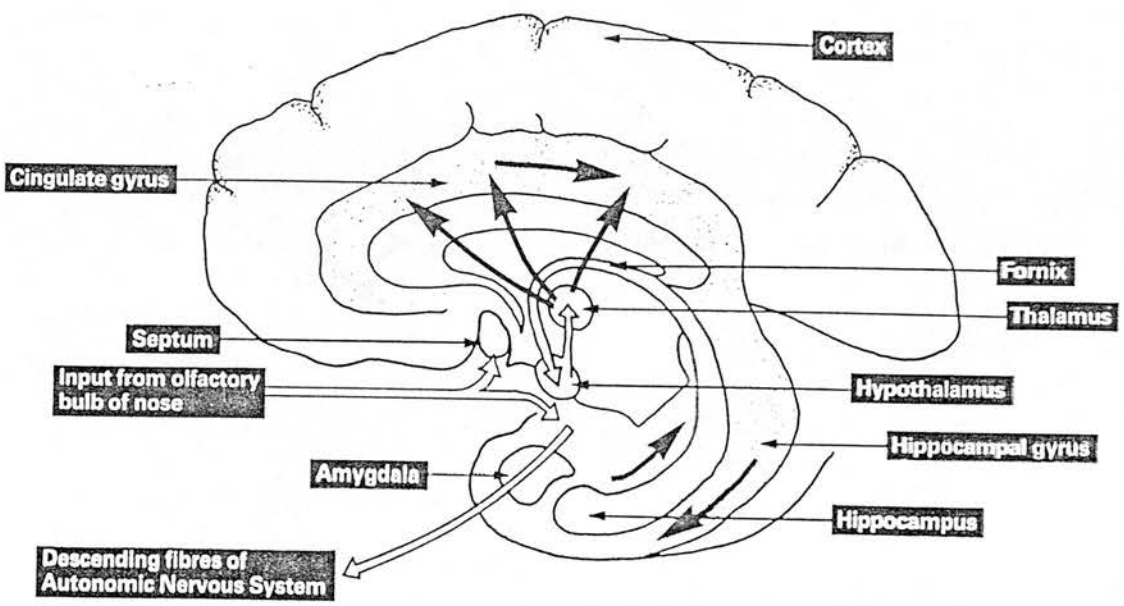
## The Psychophysiology of Stress

The physiological response to stress has two major components. The first, is located centrally in the brain, linking a number of structures in the brain known as the limbic system (Papez 1937) This includes part of the most sophisticated and highly developed area of the brain, the cerebral cortex.

The second component extending from the brain through two related branches of the nervous system called the sympathetic and parasympathetic nervous systems, is called the autonomic nervous system which extends to most of the important organs of the body. Linked to this is a chemical system which assists the nervous system activity through the release of hormones, which will be discussed later in this section.

The limbic system forms a circuit linking a number of higher brain structures:-

**Figure One:** **THE LIMBIC SYSTEM**




Source: Wycherley (1989) 'The Living Skills Handbook' Outset Publishing 4th Edition.

These structures, particularly the amygdala have been proposed to form the physiological basis of the 'fight or flight' response to stress. (De Moliner and Hunsberger 1962). From the temporal lobe the hippocampus loops over the fornix to the hypothalamus which is thought to have a major role in the production of an organised emotional response by integrating the 'fight or flight' response with the more considered influences of the cortex, which is the thinking section of the brain. It analyses and interprets incoming information from the sense organs and also plays a part in selecting the response to that information on the basis of its personal significance to the individual based on past experiences and genetic predisposition. The hypothalamus has two distinct segments, one concerning bodily activation to cope with environmental demands and the other concerned with the reduction of bodily activation to allow for recuperation. Continuous dominance of the arousal segment is associated with chronic anxiety and dominance of the inhibitory segments associated with depression. These two segments are associated with the two sections of the autonomic nervous system, arousal with the sympathetic section and inhibition with the parasympathetic section. Thus the hypothalamus forms the starting point of the two sections of the autonomic nervous system. The higher centres of the brain interpret the incoming information and send instructions to the hypothalamus which then activates one or other of the two sections of the autonomic nervous system:-

| **MAIN SIGNS** | |
|---|---|
| Parasympathic state | Sympathetic state |
| Eyes closed | Eyes open |
| Pupils small | Pupils large |
| Nasal mucus increased | Nasal mucus decreased |
| Saliva produced | Dry mouth |
| Breathing slow | Breathing rapid |
| Heart rate slow | Heart rate rapid |
| Heart output decreased | Heart output increased |
| Surface blood vessels dilated | Surface blood vessels constricted |
| Skin hairs normal | Skin hairs erect (gooseflesh) |
| Dry skin | Sweating |
| Digestion increased | Digestion slowed |
| Muscles relaxed | Muscles tense |
| Slow metabolism | Increased metabolism |

**Table One:** Sympathetic and Parasympathetic Balance

Linked to the hypothalamus by a small stalk and connected to it by both nerves and blood vessels is the pituitary gland, which produces a number of hormones which control the activity of other glands elsewhere in the body, which themselves produce hormones. One of the most important of these are the adrenal glands, which assists the body to cope with strain by producing stress hormones. These stress hormones in lower concentrations have a protective effect against invasion and infection in the short term. However, if the stress is prolonged and continuous the body's ability to fight invasion and contain infection is reduced.

**Neuroendocrine Mechanisms Associated with Stress**

Two major neuroendocrine systems have been associated with stress. The first, which is associated with acute stressful states such as fear, anger and excitement (Amkraut and Solomon 1975) is the "Sympathetic - Adrenal - Medullary System" (SAM). SAM activation has been associated with action proneness and raised effort and it has also been described as the 'fight or flight' system. It is activated when the organism is challenged in its control of the environment and, is accompanied by the release of catecholamines (epinephrine and norepinephrine) into the blood stream. Catecholamine output is increased in response to a challenge to perform well (Lundberg and Frankhauser 1980; Frankhauser, Lundberg and Forsman 1980).

The second is the "Hypothalamic - Pituitary - Adrenal - Cortical" (HPAC) system (Frankhauser 1983; Asterita 1985; Cannon and de la Paz 1911; Cannon 1932; Lundberg and Frankhauser 1980; Henry and Stephens 1977; Levine and Ursin, 1980; Ursin Baade and Levine 1978; Seyle` 1950, 1956 and 1974). The HPAC system has been described as the 'conservation - withdrawal' system and is associated with negative feelings of distress (Lundberg and Frankhauser 1980; Frankhauser 1983) and a withdrawal response (Henry and Stephens 1977). Activation of the HPAC System is most commonly associated with chronic stress and is thought to occur when threats are appraised as being overwhelming and the individual not coping. It is also accompanied by depression (Henry and Stephens 1977; Gibbons 1964; Gitlin and Gerner 1986). HPAC activation results in the release of adrenocorticotrophic hormone (ACTH) and corticosteroids (cortisol in humans). Under conditions of successful coping the HPAC system is suppressed (Levine, Weinberg and Brett 1979). More recently it has also become clear that endogenous opioids (peptides found in the brain and the periphery) are also released in

response to stress (Bandura, Cioffi, Taylor and Brouillard 1988).

The bodily responses to a stressor can be summarised in the following Figure:-

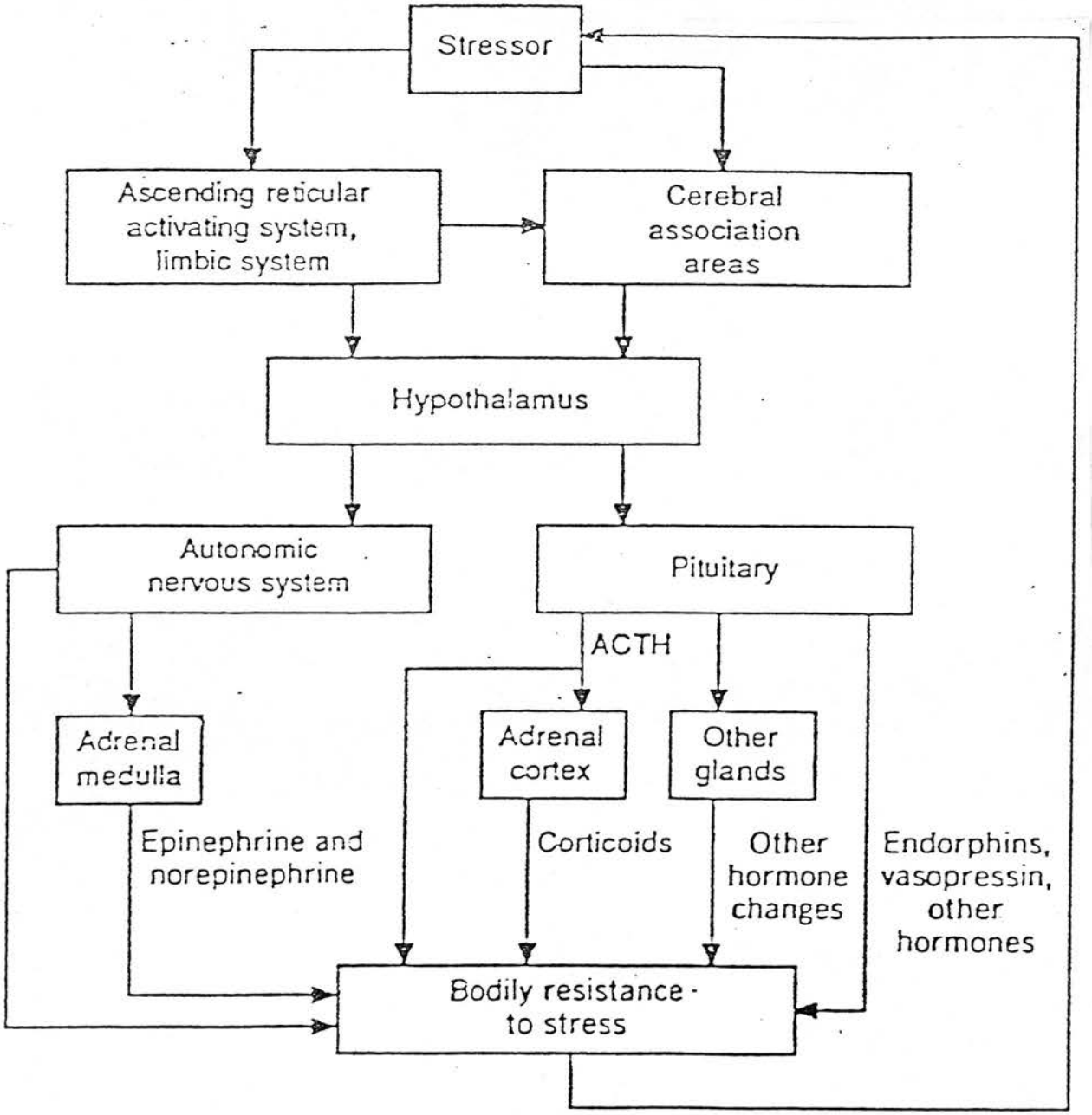



**Figure Two:** Summary of the bodily response to a stressor
(Source: Buck 1988 pg.59)

## THE IMMUNE SYSTEM

The immune system is a system of defence against harmful pathogenic micro-organisms called antigens (foreign material that does not belong to the body) which come in all shapes and sizes such as metazoa or worms (e.g. tape worm), protozoa (e.g. malaria), fungi (e.g. candida), bacteria (e.g. streptococci, salmonella) and viruses (e.g. rabies, influenza and glandular fever). It also protects the body from internal hazards such as uncontrolled cell division of mutant cell cells, which if not recognised and destroyed become neoplasms (tumours). The immune system plays a part in many diseases from colds to cancer. It is precisely regulated and when this homeostatic balance is disrupted, either by underactivity or overactivity of the immune system, the move towards disease may occur:-

| | Overactive Immune System | Underactive Immune System |
|---|---|---|
| Exogenous Antigen | Allergy | Infection |
| Endogenous Antigen | Autoimmune Disease | Cancer |

**Table Two:** Disruption of the Homeostatic Balance of the Immune System

Source: Borysenko (1987)

Basically the immune system consists of cells, tissues and organs connected via blood and lymphatic vessels, all acting in a well orchestrated integrated and holistic way. The main organs of the immune system include the 'lymphoid' organs, comprising of bone marrow, thymus, lymph nodes, spleen and lymph nodules (appendix, tonsils, Peyer's patches) which filter out pathogenic material at certain points in the circulation of the blood.

**Primary Defences**

The first line of defence in the body's fight against infection is the skin, which is impermeable to most infectious agents. Sweat on the skin contains lactic acid, fatty acids and sebaceous secretions which create an acidic environment in which bacteria fail to survive.

Mucous membranes consisting of ciliated epithelial cells line the inner surfaces of the body and secrete mucous to which microbial and foreign particles stick. Ciliary action then moves them towards the orifices of the body, for example through actions such as coughing and sneezing.

Many bodily fluids contain bactericidal components. These include the washing action of tears, saliva and urine, the hydrochloric acid in gastric juice, spermine and zinc in semen, lactoperoxidase in milk, lysozyme in tears, nasal secretions, saliva containing immunoglobulin, cellular synthesis of interferon and its secretion into extra-cellular fluids.

The 'natural flora' of the body demonstrate that the body can tolerate certain micro-organisms which are essential to it, but only in their rightful place. If they are displaced for any reason, they are destroyed by the immune system. This natural flora suppresses the growth of many potentially pathogenic bacteria and fungi by competition for essential nutrients or by the production of inhibitory substances.

If for any reason the skin is broken, the primary defences mentioned above are no longer sufficient to protect the body from bacteria, which can pass through the skin's barrier, nourish in the new environment, grow and multiply and cause local infection. In this case the body has a number of secondary local defences.

**Secondary Local Defences**

One example of secondary local defences is the 'inflammatory response'. The production of histamine which causes blood vessels in the locality of the cut to relax and so increase blood supply to the area. White blood cells called phagocytes are attracted to the area of the wound, causing severe local swelling and begin to engulf the bacteria by a process known as phagocytosis. The bacteria becomes completely engulfed into a vacuole and is then digested. After a while the phagocytes die and form 'debris' in the area of the cut called 'pus'.

Phagocytes are produced in the bone marrow and have a non-specific response to antigens. One group is known as the polymorphonuclear phagocytes (granular leukocytes) of which there are four types. Firstly, neutrophils (polymorphonuclear leukocytes) are avid phagocytizers of bacteria. Their granules contain bactericidal substances which degrade ingested bacteria. Secondly, eosinophils (eosinophilic leukocytes) are also mobile phagocytic cells with a high affinity for antigen-antibody reactions. They proliferate in response to allergies and parasitic infections and their granules contain enzymes which degrade ingested substances. Thirdly basophils (basophilic leukocytes) are least numerous but possess large granules containing histamine, which when released cause small blood vessels to become permeable and allow various leukocytes to migrate from the blood stream to connective tissues where severe local swelling may occur (as in the inflammatory response described earlier). Finally, there are mast cells which do not circulate in the blood but have an important role in allergic reactions.

Non-granular leukocytes known as monocytes (also known as macrophages) are active in loose connective tissues and organs and display non-specific phagocytosis, which is particularly common in the lungs, which airborne pollutants may enter.

Monocytes, along with granular leukocytes (neutrophils, eosinophils, basophils and mast cells form part of the 'innate' immune response). Phagocytic cells which engulf and digest microbes are attracted to them by the 'complement system' (a complex series of about twenty proteins found in the plasma), which is itself activated by the presence of microbes. Some phagocytes form a cordon around the wound, so as to prevent bacteria spreading beyond it to healthy tissue. All of this constitutes local inflammation and its function is to prevent bacteria entering the blood stream.

Also, when skin is damaged, 'blood clotting' takes place to prevent infection and excessive loss of blood. Blood platelets shatter open on exposure to air and release thromboplastin which converts prothrombin into an enzyme called thrombin. Thrombin then converts another blood protein called fibrinogen into 'fibrin fibres'. These fibrin threads form a network of fibres across the wound which entangle red blood cells to form a blood clot. This clot dries into a scab which covers the would and protects it from entry of micro-organisms and any further blood loss.

Associated with skin damage and inflammation is the 'fever response', which promotes healing and stimulates the immune system. This response is produced by Interleukin-1 stimulating the anterior hypothalamus, inducing slow wave sleep and stimulating the production of large amounts of growth hormone.

Should the local defences be insufficient to protect the body and some bacteria enter the blood stream, the organs of the blood stream (described earlier) will filter out pathogenic material at certain points in the circulation of the blood. For example lymph nodes contain armies of fixed non-mobile phagocytes, which lie in wait to trap and destroy bacteria.

Should this fail, there is a final and very powerful system of defence which is mobilised. The body starts to produce 'antibodies', which form the basis of the acquired/ specific immune response. This response has three essential characteristics. Firstly, it can recognise self from non-self. Secondly, the antigen-antibody reaction is very specific, rather like a lock to a key. Thirdly, in order to differentiate a specific antigen from a vast array of foreign substances, immunological memory is required. The immune system learns to recognise the antigen and consequently produces a secondary action which is more rapid and potent that the initial one (This forms the basis of vaccination). There are two forms of acquired immune response. The first is humoral immunity and the second is cellular immunity.

**Humoral Immunity**

Humoral immunity involves the synthesis and release of antibodies into the blood, lymph system and other bodily fluids. These are said to be free antibodies and are generally referred to as 'immunoglobulins'. Immunoglobulins are present on the surface of B cells. B cells which are produced in the bone marrow proliferate by cell division into identical clones, which will only produce the specific immunoglobulins with the same receptors for antigens as the parent cell. There are five classes of immunoglobulins (Igs) namely IgG, IgM, IgA, IgD and IgE.

IgG is the most abundant and has important extra-vascular functions for combating micro-organisms and their toxins. IgM has a large molecular weight and a short life span. It is functionally limited to the blood stream and is an effective glutinator

(i.e. dumps bacteria and erythrocytes). IgA is present in serum and the gastro-intestinal and respiratory tracts, genito-urinary surface membrane secretions and other secretions such as sweat, colostrum, nasal fluids and saliva. It functions by coating pathogens and inhibiting their adherence to mucosal cells. IgD is primarily found in the blood stream on the surface of lymphocytes in small amounts (approximately 3% of lymphocytes in adults). Its precise role is not defined but it is thought that it may act together with IgM as an antigen receptor for the control of lymphocyte suppression and activation. IgE when combined with antigens is responsible for severe and acute allergic reactions. Most of it is bound to basophils and mast cells where it induces the release of histamine, which is associated with allergic reactions. It may also help in helminthic (worm) infection.

**Cellular Immunity**

Cellular immunity is the final line of defence against infection. It is used against bacteria and viruses which live and replicate within host cells. This form of immunity is achieved through a second category of cells called T lymphocyte cells (the first being B cells as described in humoral immunity). T Cells are also produced in the bone marrow but mature in the thymus. They generally work directly by releasing toxins or indirectly by attracting macrophages. T cells first proliferate and then differentiate into helper, suppressor or killer cell, subpopulations.

Helper T cells are special T lymphocytes that stimulate the activity of B cells to produce antibodies and thus are an essential component in humoral immunity. Suppressor T cells inhibit the differentiation of B cells into plasma cells and block the activity of helper T cells. Thus, they 'switch off' antibody mediated immunity. It is the balance between helper and suppressor cells which is essential for the regulation of antibody synthesis.

Killer cytotoxic T cells are also regulated by helper and suppressor T cells in a similar way to B cells. Cytotoxic killer T cells which have been generated as a result of a pathogen are specifically toxic to that pathogen and their killing action is thought to be direct. They show specificity and memory and do require previous exposure to the antigen. They die when their function is complete.

There is also a group of T cells without absolute specificity, known as

Natural Killer cells. These are large granular lymphocytes derived from the bone marrow which destroy virally infected cells without prior sensitisation. They destroy such cells by inserting themselves into the membrane of the infected cell.

To conclude, the aim of this section has been to provide an introduction to the immune system, its structure and functioning which an non-immunologist can readily understand. It draws from numerous overviews of the topic (Borysenko 1987; Leonard 1990; Totman 1991; Fletcher 1991; Hall 1993). A useful introductory text on the subject is also provided by Roitt (1988).

## Measuring Immunocompetence

There are relatively few common measures of immunocompetence in humans, compared to those used in animals. As such one is restricted to looking through a very small immunological window using skin or blood tests. Tests used can be divided into three categories. These are assays for lymphocyte activation, assays for T cells, B cells and other lymphocyte subsets and skin tests for delayed hypersensitivity.

When lymphocytes are activated they undergo blastogenesis (or blast formation) and proliferate. The resulting increase in cell numbers can be determined by counting the cells generated or by measuring the amount of radioactive nucleotide incorporated into their DNA during the proliferation process (e.g.. tritiated thymidine uptake). Commonly, mitogens such as plant lectins are used to activate lymphocytes. Some examples include phytohemagglutinin (PHA) and concanavalin A (Con A) which predominantly activate T cells and pokeweed mitogen (PWM) which primarily stimulates B cells.

Another method used to enumerate cell sub-populations is to centrifuge the blood sample obtained. Erythrocytes and granulocytic leukocytes pass through a sucrose gradient whereas mononuclear cells (lymphocytes and monocytes) remain suspended in the gradient. These cells are counted and small samples are exposed to labelled monoclonal antibodies that react with the various subsets of mononuclear cells and they can thus identify them. Such antibodies are available commercially and each has a designated code which identifies the specific marker molecule found on each sub-population of cells. Thus, relative and absolute numbers of T cells, B cells, macrophages

and natural killer cells can be quantified. Likewise the T cells can be subdivided into helper (T4) and suppressor (T8) cells. A common expression of immune status is the helper/suppressor (T4/T8) ratio.

Skin tests for delayed hypersensitivity detect cutaneous immune reactions to antigens or groups of antigens. Measures are usually taken 24 and 48 hours after intradermal injection of antigen. Inability to react to a battery of common antigens (a hypo-reactive state) is indicative of serious diseases. In milder deficiencies one would expect some skin reaction. Commonly used antigens in delayed hypersensitivity skin tests are candida, streptokinase/streptodornase (SK-SD), purified protein derivative of tuberculin (PPD), staphylococcal antigens, mumps antigens and trichophytin. Known antigens can be given a standard.

## EVIDENCE IN SUPPORT OF THE PNI PARADIGM

Having presented overviews of the two most commonly studied variables in the psychoneuroimmunological (PNI) literature, namely stress and immunity it is now appropriate to examine the evidence which supports the PNI paradigm. This is best illustrated by an exploration of the relationship between stress and the immune system. There are two main bodies of evidence supporting the view that there are bi-directional interactions between the CNS are the immune system. The first is "physiological" and the second is "behavioural" evidence.

## PHYSIOLOGICAL EVIDENCE

There is considerable evidence that hormones (regulated by the CNS), neurotransmitters and peptides (elaborated by the CNS) influence immune mechanisms. The role of the CNS in activating the two major neuroendocrine systems (SAM and HPAC systems) has already been discussed in the overview on stress. The present discussion goes a step further by looking at the evidence for a relationship between this hormone activity and the immune system.

The SAM system stimulates the release of catecholamines (noradrenaline and adrenalin) which have been implicated as immunomodulators. For example, they have been shown to enhance the primary antibody response after a stressful stimulus in

mice (Fujiwara and Orita 1987). Immune responsiveness in rodents has been found to increase the noradrenergic content of the spleen, thymus and adrenal glands (Besodovsky and Sorkin 1981) and during the course of the immune responses the spleen concentration of noradrenaline becomes depleted (Besodovsky and Sorkin 1977). Injections of epinephrine results in increased blood circulation of lymphocytes whilst at the same time reducing their functional efficiency (Crary, Borysenko et al 1983; Crary, Hauser et al 1983, Eriksson and Hedfurs 1977; Felten, Felten et al 1985; Gader and Cash 1975). Injection of noradrenaline has also been shown to increase NK cell activity (Locke et al 1984), Amkraut and Solomon (1975) propose a mechanism whereby catecholamine release ultimately suppresses the immune system. They suggest that catecholamines act directly on alpha and beta adrenergic receptors. Alpha adrenergic, receptors stimulation decreases cAMP, whereas beta adrenergic receptor stimulation increases cAMP. Increases in cAMP suppress antibody production.
( cAMP = cyclic Adenosine Monophosphate , NK = natural killer cells).

The HPAC system stimulates the secretion of glucocorticoids and cortisol. The traditional view is that corticosteroids are primarily suppressive (Cupps and Fauci 1982; Meuleman and Katz 1985; Fauci and Dale 1975; Onsrud and Thorsby 1981). In fact, corticosteroids have been associated with suppression and enhancement (Blecha et al 1982; Niebergs et al 1979; Keller, Weiss et al 1981; Keller, Weiss et al 1983). In low concentrations, glucocorticoids exert a stimulatory effect on certain immunological responses whereas higher concentrations appear to be routinely inhibitory (Ader, Felton and Cohen 1990; Nicol and Bilbey 1960).

Opioid peptides generally demonstrate suppressive effects on the immune system (Morley, Kay et al 1987). The release of 'opioid peptides during stress can alter the percentage of T cells and the activity of NK cells (Singh and Owen 1976). Shavitt et al have suggested that the mechanism by which opioid peptides mediate the suppression of NK cell activity may be by suppression of interferon, which normally augments NK cell activity. In vitro addition of opioid peptides to immunological assays has also been found to enhance NK cell activity (Kay, Allan and Morley 1984; Biddison et al 1986; Matthews et al 1983)

Stress related neuropeptides and neurohormones significantly moderate the capacity of macrophages to attain a tumoricidal state, suggesting that alteration of macrophage function may relate to stress induced enhancement of neoplastic disease

(Koff and Dunegan 1985). A rapidly increasing body of knowledge suggests that neuropeptides play a key role in immunoregulation. Morley et al (1987) suggests that they are the most critical mediators of 'CNS - immune' transactions and describe neuropeptides as "the conductors of the immune orchestra". Some examples of neuropeptides include B - endorphine and metenkephalin, which have been demonstrated to enhance NK cell activity in vitro (Matthews et al 1983).

Other hormones apart from catecholamines and corticosteroids have also been demonstrated to have immunological affects. For example evidence suggests that serotonin exerts an inhibitory effect on immunogenesis, demonstrating that an inverse relationship exists between brain serotonin concentration and antibody synthesis (Devoino, Evamina and Ilyutchenok 1970; Idova and Devoino 1972; Devoino and Idova 1973. The central dopaminergic system appears to exert a stimulatory effect on the immune system. This conclusion is based upon changes in the immune system of patients suffering from such neurological diseases as Parkinsonism (Fujiwara et al 1966).

Numerous other studies support the finding that hormonal state and level of neurotransmitter activity influence immune responses (Berczi et al 1981; Comisa, Leonhardt and Werkerle 1982; Hall and Goldstein 1981; Nagy and Berczi 1978). In fact most hormones have been shown to be stress responsive (Asterita 1985) and have immunological effects (Grossman 1985; Kaeberle 1984). A variety of hormonal and neurosecretory systems other than the SAM and HPAC systems may be involved and stress induced modulation of immunity is a complex phenomenon involving several, if not multiple mechanisms (Stein 1989). Not only this, but there is evidence that the interaction may be bi-directional, with antigenic stimulation (or perhaps immune response to antigenic stimulation) resulting in neuroendocrinal changes (Besedovsky, del Rey and Sorkin 1983; Besedovsky del Rey, Da Prada, Burri and Honneger 1983; Besedovsky and Sorkin 1981; Shek and Sabisto 1983).

In conclusion, there is a considerable amount of evidence that stress related neuroendocrine systems release hormones, peptides and neurotransmitters which influence immune mechanism. This interaction is bi-directional in that immune mechanisms can also result in neuroendocrine changes.

**Table Three:** Effect of some Neurotransmitters on the Cellular Components of the Immune Response

| Neurotransmitter | B cell response | T cell Response | Macrophages |
|---|---|---|---|
| Serotonin increased | - | 0 | 0 |
| Dopamine increased | - | + | + |
| Beta adrenergic stimulation | - | - | - |
| Alpha adrenergic stimulation | + | + | 0 |
| Cholinergic stimulation | + | + | 0 |
| Morphine | 0 | - | 0 |
| Enkephalins | 0 | + | 0 |

Source: Adapted from Hall and Goldstein (1981) "Neurotransmitters and the Immune System". In R Ader (Ed) A "Psychoneuroimmunology". pages 521-543. New York, Academic Press.

(Key:- -, Decreased response; +, increased response; 0, no data available. )

In addition to the evidence showing that stress influences the functions of the immune system via neuroendocrine mediation, there is a considerable amount of other physiological evidence which confirms a bi-directional interaction between the Central Nervous System (CNS) and the immune system:-

'There is neuroanatomical and neurochemical evidence of direct sympathetic and parasympathetic innervation of lymphoid tissue' (Bulloch and Moore 1980; Felten et al 1981; Giron, Crutcher and Davis 1980; Williams et al 1981). There is also evidence of direct innervation of other immune structures, for example innervation of the thymus glands by the brain stem and spinal cord has been found in rats and mice (Bulloch and Moore 1980). The bone marrow (a source of B cells) also has a good nerve

supply (Calvo 1968) and it has been found that brain lesions affect marrow functions (Baciu 1962). The sympathetic nervous system has been demonstrated to mediate immune regulation (Besedovsky et al 1979).

Experimental manipulation of hypothalamus and other parts of the brain have been shown to have immunological consequences. Animal studies have demonstrated that destruction and stimulation of the hypothalamus alters humoral and cell mediated immune response. Stimulation of the hypothalamus is associated with a protective immune response pattern, whereas lesions are associated with a detrimental immune response pattern. ( Korneva and Khai 1963; Korneva 1967; Cross et al 1980; Dann et al 1979; Jankovic and Isakovic 1973; Stein, Schleifer and Keller 1981).

More recently lateralization studies have implicated that the cerebral cortex may have a role in immunoregulation in a laterally differentiated way. For example, Renoux et al (1983) found that the production of T cell inducing factors in mice is controlled by the brain neocortex in mice and that an intact left cerebral cortex is necessary to produce these T cell inducing factors.

Besedovsky et al (1977) demonstrated the bi-directional nature of the interaction between the hypothalamus and the immune response, by showing that the immune response also influences hypothalamic activity.

Immunologically competent cells have receptors sites for neuroendocrines, neurotransmitters and, neuropeptides and for substances regulated by them. Acetylcholine receptors have been found in thymus tissue (Lindstrom et al 1976). Beta-adrenoreceptors have been found on T and B cells and macrophages (Besedovsky and Sorkin 1977). Opioid receptors have been found on granulocytes, monocytes, lymphocytes and the terminal complexes of complement (Shavit et al 1984). Receptors have also been found on lymphocytes or thymocytes for hormones controlled by the CNS, including testosterone (Abraham and Bugg 1976, Growth hormone (Arrenbrecht 1974), corticosteroids (Cake and Litwack 1975), oestrogens (Gillette and Gillette 1979), insulin (Helderman and Strom 1978), histamine (Roszkowsi, Plant and Lichtenstein 1977), beta-adrenergic agents (Singh, Millson, Smith and Owen 1979). Presumably, the presence of a receptor site implies some function for its substrate. Some substrates have been identified as playing a role in stimulating the differentiation of lymphocytes and in controlling their activity (Helderman and Strom 1978).

There is evidence that feedback mechanisms in immune regulation act in part via the mediation of the CNS. Besedovsky, Sorkin and Keller (1978) found that serum levels of corticosteroids are increased in response to an antigen injection or skin graft rejection in the rat, presumably via the influence of ACTH which is controlled by the hypothalamus. This finding suggests a feedback loop between the immune system and the hypothalamic-endocrine system i.e. antigen stimulates the immune response, which leads to a rise in cortisol, which in turn tends to suppress the immune response. Besedovsky, Del Rey, Sorkin and Da Prada (1983) found that a decreased noradrenaline turnover in rats occurs at the peak of the immune response, demonstrating that the immune response evokes changes in brain noradrenergic neurones. This effect was also found by (Besedovsky et al 1986) who found an immunoregulatory feedback mechanism between interleukin-1 (a product of the immune response) and glucocorticoid hormones.

Further evidence for the bi-directional CNS-immune system link is provided by the fact that certain common biochemical substances are found in both CNS and immune system structures which are capable of influencing both. For example, thymosine which is known to influence the motivation of T cells can also be found in the areas of the brain regulating the neuroendocrine system (Hall and Goldstein 1983). Lymphocytes are themselves a source of alpha endorphin and ACTH (Smith and Blalock 1981). Activated T helper cells produce the peptide neurotransmitters, met-enkephalin (Zurawaki et al 1986). Also, animals from which the thymus has been removed, show delayed sexual maturation, presumably through neuroendocrine mediation (Besedovsky and Sorkin 1974). Russian studies have suggested that thymic hormones (important to T cell function and maturation) actually influence learning (Jancovic 1984).

If the biochemical substances mentioned above are capable of influencing both the CNS and the immune system, then it would be reasonable to assume that biochemical and functional similarities might be found between neuropeptides (substances modulating the functioning and reactivity of the CNS) and lymphokines (substances modulating the functioning and reactivity of the immune system). This does appear to be the case. An analogy has also been made between a synapse and junction between a macrophage and a lymphocyte (Solomon 1987). Similarities between the structure of specific proteins of the thymus and the cerebral cortex have also been found (Valueva and Malyzchev 1984).

There is growing evidence of a bi-directional interaction between the thymus and the neuroendocrine system. Neuroendocrines have been shown to influence the production of thymic hormones (Fabris 1984). Thymectomized mice display a profoundly disturbed endocrine balance (Fabris et al 1983). A peptide has been extracted from the anterior pituitary which has thymocyte - stimulating properties (Saxena and Talwar 1977). Also, oxytocin, neurophysin and neurohypophyseal peptides have been identified in the human thymus, supporting the view that the thymus has a neuroendocrine function (Greener et al 1986). Other evidence for the PNI hypothesis includes the finding that neurotropic viruses show an affinity for lymphocytes and vice versa (Shaw et al 1985; Weigent et al 1986) For example, the measles virus is found in both the brain and lymphocytes (Fournier et al 1985). Some psychotropic drugs have receptor sites on and functionally affect, immunologically competent cells. For example, benzodiazepines which are widely used for anxiety effects are potent stimulators of human moncytes (Ruff et al 1985). Tricyclic antidepressants have binding sites on splenic lymphocytes and suppress mitogen response (Audus and Gordon 1985). Also, the immune system and central nervous system have some cell types in common (Angeletti and Hickey 1985) and there are biological similarities between cell surface consituents of neurones and immunological cells (Tse et al 1985).

Finally, sleep has a role in immunological as well as CNS function. Studies suggest that sleep may have an important role in the recuperative process, whether it is recovery from a day's activity or from damage induced by a disease. The production of interferon enhances slow wave sleep and stimulates the immune system to do its work. Interleukin-1 has also been found to increase in conjunction with the onset of slow wave sleep (Moldovsky et al 1986; Reite 1987; Hall 1993).

In conclusion, there is a considerable body of physiological evidence supporting the view that the CNS and the immune systems interact and that these interactions are bi-directional in nature. From the evidence presented so far a pathway is emerging:-

## BEHAVIOURAL EVIDENCE

### Classical Conditioning of the Immune Response

Much of the literature on behavioural phenomena pre-dates the evidence provided by physiological studies. Perhaps one of the most striking illustrations of how behavioural phenomena can have immunological consequences is provided by demonstrations that the immune response can be classically conditioned.

Ader and Cohen (1981) provide a historical account of 'conditioned immunobiologic responses' and report on numerous early experiments of this phenomenon (pages 321-351). The findings of these experiments provide compelling evidence supporting the CNS - immune system interaction and are consistent with the PNI paradigm.

The 'pioneers' in this area were Metal'nikov and Chorine (1926; 1928). They applied Pavlov's methods to the study of immunity. In the first experiment reported Metal'nikov and Chorine (1926) used guinea pigs. The guinea pigs received paired conditioned stimulus (CS) involving scratching the skin with an unconditioned stimulus (US) of intraperitonial (ip) injection of staphylococcus filtrate. The CS was then presented alone several times without the US. An increase in polynucleated cells was demonstrated although somewhat weaker and more transient than to the US. Also in this study they used the same procedure to show that the method could be used to combat infection.

In a later study Metal'nikov and Chorine (1928) used daily pairings of scratching the flank of three rabbits (CS) and i.p. injection of 2cc of an emulsion of vibrocholera for 12 days. Three weeks later two of the rabbits were exposed to the CS alone three times in 24 hours. Antibodies rose in these animals but not in the third animal not exposed (which showed no change in titre). A similar result was found when the CS was presented two months later.

Because of both the novelty and importance of this phenomenon several experiments were undertaken to confirm these initial observations. For example, Nicolau and Antinescu-Dimitriu (1929a) replicated Metal'nikov and Chorine's 1928 study and confirmed their results.

More recently a famous experiment carried out by Ader and Cohen (1975) again confirmed the earlier findings. Ader and Cohen paired cyclophosphamide a potent immunosuppressive drug (US) with the consumption of saccharin drinking solution (CS)

in rats. Subsequently, the saccharin (CS) was presented on its own and was found to elicit an immunosuppressive response. Other researchers (Rogers et al 1976; Wayner, Glannery and Singer 1978) have found similar results. Ader and Cohen (1985) review the literature in this area and conclude that this phenomenon can be observed in both humoral and cell mediated immune response to antigenic stimuli. Attempts have been made to dismiss the conditioning phenomena as non-specific stress i.e. adrenocortically mediated effects (Dwyer 1983) but the arguments against it are not persuasive (Bovbjerg, Cohen and Ader 1983) and the hypothesis that the conditioning effects are mediated by elevations in adrenocortical steroid levels receives no support from available data.

## The Life Events Literature

Much of this research has focused on the effects of environmental stressors on the immune system in healthy humans and animals, as opposed to diseased populations. In psychology this is referred to as the 'life-events' literature.

Paykel and Rao (1984) define a life event as:

"a discrete change in an individual's social or personal environment".

This change refers to an externally verifiable one as opposed to an internal psychological one. It is not necessary for such events to be major to precipitate strain (Fletcher 1991). Historically, the first researchers in this area observed that reported illness was associated with a greater number and severity of life events (Hinkle and Plummer 1952; Hinkle and Wolffe 1957; Hinkle et al 1958; Holmes and Rahe 1967). In 1967 Holmes and Rahe established for the first time a self report questionnaire to assess the magnitude of potential psychosomatic impact of a number of life events, some of which everyone is likely to experience from time to time (The Social Readjustment Rating Scale - SRRS), which was shown to predict minor illnesses such as colds, backaches and stomach aches (Holmes and Holmes 1970). This research has spawned a massive literature by other researchers investigating almost every disease and psychological disturbance. The approach is not however without its critics. Lazarus and Folkman (1989) for example criticise it on the grounds that it does not distinguish between positive and negative stressors and ignores the effects of moderating effects of variables such as personality, coping processes and individual appraisal of events. The life events listed are not representative of many changes experienced by many groups (such as children, adolescents,

elderly for example and tend to focus on major events, such as death, divorce and loss of job) which occur rarely in the lives of most people. Other criticisms include the observation that statistical correlations in the research are rather small and may account for at best 9% of the variance in illness. This does not however mean the association is of no practical significance. (Rabkin and Struening 1976) Life events are a necessary but not sufficient in themselves to lead to illness.

Studies which have separated negatively and positively evaluated life events tend to show that negatively evaluated events are correlated more with illness than positive ones (Sarason, Johnson and Siegal 1978; Sarason and Sarason 1984, 1985; Lazarus and Folkman 1989).

Other potentially confounding variables in the life events literature include age (Holmes and Masuda 1974; Masuda and Holmes 1978), socio-economic status (Liem and Liem 1984; Caplan et al 1975), adoption of the sick role and care seeking behaviour (Craig and Brown 1984; Dohrenwend and Dorehrenwend 1984; Mechanic 1974; Rabkin and Struening 19767), life events post-dating the illness (Hugdens 1974; Paykel and Rao 1984); retrospective reporting (Fletcher 1991), life event clusters (Kasl 1983) and life events being intimately embedded in personal traits and lifestyle dynamics (Kasl 1983; Matthews and Glass 1984).

**Acute stressors**

In most studies of the relationship between environmental stressors and immunity, the effects of acute short-term stressors have been examined. 'Acute Stress' is that associated with a single environmental event, even though the anticipatory or consequent stress may vary. In early research the effects of space-flight was examined. In one study Apollo astronauts, immediately after splashdown had higher White Blood Cell Counts (WBC) than during the pre-launch period (Fischer et al 1972). In another, the Skylab programme, WBC counts were elevated at recovery as were the percentage of T-lymphocytes and absolute number of polymorphonuclear leukcytes (Kinsey 1975). Neuroendocrine measures of cortisol and catecholamines confirmed that the splash down was very stressful for astronauts (Leach and Rambout 1974). The combination of physiological and presumably psychological distress was associated with alterations in cellular immune functioning, in a number of cases activating the immune response.

Another early stress related phenomenon was sleep deprivation. Interferon production was found to increase both during and after a long vigil (77 hours) continuous attention task. Phagocytosis decreased initially during the vigil but later rose to above baseline levels after the vigil (Palmblad et al 1975; 1976). This study demonstrated the critical role of timing and duration of stressor exposure plays in determing the nature of stress induced immune alterations. In a later study (Palmblad, Bjorn et al 1979) found sleep deprivation to be associated with diminished response of lymphocytes to mitogen. Sleep deprivation studies should however be interpreted with caution since they may confound psychological and physical effects of the stressor i.e. have an effect secondary to stress.

Animal studies have also demonstrated that a variety of environmental stressors such as noise, bright light and overcrowding (Vessey 1964; Hill, Greer and Felsenfeld 1967) have been shown to alter humoral immune response by suppressing the production of specific antibodies. Gisler (1974) found that repeated low voltage electric shocks given to mice could enhance the body's antibody response.

Inconsistencies in findings using experimental manipulations and difficulties in generalising findings from animals to human subjects have led to attempts to design studies using naturally occurring environmental stressors in normal populations or populations at high risk (Locke 1982).

The stress of academic examinations has been used in a number of studies. Dorian, Keystone, Garfinkel and Brown (1982) compared a group of psychiatry students preparing to take an important exam with a control group not taking the exam. Two weeks before the actual exam the exam group had higher B and T cell counts and lower response to mitogens. Surprisingly, cortisol levels were higher in the non-stressed group. Catecholamines were not measured. Bovbjerg et al (1990) collected blood samples from two measured stress levels in 26 medical students at the end of a week of exams. The students were then immediately immunised with trivalent influenza vaccine. Three weeks later psychological and blood samples were collected. Students with high stress levels following the exams had significantly smaller increases in antibodies in response to influenza three weeks later. Thus, psychological 'state' influences immune response following in vivo challenge with an antigen (in this case life events associated with taking examinations). In a comprehensive series of studies Kiecolt-Glaser, Glaser et al (1985) investigated a

variety of immune changes resulting from examination stress. Changes in antibody titres to HSV-1, EBV and cytomegalovirus (CMV) were found to be higher at exam time. In a subsequent study Glaser et al (1987) demonstrated alterations in leukocyte migration - inhibition factor resulting from examination stress. Glaser, Kiecolt-Glaser, Stout et al (1985) demonstrated reductions in the percentages of helper T cells. Kiecolt-Glaser, Garner et al (1984) found that during exams lytic activity of NK cells was reduced but plasma levels of immunoglobulin A increased. Glaser, Rice et al (1986) found that lymphocyte production of interferon was greatly suppressed during exams. Interferon is a regulator of NK cell activity and changes in NK cell activity could be ascribed to reduced interferon production.

A frequent criticism of research employing healthy subjects is that alterations in immunity may be of little clinical significance. Another one is that the apparent relationship between the environmental stressor and the immune function may be mediated by alterations in diet, sleep patterns or activity level secondary to stress, the stress itself neither being a necessary or sufficient cause of immune changes (O'Leary 1990).

In summary, acute environmental stressors have been shown to elicit mixed effects. In some studies lymphocyte numbers have been demonstrated to increase, whereas in others they decrease. When assessed the functional capacity of immune cells tended to be reduced. Acute stressors have been associated with activation of both the SAM and HPAC systems and the differing immunological effects of these systems may account for the diverse findings.

## Chronic Stressors

To date, relatively little well conducted research has been carried out on the effects of chronic stressors on the immune response. This is unfortunate because there is evidence from animal research that the effects may change over time (Monjan and Collector 1977).

Unemployment if prolonged is a chronic stressor that has been shown to affect mortality and morbidity (Brennan 1979; Iverson and Anderson 1987; Jackson and Warn 1987; Kessler et al 1987; Fryer D 1988; Westin 1988; Moser et al 1987). A recent

study in Sweden examined the effects of unemployment on immune function in women. After nine months of unemployment subjects showed reduced lymphocyte response. When compared to employed women (Arnetz et al 1987), the results indicate that some aspects of the immune system may be altered at a specific time period following the loss of work.

Kiecolt-Glaser, Glaser et al (1987) examined the effects on immunity of the chronic stress associated with caring for relatives afflicted with Alzheimer's Disease. Compared to control subjects the care-givers had higher antibody titres to EBV (reflecting impaired cellular immunocompetence) and lower percentages of T lymphocytes and helper T cells, with lower helper: suppressor T cell ratios.

Marital quality has been found to have effects on immunity. A poor marriage can be described as a chronic stressor. Marital disruption is associated with significant increases in psychological distress (Bloom et al 1978) and is the single most powerful sociodemographic predictor of stress related physical illness (Somers 1979). Poorer marital quality has also been associated with greater depression and a detrimental effect on immune functioning (J. Kiecolt-Glaser 1987).

Separated or divorced individuals have about 30% more acute illnesses and physician visits than married adults (Somers 1979) and amongst those who have been separated for a shorter period of time and those with greater attachment to their ex-spouse poorer immune functioning has been observed (Kitson 1981; J. Kiecolt Glaser 1987). It has also been observed that there is a greater decline in the physical health of men following divorce than in women (Cochrane 1988).

Perhaps the most severe human stressor is bereavement following the loss of a spouse or close relative. The psychological and physiological effects of bereavement are profound. Risks of psychiatric, physical illness and death are greatly increased amongst the bereaved (Stroebe, Stroebe et al 1982; Rowland 1977; Clegg1988; Murray-Parkes 1972; Maddison and Viola 1968; Rees and Lutkins 1967; Jacobs and Ostfeld 1977). Bartrop et al (1977) found the lymphocyte response of bereaved subjects was reduced six weeks often the spouse's death. Schleifer et al (1980) observed a similar depression of lymphoblast transformation 5-7 weeks post bereavement. (In neither study could immune suppression be explained by simultaneous neuroendocrine charges, suggested that there may be a primary mechanism or a direct brain immune system link

through which immune suppression works). Schleifer, Keller et al (1983) examined immunity in a group of men whose wives have died from breast cancer in the first two months following bereavement and found response to mitogens was reduced. Reduced NK cell activity has been observed in women who have recently become bereaved (Irwin, Daniels, Smith Bloom and Weiner1987) compared with an age-matched control group (Linn et al 1987)

Lonely individuals have been found to have lower NK cell activity and higher antibody titres to HSV (Herpes Simplex Virus) than non-socially deprived individuals (Glaser, Kiecolt-Glaser, Spiecher et al 1985; Kiecolt-Glaser, Garner et al 1984) Higher levels of urinary cortisol have been reported in lonely subjects, as well as poor T cell response to mitogen (Kiecolt-Glaser, Ricker et al 1984). Meaningful long term social contacts can have a marked positive effect in terms of resistance to disease (Cassel 1976; Bruhn et al 1966; Berkman and Syme 1979).

Social support has been defined (Ganster and Victor 1988) as the

> "presence of others, or the resources provided by them, prior to, during and following a stressful event".

Level of social support has also been linked to mental health (Broadhead et al 1983; Cohen and Wills 1985; Gottlieb 1983). It is thought that social support acts through relaxing the fight on flight response and/or strengthening the immune system response. Broadhead et al (1983) described some evidence that a positive CNS response which acts to reverse hypertensive effects of stress, might be related to socially supportive stimuli. The precise mechanism appears to be the release of certain neuropeptides, especially B-endorphin, in response to supportive stimuli.

Early life experiences have been shown to influence adult immune functioning. This was recognised in the work of Freud (1953). Handling rats for 3 minutes a day from birth until weaning enhances primary and secondary antibody response to a novel antigen (Solomon 1969). Early losses in incidence of leukaemia (Green and Miller 1958) and poor child-parent relationships have been associated with a greater propensity for that child to develop cancer in adulthood. (Bahnson 1981; Bahnson 1979; Wrye 1979; Thomas et al 1981).

In summary, the effects of chronic stressors on immunity suggest that adaptation fails to take place and prolonged stress results in prolonged immunosuppression,

the consequences of which could conceivably be severe. Additional research in this area is clearly needed. For example, in the area of occupational stress (potentially one of the most protracted and chronic of stressors) although most of the research makes claims that such stress has health implications, there is surprisingly little evidence for or against this claim. For example, current 'burnout' research (Maslach 1982; Perlman and Hartman 1982) surprisingly provides little evidence of health outcomes. Maslach and Jackson (1986) state that further research is required particularly on the effects of burnout on physical and mental health. Some aspects of work have been studied in more detail, such as the effects of shift work. Nakano et al (1982) for example, demonstrated that T cell function is significantly more depressed in permanent might shift workers than those on permanent day shift or who rotate over three shifts. So, clearly other protracted stressors need to be studied but overall there is convincing evidence that chronic stressors do have a detrimental effect on the immune system.

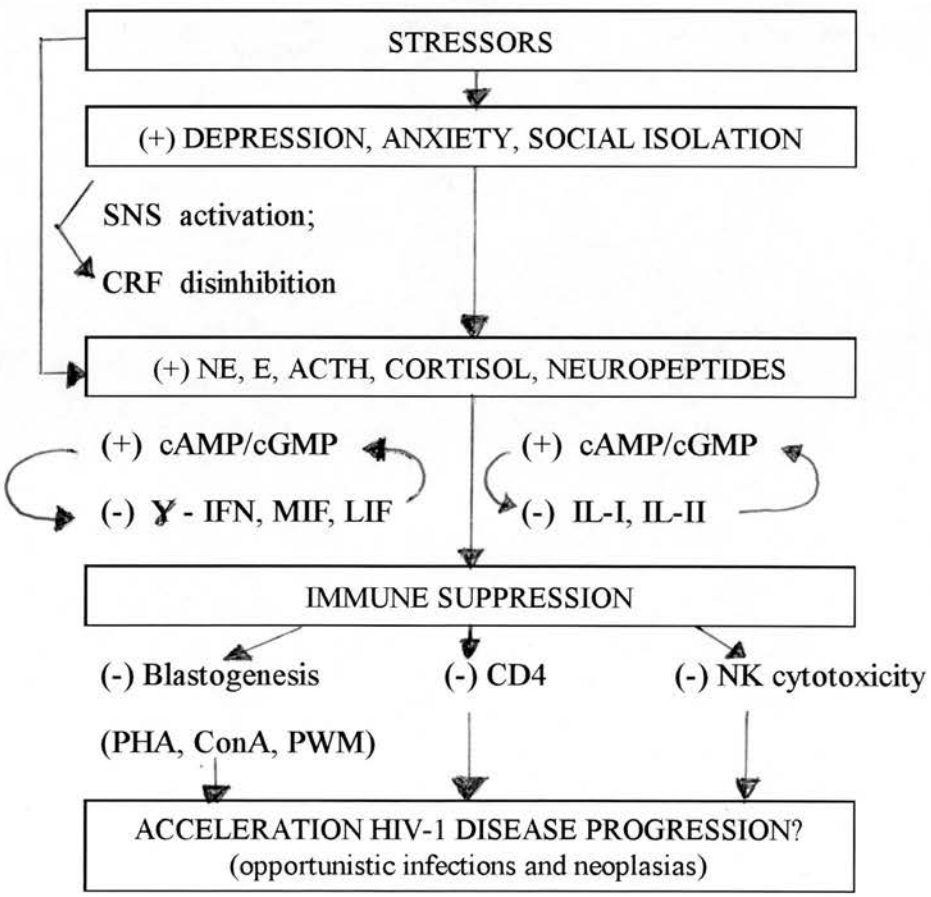
The life event literature discussed up to this point has looked at the relationship between environmental stressors and immune functioning in healthy subjects. However, there is also a body of literature which identifies a relationship between specific diseases and life events. Combined, these findings contribute to a fuller understanding of the processes that have biological, if not clinical significance. For example, there is clear evidence of a psychosomatic component in the common cold (Totman et al 1980). Also, it has been found that stressful life events may contribute to the likelihood that a person will develop coronary heart disease (Rahe and Paasikivi 1971; Theorell and Rahe 1971; 1972; Connelly 1976). There has also been a relationship found been certain life events and cancer. For example, Joseph and Syme (1982) weighed up the evidence and found that 90% of the studies looking at life events and cancer found that there was an association between loss of a significant relationship through death or divorce and cancer. LeShan (1977) studied four hundred cancer patients and found that 70% had lost a significant close relationship through death or divorce within eight years preceding the illness, compared to only 10% of controls.

**Emotional Distress**

The emotional manifestations of stress (both psychological and physiological), commonly known as 'strain' have been demonstrated to alter the incidence, course and severity of diseases that are "immunologically resisted":-

For example, there are numerous studies which support the view that high levels of emotional distress (namely anxiety and depression) create the right conditions for Human Immune-deficiency Virus-HIV) to take hold and accelerate the disease process through opportunistic infections acting on an already disabled immune system (Solomon, Temoshok, O'Leary & Zich 1987; Temoshok, Zich, Soloman and Stites 1987; Goodkin 1988; Tross 1987). Antoni et al (1991) propose a model to represent the manner in which psychological stressors may ultimately accelerate HIV disease progression:

**Figure Three:** The Role Of Psychosocial Stressors in HIV-1 Progression




Source: M.H. Antoni, A. Lapperriere, N. Schneiderman and M.A. Fletcher (1991)

**Figure Three:** Schematic representation of the manner in which psychological stressors are hypothesised to increase neurohumoral activity, produce immune suppression and possibly accelerate HIV-1 disease progression. SNS, sympathetic nervous system; CRF, corticotropin releasing factor; NE norepinephrine; E. epinephrine; ACTH. adrenocorticotripin hormone; Y-IFN, gamma interferon; MIF macrophage migration inhibitory factor: LIF, leukocytemitogen: CD, cluster designation; NK, natural killer.

There is a widespread notion that depression increases susceptibility to cancer. Some prospective studies have demonstrated that individuals who are more prone to depression are more likely to develop cancer later in life (Schekelle et al 1981) and that there is a link between depression and malignancy (Bieliauskas and Garson 1982). These results have been contradicted by studies which find no association between depression and cancer (Kaplan and Reynolds 1988; Schmale and Iker 1971). In conclusion, the findings are mixed and there is not a lot of evidence to suggest that depression plays a major role in the aetiology of cancer.

There is considerable evidence from human studies that acute and chronic psychological distress may modulate latent herpes simplex virus (HSV) expression and recurrent infection (Glaser et al 1985; Glaser et al 1987; Kasl et al 1979; Katcher et al 1973). Under conditions of psychological distress cellular control by T cells may be impaired. Negative mood states such as anxiety and depression have been significantly associated with fewer T8 (suppressor and cytotoxic) cells. Also, higher levels and depression have been associated with more recurrences of the disease (Kemeny, Cohen, Zegans and Conant 1989). One mechanism suggested is that psychological distress triggers the hypothalamic - pituitary-adreno-cortical and sympathetic-adrenal-medullary axes to release corticosteroids and catecholamines respectively, which in turn act upon the immune system creating the right conditions for the latent HSV to act on the body; (Bonneau et al 1991; Cotman et al 1987).

Ulcerative gingivitis (trench mouth) is another disease which psychological distress is thought to affect the immune response. The bacteria involved are the very ones normally present in the mouth, which under normal conditions do not produce ill-effects. However, under conditions of emotional distress there is a reduction in

immunoglobulin A (IgA), the antibody found in saliva to protect the mouth from such bacteria (Solomon 1990).

Upper respiratory tract infections occur more frequently in individuals experiencing high levels of emotional distress (Meyer and Haggerty 1962; Graham, Douglas and Ryan 1986)

Some physical illnesses have been often diagnosed as psychiatric depression because psychological factors do play a part in the clinical presentation. However, it is difficult to establish whether the state of psychological distress is a cause or a consequence of the physical illness. For example a condition found mostly in younger adults who are having trouble with what are ordinarily stressful phases of life is known as "chronic fatigue syndrome". Symptoms include fever, swollen lymph nodes, muscle weakness and discomfort, headaches, forgetfulness, irritability and fatigue. Other names for this syndrome have included 'yuppie flu' and chronic Epstein-Barr Virus. Psychological distress has been shown to be associated with the syndrome (Kibler et al 1985; Straus et al 1985). Also an association between Chronic Fatigue Syndrome and low natural killer NK cell activity has been found (Caliguiri et al 1987). There is some evidence that such individuals have a deficiency in the ability to produce the major stress hormone cortisol which is necessary to mobilise stored energy (Hall 1993). Whilst a viral link is highly suspected, it is not yet proven (Hall 1994).

Associated with the EBV syndrome is a similar condition also showing a clinical resemblance to depression known as low Natural Killer Syndrome (LNKS) which is characterised by feelings of fatigue, decreased interest in mental and physical activity, general dullness and a remittent low grade fever. Normal number of NK cells are present in such individuals but a specific deficit in NK cell activity has been identified (Usuda, Aoki et al 1985; Aoki, Usuda et al 1987). Again it is difficult to sort out whether the psychological state is a cause on a consequence of physical illness.

Psychological distress (or strain) has also been demonstrated to alter the incidence, course and severity of diseases associated with "aberrant immunological function", for example, allergies and autoimmune diseases. Auto-immune disease differs from immunologically resisted disease in that it is characterised by enhanced activity in some component of immunity. Also, the immune system is doing what it is supposed to do but on a person's healthy cells instead of a virus or bacteria. There is increasing evidence that stress has effects on such 'hyperimmunity' in the following diseases:-

Grave's disease (exophthalmic goiter), Hashimoto's disease (status lymphaticus), systemic lupus erythematosus (SLE), psoriasis, myasthenia gravis (muscular weakness) pernicious anaemia, polymyositis and multiple sclerosis (Kaplan and Sadock 1985; Grade and Zegans 1986)

If negative affective states are associated with worse disease outcome (as the evidence already presented suggests) then negative affect in such auto-immune diseases ought to be associated with increased immunological response and reduction in distress (e.g. through psychological therapy) associated with a reduced response. In fact, for two diseases Rheumatoid Arthritis (RA) and Multiple Sclerosis (MS) there is some evidence that this is the case, namely a malfunction in the suppressor T cell system which is associated with failure to control autoimmune processes. Inadequate suppressor T cell functioning has been causally implicated in RA (Abdou et al 1979; Decker et al 1984) and in Multiple Sclerosis (Foley et al 1988). Zautra et al (1989) found that in a population of RA suffers greater psychological distress was associated with lower helper suppressor T cell ratios and cognitive - behavioural therapeutic interventions have been found to reduce both the symptoms and the level of rheumatoid factor (a type of immunoglobulin found in serum which attacks other antibodies as though they were pathogens). Foley et al (1988) found that MS sufferers who were high on anxiety and/or depression had significantly higher numbers of T4 (helper cells) than those low on anxiety and/or depression, presumably exacerbating or accelerating the disease.

Further evidence for the interaction between stress and the immune system is provided by the literature which demonstrates that clinical levels of emotional distress (i.e. emotionally disturbed individuals) and mental illness are accompanied by immunological abnormalities. Numerous studies have demonstrated immunological abnormalities in clinically depressed patients. In particular lowered lymphocyte responsiveness has been found in depressed individuals (Cappel, Gregoire, Thiry et al 1978; Murphy, Gardner, Greden et al 1972; Schleifer, Keller, Meyerson et al 1984; Clayton, Halikes and Maurice 1972; Kronfol et al 1983; 1984; 1986; Claman 1972; Chang 1984; Albrecht, elderman, Schlesser et al 1985; Kronfol and House 1989; Schleifer, Keller, Siris, Davis and Stein 1985) and reduced phagocytic response (Kronfol and House 1989; Irwin, Patterson et al 1990; Locke et al 1984).

Whilst there appears to be a considerable amount of evidence supporting the detrimental effects of depression on immune functioning, the results are not

unequivocal. For example, Stein (1989) in a review of the literature in this area concluded that some but not all patients with major depressive disorder may show immune changes and that altered immune system measures do not appear to be a specific biological correlate of major depressive disorders but may occur in subgroups of depressed patients. There is often an assumption made that depressed individuals are a homogenous group which in fact they are not. Differences in immunological functioning have been found for variables such as age, seventy of depression and hospitalisation status (Schleifer, Keller, Bond, Cohen and Stein 1989), between unipolar and bipolar depressives, (Murphy, Gardner, Greden and Carrol 1987) and behavioural variables such as alcohol intake, sleep, exercise, diet and tobacco consumption (Kiecolt Glaser and Glaser 1988; Palmblad, Petrini, Wasserman and Adkerstedt 1979). Neither are patients suffering a single episode of depression are well differentiated from those experiencing recurrent episodes of depression (Levy and Heiden 1991).

With respect to the relationship between the immune system and anxiety there are relatively few studies compared to those on depression and immunity. However, many of the neurobiological processes associated with stress and depression have been observed in anxiety and are known to influence the immune system (Stein, Keller and Schleifer 1988). The findings of a study by Locke et al (1984) suggest that clinical anxiety may reduce Natural Killer Cell (NK) activity. Further research in clearly delineated and diagnosed anxiety states and disorders is required to elucidate the pathophysiology of anxiety disorders (Stein et al 1988).

Some immunological abnormalities have been found in more severe mental illness such as schizophrenia (Solomon 1981; Fessel, Hirata-Hibi 1963). Other psychiatric conditions may also be associated with immunological abnormalities (Colligan 1985; Dahlstrom Welsh and Dahlstrom 1972; Heisel, Locke, Kraus and Williams 1986). Generally speaking poorer mental health has been found to be associated with lower NK cell activity (Locke et al 1984). Increased emotional distress generally is associated with significant dysfunctional differences at the molecular level which may have important implications for health (Kiecolt-Glaser, Stephens et al 1985).

If states of emotional distress have been demonstrated to have largely negative effects on the immune system, it is reasonable to assume that "distress free" states can be demonstrated to have positive effects upon immune functioning. The evidence tends to support this hypothesis. 'Dispositional optimism' and the absence of depression

are associated with better physical health, which is suggestive of the immune-enhancing effects of such traits (Scheier and Carver 1987; Cousins 1977; Peale 1956; Kaplan and Camacho 1983; Levy 1986; Roger and McWilliams 1988). The therapeutic effects of 'laughter' and 'jovialism' have also been demonstrated (Cousins 1989; Kenton 1988; Dillon, Minchoff and Baker 1985).

It follows that interventions which aim to reduce and alleviate emotional distress, which form the basis of most forms of psychotherapy will have positive health effects and result in immunological enhancement. This has in fact been demonstrated for relaxation and guided imagery techniques (Kiecolt-Glaser, Glaser et al 1985), meditation (Smith, McKenzie et al 1985), visualizstion (Hall, Longo and Dixon 1981) and for psychotherapy which aims at disclosure of negative thoughts and feelings (Pennbaker, Kiecolt-Glaser and Glaser 1988a) hypnosis (Hall, Longo and Dixon 1981. Bowers and Kelly 1979; Hall 1983; Jemmott and Locke 1984) Indeed, it is claimed that a wide range of immunological disorders have been positively influenced by hypnosis, including contact dermatitis (Ikemi and Nakagaua 1962), chronic urticaria (Kaneko and Takaishi 1963), allergic skin reaction (Clarkson 1937), asthma and hay fever (Mason and Black 1958) and allergy to dogs (Perloff and Spiegelman 1973).

The research on hemispheric lateralization of functions provides further support for a physiological basis to the interaction between stress and immunity. The left hemisphere is thought to be involved in processing positive emotions and stimulation of the immune system, whereas the right hemisphere processes negative emotions and suppresses the immune system, either directly, or by mediating in, or inhibiting the activity of the left hemisphere (Ley 1983; Silberman and Weingartner 1986). Left handed people are more prone to auto immune disorders (Geschwind and Behan 1982; Pelletier and Herzing 1988).

Diseases of immunological aberration are at times accompanied by psychological and/or neurological symptoms, suggesting a bi-directional interaction between psychological distress and immunity. Evidence for this is provided by the disease systemic lupus erythematosus. This is a disease where the body's immune system attacks healthy organs with all the ferocity it usually reserves for life threatening intruders. The psychosis which is associated with this auto-immune disease can be very similar symptomatically to schizophrenia (Fessel and Solomon 1960).

In conclusion, there is a considerable volume of evidence which suggests that the emotional manifestations of stress can alter the incidence, course and severity of diseases that are immunologically resisted and diseases associated with aberrant immunological functioning.

Milder non-clinical levels of anxiety and depression as well as clinical levels of disturbance and mental illness have been shown to be associated with changes in immunological functioning. There is also evidence to suggest that the interactions between the emotional manifestations of stress and the immune system may be bi-directional.

One hypothesis put forward is that in the normal healthy state, resistance is generally adequate to prevent disease. However, emotional distress, by causing small changes in immune functioning, alters the state of immune balance which normally exists between pathogenic events and bodily defences and allows inapparent or mild illness to manifest itself as severe illness (Amkraut and Solomon 1975; Totman 1979).

**Personality**

Personality has been defined (Eysenck 1970) as a :-

> "more or less stable or enduring organisation of a person's character, temperament, intellect and physique that determines his/her unique adjustment to the environment".

There is a wealth of evidence that personality acts as a moderating variable between life events and the potentially harmful effects of stress. Some individuals are relatively resistant to the effects of environmental stressors whereas others are quite vulnerable (Cohen et al 1982; Cohen and Wills 1985; Gentry and Kobasa 1985; Johnson and Sarason 1979).

The literature suggests that there is actually a "stress-prone" personality (Taylor and Cooper 1989). Perhaps the best known and most reported stress-prone personality type is the Type A personality (Rosenman and Friedman 1974). The idea that certain individuals are more prone to disease however dates back much further than this.

Rosenman and Friedman (1974) were the first to identify a particular cluster of traits associated with coronary heart disease (CHD). The traits associated with the "coronary prone Type A" individual included an over riding need to achieve, constantly

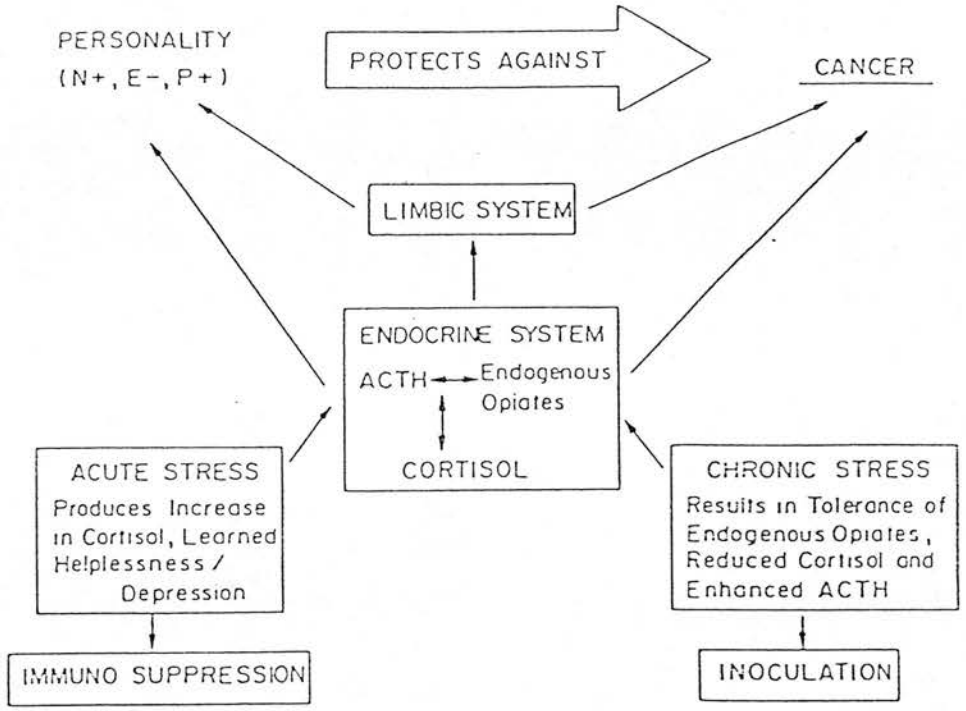
working against the clock, often in the face of real or imagined opposition from others, being highly competitive, hostile if blocked in achieving one's goals and a tendency to deny getting tired. The opposite to this is the Type B individual who is relaxed and unmotivated to the point of lethargy. Most individuals lie somewhere in between the two extremes.

The evidence linking Type A personality with heart disease is impressive, though not conclusive. A solid core of studies link extreme Type A behaviour with risk of heart disease (Matthews and Haynes 1986; Hecker et al 1988; Haynes and Feinleib 1982). Two further studies showed that one particular component of Type A behaviour, namely 'hostility' to be risk factor for heart disease over periods of twenty and twenty five years (Barefoot et al 1983; Shekelle et al 1983). There is also some evidence that the Type A behaviour pattern may be a contributory factor in other diseases such as peptic ulcers, allergies and respiratory infections (Wrzesniewski et al 1987).

Kissen (1966) was the first to propose that there may also be a "cancer prone" personality. Kissen observed that cancer patients showed an abnormal pattern in the expression of emotions. Such patients have a tendency to suppress, repress and deny negative feelings such as anger, depression and guilt. They also show a diminished outlet for emotional discharge during childhood and adulthood. Subsequent studies have supported this hypothesis (Bahnson and Bahnson 1969; Greer and Morris 1975; Wirsching, Stierlin et al 1983). A relationship between personality and disease has also been found for women with cervical cancer (Antoni and Gookin 1988) and men with colorectal cancer (Thomas et al 1988).

Eysenck (1988) goes much further by stating that personality vaiables are much more predictive of death from cancer or cardiovascular disease than smoking! He identified two different personality types which are susceptible to either of these two diseases. Eysenck defined personality in this study in terms of differential ways of dealing with interpersonal stress and found stress to be a very potent cause of death. Stressed individuals were found to have a 40% higher death rate than non-stressed individuals. Eysenck does not claim at the present time to have a model worked out sufficiently but does assert that there is too much empirical evidence to doubt that stress-strain, interacting with personality, plays a causal role in the genesis of cancer, probably in a synergistic interplay with other factors such as smoking and drinking and that simplistic formulations, such as 'smoking causes cancer' have no part to play in the scientific study of this disease

Figure Four: Personality-Cancer Relationship as Mediated by Stress Factors and the Endocrine System




Source: Eysenck H.J. (1986)

(In: 'Smoking and Health' in Tollison (Ed) Smoking and Society p17-88 Lexington, Lex.)

If Eysenck's assertions are correct that stress is a very potent cause of death from cancer and that personality is a moderator of stress, it would suggest that death from cancer could be avoided or at least postponed by use of cognitive-behavioural therapy. This is particularly important because of the relatively poor evidence traditionally cited in an attempt to avoid or postpone cancer (Eysenck 1980; 1986).

Some researchers have identified a 'hypertensive personality' Alexander (1939) characterised such an individual as exhibiting chronic hostile and angry impulses, which were inhibited or repressed. Such 'unconscious' conflict it was hypothesised, results in chronic elevations in blood pressure and anxiety. Although it is recognised that there is a familial component to hypertension, there is still a lot of interest in the contribution of psychological factors in the development of the disorder (Krantz and Glass 1984; Matthews 1985; Esler 1977). This interest has been boosted by studies showing that blood pressure can be significantly reduced by psychologically based interventions (Agras and Jacob 1979; Charlesworth et al 1984; Goldstein et al 1984; Shapiro 1983).

In 1987, Friedman and Booth - Kewley examined in detail the 'disease-prone' personality. They carried out a meta-analysis of 229 studies looking at the relationship between six personality variables (depression, anger, hostility, aggression, extraversion and anxiety) and disease. They found the average magnitude of correlations to be in the range of .1 to .25. Although these correlations might initially seem low, they are moderate or even high when compared to other 'well established' medical risk factors. For example, correlations between smoking and CHD and cholesterol and CHD are all under .15. All the personality variables were shown to be associated with asthma, arthritis, ulcers, headaches and heart disease. More specifically extraversion was associated with heart disease and headaches and introversion was associated with asthma ulcers and arthritis. These findings give some credence to the possibility of 'illness specific' disease - prone personalities, such as the arthritic prone or headache prone personality.

Recent evidence suggests that personality may affect disease through causal physiological mechanisms. Type A personalities show greater physiological 'reactivity' to stressful conditions than Type Bs. They show greater elevations in systolic blood pressure and heart rate in response to challenging tasks. This is one of the leading hypotheses concerning the means by which Type A Behaviour pattern may ultimately become manifest in CHD (Dembroski et al 1979; Dembroski et al 1978; Herd 1978)

Type As have higher catecholamine levels during the day (but similar at night) compared to Type B individuals providing further evidence that they show a different pattern of reactivity to daily events (Friedman et al 1960). Some researchers have found that Type A individuals secrete higher levels of stress related hormones generally (Matthews and Haynes; Boman 1988) and chronically high levels of stress related hormones (as already discussed) are known to effect the immune system and ultimately make the individual more susceptible to disease.

In conclusion, it appears that the relationship between personality, the immune system and illness works through physiological mechanisms and the effect of stressors on physiological mechanisms is moderated by personality variables.

## Coping Style

Coping style is considered to be another important moderating variable between stress and Health (Jenkins 1979; Lazarus 1981; Rahe and Arthur 1978). Coping

is defined by (Cohen and Lazarus 1979) as:

> "efforts both action oriented and intrapsychic to manage (that is tolerate, reduce, minimise) environmental and internal demands and conflicts among them, which tax or exceed a person's resources".

Lazarus (1966) described a cognitive model of the coping process. He considers that 'cognitive appraisal' is the central concept and that appraisal takes place in two stages, primary and secondary appraisal. This evaluation may be conscious, or unconscious and takes into account a person's understanding of the power of a situation to produce harm, as well as their resources to deal with it. 'Primary appraisal' can be of 'harm-loss' (where the damage has already occurred), 'threat' (anticipated harm) or 'challenge' (focusing on the potential for mastery rather than the risks). "Secondary appraisal" consists of an evaluation of the individual's coping resources and options (Lazarus et al 1970; Lazarus et al 1974; Lazarus and Launier 1978). The type of secondary appraisal made depends upon factors such as the individual's beliefs, motivation, intellect and skills. If for example, the person believes a situation to be manageable they are more likely to perceive it as challenging than threatening and are more likely to adopt a problem solving approach. If however, they believe the situation to be unmanageable they are more likely to adopt an emotion-focused approach and avoid the problem (Cronkite and Moos 1984; Cohen, Evans, Stokols and Krantz 1986; Lazarus and Folkman 1984)

How one copes with stress is thought to have health implications and there are a number of conceptional models which attempt to explain the relationship between coping style and health (Rotter 1966; Kobasa 1979; Antonovsky 1979;1987; Fisher 1986).

Rotter (1966) developed the 'Locus of control' concept, which is concerned with the belief that an individual has in their ability to control events. People towards the 'external' end of the dimension perceive that they have little control over powerful external forces, whereas those towards the 'internal' end believe that they do have control over events and their destiny by their own individual action. Individuals who are towards the internal end of this dimension tend to cope more effectively with stressful situations and remain healthier.

Kobasa (1979) described the 'hardiness' concept, which is a global personality construct which acts as a moderator between stress and illness. Kobasa noted that some individuals are able to cope better with adversity and high levels of stress

and yet still remain healthy. The concept is composed of three inextricably intertwined components. The first is 'commitment', which relates to ones own values goals and capabilities and having an idea of what one wants from life and an overall sense of purpose. The second is 'challenge', which relates to an involvement in situations as a means of expressing ones values and abilities and making use of opportunities to do this. The third one is 'control', which relates to seeing oneself as being able to influence and change situations, so that they go in the direction one wishes (similar to Rotter's 1966 Locus of Control concept). Individuals who have all three components to a high degree are described as 'hardy' and according to Kobasa are able to cope with higher levels of stress without being affected and are less likely to become ill than less hardy individuals, independent of other variables such as Type A personality (Kobasa, Maddi and Kahn 1982; Kobasa, Maddi and Puccetti 1982; Kobasa and Puccetti 1983; Kobasa, Maddi and Zola 19834; Rhodewalt and Agustdottir 1984).

Antonovsky (1979; 1987) described another global concept called the 'Sense of Coherence', which correlates significantly with a wide range of illness measures. Individuals with a high sense of coherence tend to perceive their internal and external environments as predictable and that there is a high probability that things will turn out well for them. Such individuals according to Antonovsky, are able to cope more effectively with higher levels of stress without becoming ill. It consists of three components. The first is 'comprehensibility', which relates to the extent to which an individual perceives a stimulus to make cognitive sense. The second is 'manageability', which refers to a sense that whatever happens, one will be able to cope and maintain some control over events, or at worst learn to live effectively with a problem. The third component is 'meaningfulness', which relates to the extent that something makes sense and gives life meaning to the extent that one wants to invest in it and cares about what happens. Antonovsky's 'Sense of Coherence' concept shows a statistically significant correlation with Rotter's 'Locus of Control' and Kobasa's 'Hardiness' concepts (Antonovsky 1987), indicating that there must be some similarities between these measures.

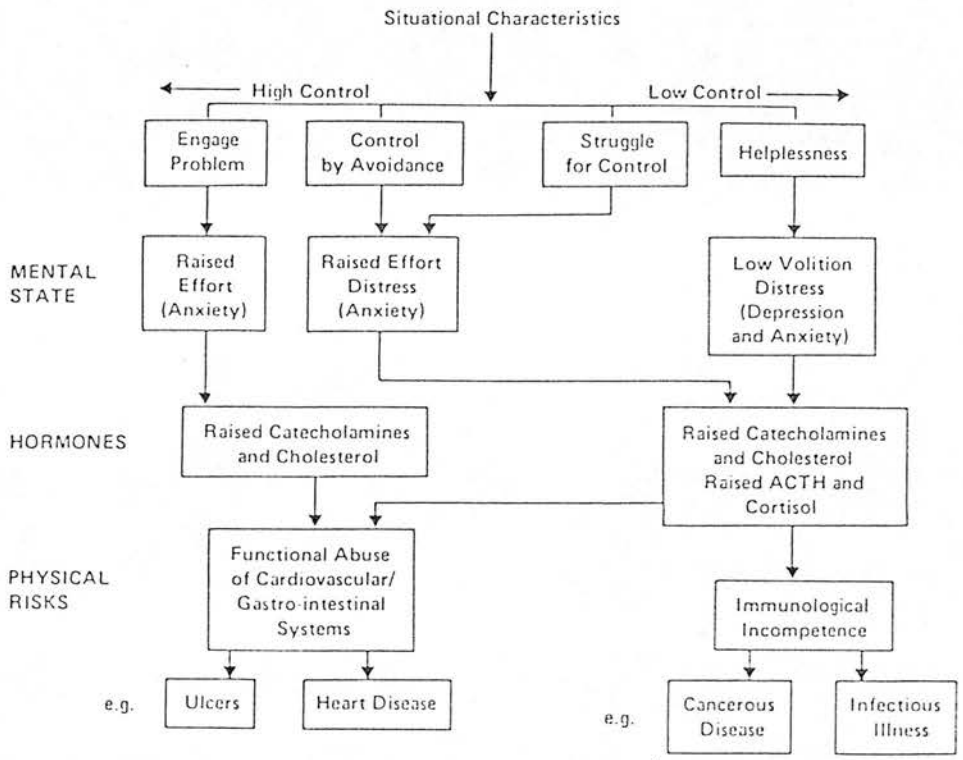
Coping ability has been demonstrated to be related to the immune response, such that better coping is associated with greater immune responsiveness. (Roessler et al 1979; Locke, Hurst and Heisel 1978). One possible way in which coping may affect the immune response and ultimately influence the aetiology of disease is through physiological mechanisms (Elliott 1979). Where an individual appraises that a situation has potential

for mastery it is seen as a challenge (Lazarus 1966) and an attempt is made to gain mastery over it by a process of 'dominant challenged control', which leads to activation of the SAM system, elevating sympathetic activity and raising catecholamines levels. However, where an individual perceives that they have little or no control, a state known as 'subordinate loss of control', the HPAC system is activated, raising ACTH and cortisol levels. Raised levels of stress hormones influence the functioning of the immune system and consequently the poorer coper will become more prone to disease states. (Henry 1976; 1982; Henry and Stephens 1977).

The key variable which emerges again and again in the literature on coping styles, is that of perceived 'control'. It is found in the control dimension of Kobasa's 'Hardiness' concept (1979), in Rotter's 'Locus of Control' dimension (1966), the 'manageability' dimension of Antonovsky's 'Sense of Coherence' concept 1979; 1987) and the 'potential for mastery' dimension of Lazarus's appraisal construct (1966). It appears that one's perception of being in control is a decisive factor in the coping process. Feelings of control act as a buffer between stressors and emotional distress and ultimately disease aetiology (Lefcourt 1985; Wheaton 1982; Steptoe and Appels 1989). A lack of control is associated with feelings of emotional distress and according to Frankenhaeuser and Johansson (1986) different levels of personal control are differentially associated with catecholomine and cortisol secretion and also with the level of effort displayed. A state of challenged control is associated with raised effort and raised catecholamine levels, whereas loss of control is associated with higher levels of distress, reduced effort and increased cortisol secretion (Frankenhaeuser and Johansson 1986).

Fisher (1986) attempts to integrate the control dimension with the physiological mechanisms described earlier in a 'Cognitive-control' model:-

**Figure Five:** "A Cognitive - Control Model" (Source: Fisher 1986, pg 170)




The 'cognitive-control' model proposes that raised effort and associated catecholamines may be helpful if they lead to successful resolution of a problem but if prolonged could do functional damage to bodily systems and result in 'somatic' health problems. However, if effort strategies are unsuccessful and 'failure to control' results an increased level of distress and raised secretion of ACTH and cortisol occurs, with an associated risk of immunological changes rendering the individual more prone to diseases of immunological incompetence! These two conditions are extremes and more typically effort and distress are both present in a situation of challenged control. In the figure above, increasing loss of control is associated with moving to the right. If repeated failure to control occurs, pathological arousal increases, initially through increased efforts associated with a struggle for control and ultimately results in a passive state of helplessness and depression when the individual 'gives up' making an effort to control.

**The Interaction of Personality and Control**

Type A personalities appear to be motivated by an intense need to assert and maintain control over their environment (Lazarus 1971; Glass 1977; 1983; Matthews and Glass 1984; Strube and Werner 1985). Some authors suggest that this is motivated by a strong fear of failure (Price 1983; Musante, MacDougall and Dembroski 1984; Brunson and Matthews 1981; Matthews and Siegal 1983) and the belief that one's self worth is a function of one's achievements (Furnham and Linfoot 1987; Burke and Deszca 1984).

Glass (1977) identified two stages in the Type A individual's response to try and gain control over often uncontrollable events. The first one, which occurs with brief exposure to uncontrollable stress is characterised by an exaggerated physiological arousal response, known as 'hyper-responsiveness'. Associated with this is raised effort and enhanced secretion of the SAM system hormone adrenaline (Frankenhaeuser, Lundberg and Forsman 1980a, 1980b). However, prolonged exposure to uncontrollable events results in a condition known as 'hypo-responsiveness' which is accompanied by enhanced secretion of the HPAC system hormone cortisol as a state of 'distress without effort' is reached (Frankenhaeuser, Lundberg and Forsman 1980a, 1980b). Associated with a state of hyporesponsiveness is a state of helplessness, despondency and depression which is described by Seligman (1975) as 'learned helplessness'. The pattern of responses described by Glass (1977) matches that predicted by the 'learned helplessness model and 'reactance' theory and emphasises the importance of the control construct with respect to Type A behaviour (Wortman and Brehm 1975).

One consequence of a Type A individual's reaction to repeated failure is an erosion of 'self esteem' Musante et al (1984) Price, (1982) describes self esteem as a direct function of one's tangible accomplishments. Thus, in the face of repeated failure to control events, the Type A individual is more prone to feelings of inadequacy, insecurity, self doubt, depression and negative feelings of self worth, that is, lower self esteem (Price 1982; Tramill et al 1985).

## CONCLUSIONS REACHED FROM THE LITERATURE REVIEW

In conclusion, a review of the literature exploring the relationship between psychosocial stressors and the immune response in humans suggests that dualistic notions about the mind and body being separate entities are inadequate to explain the research findings. There is a wealth of evidence both physiological and behavioural which indicates that the traditional biomedical paradigm should be abandoned in favour of the PNI paradigm in which mind and body are seen as a continuum and bi-directional interactions between the Central Nervous System and the Immune System readily acknowledged.

The inter-relationships between psychosocial and physiological variables are not simple unidimensional ones but consist of complex interactions of at least a few but more likely multiple factors operating to influence the individual's immune system.

The literature suggests that it is not so much life events themselves that are stressful but that the manifestations of stress both psychological and physiological are more influenced by the individual's unique response to them. Trait characteristics such as personality and coping style, in particular the individual's appraisal of threat and perception of controllability over life events appear to play a key moderating effect on psychological and physiological states and ultimately the individual's state of immune-competence.

The literature on the psychophysiology of stress suggests that the psychological and physiological manifestations of stress by reducing the immune competence of the host, create the necessary preconditions for illnesses which are immunologically resisted (e.g. colds, opportunistic infections)

## METHODOLOGICAL CONSIDERATIONS

Whilst the evidence presented in the literature review supports the notion that CNS factors influence the immune system, the PNI research on closer examination does contain a number of methodological shortcomings. This has perhaps occurred because even though there is an increasing acceptance of the role that psychosocial factors play, the focus of much of the research has been very much within the tradition biomedical paradigm and in particular upon cellular and biochemical activity, to the neglect of the

mind part of the Mind-Body Continuum.

There is a focus upon the chronic disease consequence of stress and upon diseased populations. Little attempt is made to demonstrate how subtle psychological factors might influence the 'nuts and bolts' workings of the immune system, nor using subjects in the normal healthy population. The populations being studied could therefore be a biased sample which is unrepresentative of the general population.

Similarly, there is an excessive focus upon stressors that are severe or chronic in nature and very little upon more subtle everyday stressors. There is almost a universal neglect of the factors which contribute to positive health states, in favour of the pathological end of the health-disease spectrum. The beneficial effects on health of interventions which lead to distress free states and effective coping styles, which form the basis of many psychological therapies remain largely unresearched.

Many of the studies carried out select only one or two psychosocial variables with little or no explanation as to why those variables have been chosen in preference to others. Consequently they fail to address the complexity of the wide range of possible interactions involved.

In a number of studies stress is not clearly defined and terms such as stress, stressor, strain and distress are used interchangeably. Also, there appear to be very few standardised stressors studied in the literature (e.g.. bereavement, examinations and sleep deprivation) and not enough emphasis placed upon the need to use specific well validated and reliable psychological measures based upon the most recent research. Similarly some measures of immunity are more sensitive than others and often not enough caution is taken to ensure the most sensitive measures available are used.

Also, in many studies there is a lack of stringent study design which addresses the need to control for the wide range of possible confounding variables identified in the literature. Very few are prospective in design. Many are conducted over a short time span and consequently are unable to provide information about or explain change over time.

In conclusion, there do appear to be considerations which need addressing. In particular more well designed and controlled prospective studies are needed which are conducted over a larger time span using clearly defined concepts and a broader range of

well validated and reliable measures which look at subtle psychological changes in response to everyday stressors in the normal healthy general population.

## TOWARDS A CAUSAL PATHWAY

Simply demonstrating statistically significant associations between two or more variables does not tell us enough about those variables to make causal inferences. It is not sufficient to use guess work or assumptions to make decisions about causal order. The work of Davis (1985) helps us make decisions about the logic of causal order. Davis (1985) argues that there are a number of simple 'rules' that can be followed which allow one to make causal inferences:-

One example being that 'after' cannot follow 'before'. Thus, it is impossible for disease to follow death in a causal sequence. Death must always follow disease. Another example given is that some variables are part of a well known sequence of events. Thus, something which is known to be a stimulus must logically come before the response in the causal sequence. Davis argues also that it is logical to assume that constants (unchanging) or variables that remain fairly unchanging come earlier in a causal sequence than more volatile and changing variables. Thus for example, personal characteristics or 'traits' come earlier in the causal sequence than 'states', which can change relatively quickly compared to traits which may remain fairly constant throughout one's life. Davis states that the standard consensus about the relative position of variables is thus:-

Prior——> Independent—> Intervening—> dependent—> consequent

Using such rules one is able to reach some conclusions about the causal sequence of events between the environmental stimuli impinging upon an individual and the final stage of disease. Using the rules of logic described by Davis (1985) an attempt is made to integrate the vast number of research findings discussed to build a causal pathway between psychosocial stressors and the immune response. It is reasonable to assume according to Davis (1985) that:-

1. The 'prior' starting point would be the life events impinging on the individual.
2. The 'consequent' or final state is presumably disease.
3. Personal 'traits' such as personality and coping style precede psychological,

physiological and immunological 'states'.

4. The immediate antecedent of the disease state is a state of altered immunity, which leaves an individual more susceptible to disease.

5. The immediate antecedents of altered immunity appear to be the changes in physiological 'states' associated with neural and hormonal events.

6. A mental schema results from the perception of environmental stimuli.

7. Psychological and biological vulnerability factors act as intervening variables between the mental schema and the resulting emotional state.

8. Neural and neurohormonal events are triggered by a state of emotional distress.

'Life Events' include changes in Social supports and a range of other environmental psychosocial stimuli contained in the life events literature. Psycho biological 'Vulnerability factors' include both genetic factors which appear to be related to one of the most important personality variables 'neuroticism', as well as learned patterns of coping and responding developed through one's early life experiences, parenting and so on (Goldberg and Huxley 1992).

NOTE: As one moves further along the 'causal' pathway the factors later in the chain of events have been increasingly more researched within the context of the biomedical paradigm. One also needs to accept that there are continuous feedback loops at every level in the causal pathway to every other levels.

## MIND - BODY MODELS

Totman (1979) outlines what he considers to be the four essential criteria necessary to build a workable Mind-Body model which is capable of explaining the relationship between psychosocial stressors, the immune response and ultimately health outcomes:-

1. A workable model must be 'practical'. It needs to be cast in a form which is able to lead on to testable physiological hypothesis. It needs to be able to explain the vast amount of findings presented in the research and incorporate the notion of genetic vulnerability. Also, it should relate to real life, observable predicaments in a clear way.

2. A workable model must be 'logical'. It must take the individual as the fundamental unit, since disease is something which happens to individuals. It needs to be able to account for the finding that life events causing one person to experience symptoms will hardly affect another individual. The unique significance or personal meaning of events to individuals needs to be explained by such a model.

3. A workable model would need to provide the 'psychological structure' which would provide the scaffolding upon which the vast number of research findings can be grafted.

4. A workable model needs to be able to demonstrate a causal sequence which would comply with the rules of causal inference described earlier (Davis 1985).

Several models of Mind-Body Interactions in the link between stress and illness have been proposed in the literature over the years (e.g.. Kagan and Levi 1974; Engel 1977; Cohen and Edwards 1988; Cunningham 1991; Goldberg and Huxley 1992).

Kagan and Levi (1974) published a review of the role of what they called psychosocial stimuli in disease. Essentially they proposed that external psychosocial stressors (which are stimuli that originate in social arrangements and relationships and act through higher nervous system processes) and the individual's psychobiological programme (influenced by genetics and early environmental influences) additively determine the psychological and physiological stress reaction. These reactions lead to mental and physical precursors of disease which, if they persist, lead to clinical manifestations of the disease and eventually death. This sequence of events is moderated by interacting variables which promote or prevent the process that might lead to disease.

The system is a cybernetic one with continuous feedback between each of the elements:-

**Figure Six:** "A Theoretical Model for Psychosocially Mediated Disease"
Source: (Kagan and Levi 1974)

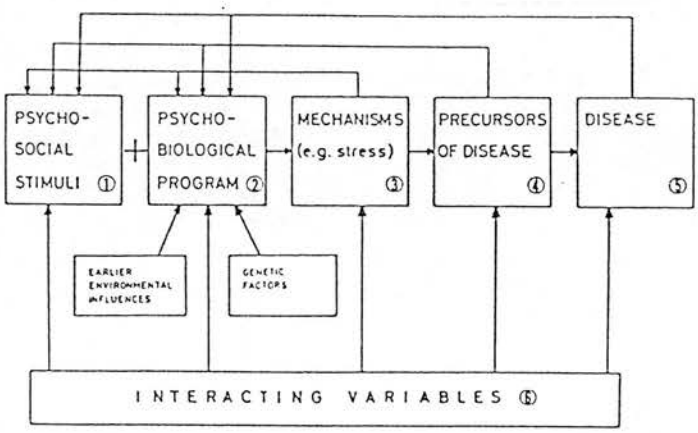
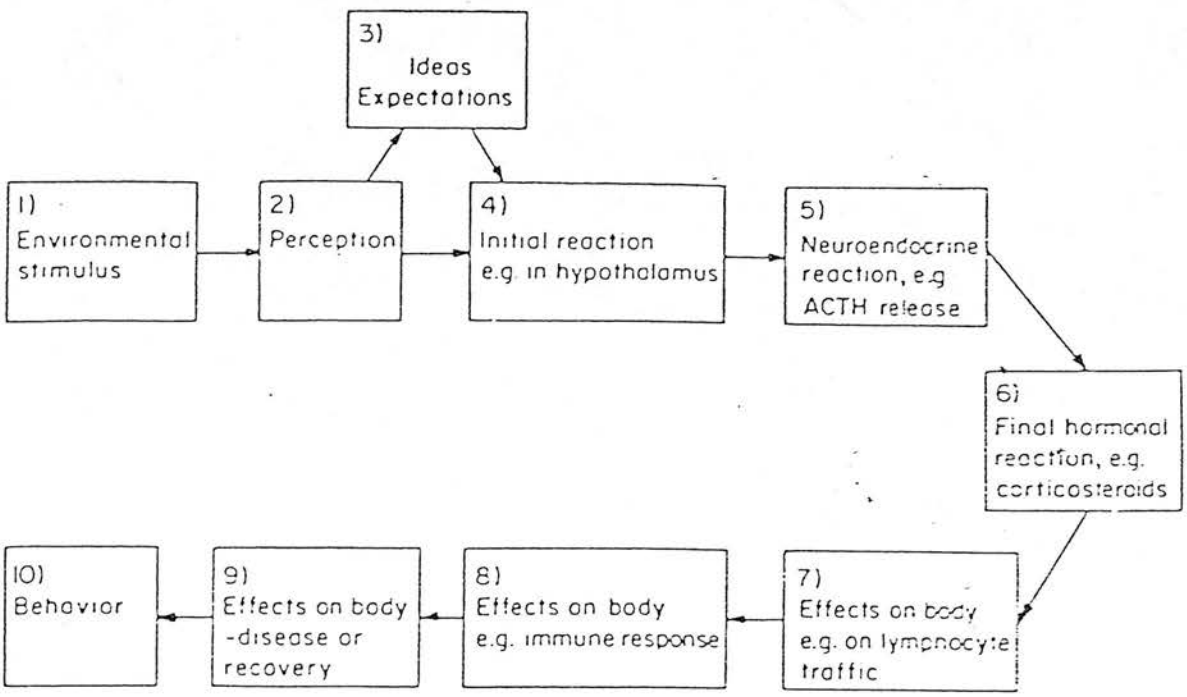



Fig. 1. A theoretical model for psychosocially mediated disease. The combined effect of psychosocial stimuli (1) and the psychobiological program (2) determines the psychological and physiological reactions-mechanisms (3), [e.g. stress] of each individual. These may, under certain circumstances, lead to precursors of disease (4) and to disease itself (5). This sequence of events can be promoted or counteracted by interacting variables (6). The sequence is not a one-way process but constitutes part of a cybernetic system with continuous feed-back.

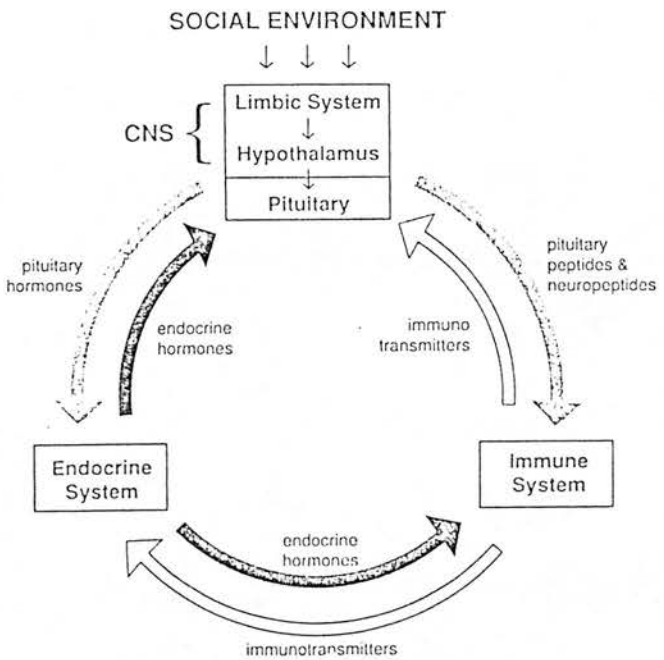
Cunningham (1991) describes a model of how nervous and immune systems interact and identifies some of the levels through which an environmental stimulus, perceived by the mind may affect the immune response and eventually health and behaviour:-

**Figure Seven:** "How Nervous and Immune Systems Interact" (Cunningham 1991):-



Events at each stage in the pathway are enormously complex. Traditionally behavioural psychology has focused on 1 and 10. Much of the research literature described in this study relates levels 4,5 or 6 levels 8 or 9. Stress research tends to compare 1 or 2 to 8 or 9. The very important work on psychological conditioning of the immune response relates to levels 3 and 8.

**Figure Eight:** "Relationship Between Social Events and Three Bodily Symptoms" Goldberg and Huxley (1992):-




The CNS acts as the major controller, translator and integration of stimuli from the environment. Within the CNS the limbic system is the major control system involved in adaptation and in the neuroendocrine and emotional response to stressful signals. The limbic system serves as an important connection between cerebral cortex and the hypothalamus and evaluates stressful stimuli and compares them with past experience. They hypothalamus receives information from the periphery and integrates it with the internal environment and adjusts important functions like sympathetic activity and endocrine secretions. It does this by means of its intimate connection with the pituitary

gland (sometimes referred to as the hypothalamo - pituitary axis). It controls ACTH release in response to stressful stimuli. Thus, the CNS modulates the relationship between the external social environment and the internal environment of the body. It influences the endocrine system by secretion of pituitary hormones and influences the immune system by neuropeptide secretion and by autonomic control of lymphoid tissue. The CNS is itself influenced by various hormones and by the immune system by substances called neurotransmitters. The endocrine system and the immune systems are also capable of directly influencing one another (Goldberg and Huxley 1992).

The models presented earlier vary in the extent to which they meet Totman's (1979) criteria. Kagan and Levi's (1974) model focuses on the individual as the fundamental unit, attempts to demonstrate a causal sequence, addresses the importance of personal significance of events and differences in appraisal, incorporates the notion of 'appraisal' of stimuli from the environment and acknowledges the role of moderating variables in the response to stress. In addition it has the advantage that the continuous feedback provided by interacting variables allows for changes in the environment over time, thus accommodating the differences between acute and chronic effects as the system adapts to changes. The explanatory predictive value of the model is greater as one moves further along the causal sequence towards the cellular and biochemical end and the model pays particular attention to neuroendocrine responses. On the negative side however, the model fails to address how all these important mechanisms might have their actions and is not specific enough in clarifying the different types of psychosocial stressors or moderators of stress found earlier in the causal sequence of events. As such it would be difficult to draw out clear testable hypotheses from this model.

Cunningham's (1991) model also focuses on the individual, attempts to demonstrate a causal sequence of events and acknowledge to some degree the personal significance of events. However, the model underplays the role played by psychological moderating variables in the causal sequence of events; placing cognitive factors on the periphery of the model. Neither does it specifically address the notion of genetic vulnerability. The focus of the model is again more heavily upon the biochemical events

occurring later in the causal sequence. Whilst the model does acknowledge that most of the stresses affecting western man are not physical but initiated by his own mental reactions to intrinsically harmless stimuli, does not specifically clarify categories of psychosocial stressors. Again, the explanatory and predictive value of the model becomes greater as one moves further along the causal sequence to biochemical and cellular phenomena.

Goldberg and Huxley's (1992) model comes closest to meeting the criteria outlined by Totman (1979). It takes the individual as the fundamental unit, provides a psychological structure and relates psychological phenomena to physiological systems in the brain. It addresses the notions of genetic vulnerability, the unique personal significance of incoming stimuli in relation to past experiences and the importance of moderating variables such as personality and coping style. It is able to accommodate the wide body of research findings and lead on to testable physiological hypotheses. It also demonstrates a bi-directional causal sequence between psychosocial biochemical and cellular factors. It is much more specific about the psychological structures involved than the other models outlined.

In conclusion, Goldberg and Huxley's (1992) 'biopsychosocial model' comes closest to meeting the criteria outlined by Totman (1979) for a workable 'mind-body' model which is capable of explaining the relationship between psychosocial stressors, the immune response and ultimately health outcomes. Kagan and Levi's and Cunningham models are more of a conceptual framework than a predictive model (Warr 1980).

## AIMS OF PRESENT STUDY

1. To carry out an empirical investigation of the relationship between psychosocial stressors and the immune response in humans, which takes into account the methodological considerations outlined in the introductory section of this study.

2. Demonstrate that subtle psychological changes in response to every day stressors in the normal healthy population will influence the workings of the immune system and ultimately have pathological outcomes.

3. Construct a theoretical framework based upon the findings outlined in the literature search, which is also capable of explaining the results obtained in the present study.

## HYPOTHESES

On the basis of the literature reviewed it is hypothesised that:-

1. • **Life events in isolation are 'neutral'. They are not associated in any direct causal way with emotional distress or the workings of the immune system.**

2. The relationship between life events and emotional distress experienced is moderated by personality factors:-

   a) Personality factors play a role in determining whether or not a life event is perceived as stressful:-

      • **Type A personalities will report a greater number and severity of life events than Type B personalities**

   b) Personality factors play a part in determining the physiological reactivity of an individual to stressful life events:-

      • **Type A personalities will report higher levels of anxiety than Type B personalities.**

3. The relationship between life events and emotional distress experienced is moderated by coping factors. ( Note: Coping in this context is defined as a 'trait' not a 'state' measure-see page 108).

   a) Coping factors play a role in determining whether or not a life event is perceived as stressful:-

   • **Poor copers will report a greater number and seventy of life events than good copers.**

   b) An individual's perception of coping is associated with the amount of emotional distress experienced:-

   • **Poor copers will experience higher levels of anxiety than good copers.**

   • **Poor copers will experience higher levels of depression than good copers.**

c) An individuals perception of control over stressful life events is associated with the amount of emotional distress experienced:-

- **Individuals reporting low perceived control over life events will experience high levels of anxiety and depression than those reporting high levels of control.**

4. Personality and coping factors work together in an interactive way:-

- **Type A individuals in situations of low perceived control will experience more emotional distress (anxiety and depression) than Type B individuals in situations of low perceived control.**

5. Emotional Distress is the mediating variable through which life events personality and coping factors influence the immune system:-

- **Subtle changes in emotional state in response to everyday stressors will have an effect on the immune system.**
- **Depression will be the key mediating variable through which immuno-suppression takes place.**
- **Anxiety will be the key mediating variable through which immune-enhancement can take place.**

6. Subtle psychological changes in response to every day stressors in a normal healthy population will be associated with sickness behaviour:-

- **More vulnerable individuals (high Type As and poor copers) will display more sickness behaviour.**
- **Individuals reporting higher levels of emotional distress (anxiety and depression) will display more sickness behaviour**

7. There will be an association between sickness behaviour and immune response.

- **Specifically, individuals demonstrating more sickness behaviour will have a poorer immune response.**

8. The results of this study will comply with the sequence of events predicted by the rules of causal logic outlined in the introduction (see pages 49 - 50).

| LIFE EVENTS | → | PERSONALITY COPING | → | STATE OF EMOTIONAL DISTRESS | → | IMMUNE FUNCTIONING |
|---|---|---|---|---|---|---|

# METHODS

## DESIGN

The present study was prospective over a six month time span. The dependent variables (antibody titre levels and sickness absence statistics) were measured at the end of the six months. Further sickness absence data was also collected over the six months following the completion of the study.

Data on the selected independent variables (measures of psychosocial stress) were collected at four points in time over the six months. The independent variables were categorised into three major groups:-

a) environmental variables.

b) personal variables.

c) measures of emotional distress.

At the end of the six months, data on the dependent variables was allocated to one of two groups for the purpose of statistical analyses, using the 'median split' method. For the measure of immune response, 'Group One' was the high immune response group and 'Group Two' was the low immune response group. For the measure of sickness absence, 'Group One' was the low sickness group and 'Group Two' the high sickness absence group. Stepwise multiple regression analysis was also carried out to assess the extent to which selected independent variables are associated with each of the dependent variables. Further statistical analyses were conducted as considered appropriate.

## SUBJECTS

### Rationale for Sample Selection

The main considerations in selecting a sample for this study were as follows:-

### Sample Size

It was necessary to obtain a large enough population of subjects to make

the study a valid one in a statistical sense. Health Service Workers were chosen, firstly because large numbers of them are immunised 'routinely' on commencement of employment with the National Health Service and secondly, the 'dropout' rate from the study could be reduced, since it would be relatively easy to monitor an individual subject's whereabouts at any given time in the six month duration of the study and provide 'reminders' when necessary. The largest employee group recruited annually who are immunised routinely were found to be student nurses with an annual intake of approximately 70 student nurses per year, which would provide sufficient numbers of subjects to generate a valid sample size. This was one of the reasons why the student nurse population was eventually chosen for this study.

**Minimising the Variance due to Non-Psychological Variables**

There were a multitude of possible 'non-psychological' variables which could confound the results obtained. These included physical characteristics and environmental variables .The present study attempted to minimise the variance due to these variables by selecting subjects closely controlled interms of physical characteristics and life experiences over the duration of the study. It was again decided that student nurses would be the best population to fit these criteria, for the following reasons:-

1. The Immune Response in humans has been shown to be influenced by a number of physiological variables, such as age Deinhardt 1982), sex, body mass (Cockcroft et al 1990), physical fitness (Eskola 1978; Targan 1981) and circadian variations (Cove-Smith et al 1978). To a large extent, these variables are controlled for by selecting the student nurse population (see 'subject characteristics' in the results section - page 78).

2. Most of the population selected would have experienced a number of similar 'life events' associated with commencing nurse training (e.g. change of employment or starting a new career altogether, interviews, change in supports, moving away from the parental home for the first time or simply moving away from home and friends to commence training). Unfortunately, it was not possible to control for other life events of a personal nature which might occur during the course of the

study (e.g. divorce, marital problems bereavement and so on) in the design stage. However, these could be looked at in the analysis stage of the study.

3. All the student nurses would be confronted by similar work experiences (e.g. level of responsibility, course-work assignments, practical placements and shiftwork) at approximately the same times, thus controlling to a greater degree for variations in occupational stress levels than would have been possible had another population been selected. Research has shown that even amongst an apparently 'homogenous' population as student nurses, significant variations in occupational stress levels do exist between the initial period of training(first year) and later on in training(second and third years),with most studies identifying the first year as being most stressful (e.g. Garrett et al 1976; Williams 1979). All the subjects selected for the present study were first year students commencing their training, thus controlling for any variations due to length of time in training .

**Exclusion Criteria**

Those student nurses who had previously been vaccinated for the antigen used in this study prior to its commencement were excluded, since the design of this study was 'prospective' in nature.

## METHODS OF DATA COLLECTION
## DEPENDENT VARIABLES

### *A) Antibody Titre Levels*

Hepatitis B Vaccine

Hepatitis B vaccine is usually given routinely to anyone who may have direct contact with infected persons or their bodily fluids and hence will be at risk of contracting the disease. 'Needlestick' injuries are the major risk factor in the risk of transmission of hepatitis B infection to health-care workers. The antibody response built up over the six month course of vaccinations is measured by 'blood titre' levels. Before 1990 the subject was said to display either an antibody +ve response or an antibody -ve response. Since 1990 however, a more sensitive measure has been developed which

measures the subjects immune response on a scale of 0 to 1000, where 0 = no immunity and 1000= maximum immunity.

The manufacturers of Engerix B estimate that 84% of subjects given the course of hepatitis B vaccine develop an immune response(>100) and 54% develop a maximum immune response of 1000. These statistics are supported by subsequent research of healthcare workers in Sweden (Struve et al 1992). A further study amongst nursing students (Dentico et al 1991) demonstrated that the high percentage of immune responders were maintained up to five years after the commencement of vaccination (75% of responders).

Only three previous studies could be found in the literature which make use of the antibody response to Hepatitis B vaccine to explore the relationship between stress and the immune response in humans (Jabaaij 1992; Glaser et al 1992 and Petry et al 1991). All of these studies show that psychosocial factors appear to affect the immune response to a recombinant Hepatitis B vaccine, although they do not all agree in which direction the effect is. Two of the studies (Jabaaij 1992; Glaser et al 1992) demonstrate that psychosocial stress affects the immune response in a negative direction and the results of the other (Petry et al 1991) suggest the opposite to this, namely that psychosocial stress actually enhances the immune response. Further, in the study by Petry et al (1991), Multiple Regression analysis demonstrated that psychosocial factors accounted for 5.8% of the variance in the immune response and as such they are considered to be as strong a determinant of antibody titre levels as other well established variables such as 'age' (Deinhardt 1982) for example.

Rubella Vaccination

Rubella is a mild infectious disease most common amongst children aged 4 to 9 years. Maternal rubella can result in multiple defects in the foetus. For both children and adults the dose is 0.5 ml, given by subcutaneous injection. One dose of vaccine promotes an antibody response in over 95% of vaccines and protection has been shown to persist over fifteen years. It is given to all girls between their 10th and 14th birthdays and non-pregnant seronegative women of child-bearing age.

All health service workers, both male and female are screened before employment by a blood test to ascertain whether they are seronegative or seropositive. Those found to be seronegative are vaccinated again. In the present study all student nurses were screened by serological testing as part of their pre-employment medical and categorised as either seronegative or seropositive and this data on immune-responsivity was used in this study.

## Previous Studies using Antibody Response to Hepatitis B Vaccine to explore the Relationship between Stress and the Immune Response in Humans

### Petry et al (1991)

This American study used eighty one seronegative medical students who received a standard protocol of a recombinant hepatitis B vaccine (0, 1 and 6 months). Six months after the first dose each subject completed both the Survey of Life Experiences and Symptom Distress Check List to assess levels of stress and distress during that period. Three months after the third dose, corresponding to the booster phase of immunisation, each subject completed the same questionnaires and was also tested for quantitative hepatitis B antibody titres. Correlations were statistically analysed using Pearsons Correlation Coefficient and Stepwise Multiple Regression Analyses.

Results indicated that higher levels of perceived stress, irascibility (interpersonal sensitivity and hostility), depression and anxiety during the induction phase of immunization were significantly associated with higher peak antibody titres. Jointly, these psychosocial variables accounted for 5.8% of the variance and were as strong a determinant of peak antibody titres as was age.

This study has a number of methodological drawbacks however. It did not control for biological variables such as age, sex, weight or smoking status. The data collected on the psychosocial variables was retrospective in nature, asking subjects to report on subjective status such as depression and anxiety over the previous six months. There is consequently no way of knowing what fluctuations or changes occurred over this time span. The study does not report on the reliability or validity of psychosocial measures used. In addition, a smaller antigen load (10 g/ml) and a different timescale for measuring peak antibody levels was used (at nine months rather than seven months) to that used in the United Kingdom.

**Jabaaij et al (1992)**

This Dutch study used a low dose (2 g/ml) of hepatitis B vaccine to vaccinate eighty medical students using the standard protocol (0, 1 and 6 months). Questionnaires measuring daily hassles and psychoneurotic symptoms were completed twice during the study at months two and six. Based on the questionnaires, two different distress measures were calculated, a stress index score at month two and at month six. Regression analyses revealed a significant negative association between stress at month two and antibody titre levels, indicating lower titre levels for more distressed patients.

This study used a much lower dose than is the standard protocol and excluded subjects who did not achieve protective levels of antibodies from the study. Two different vaccines were actually used in the same study and two different schedules for administering these vaccines were followed. Also, there is no information given about why 43% of the total subject population did not participate in the study. As such this study has some serious methodological flaws.

**Glaser et al (1992)**

This American Study is perhaps the most well designed of the three studies discussed. Each of a series of three hepatitis B vaccinations were given to forty eight second year medical students on the third day of a three day examination series to study the affects of examination stress and the ability to generate an immune response.

The results indicated that those subjects who seroconverted after the first injection (25%) were significantly less stressed and anxious than those who did not seroconvert at that time.

The study was quite well designed, using a standardised stressor (examination stress) and reported on the reliability and validity of the psychosocial measures used. However, it is not the standard practice in the United Kingdom to measure blood antibodies after only one month and it appears from the results that this finding was not replicated at the end of the course of vaccinations. The study does not say if the anxiety questionnaire was given before or after the blood test and second vaccination. If given before, this could have had a confounding effect in that subjects' anxieties may well have been raised in anticipation of the injections to follow! Again the dose of hepatitis B vaccine was lower than that administered in the United Kingdom. However, of the three studies this was perhaps the most well designed.

Some previous studies have demonstrated an association between mental health and serum antibody virus. For example, King et al (1985) found a statistically significant reduction in serum anti body levels for rubella virus in mentally ill patients (chronic schizophrenics). The present study aims to establish whether such a relationship can be demonstrated in otherwise healthy subjects.

***B) Sickness Absence Records***

Sickness absence for each subject was recorded over the six month duration of the study and over the six month period following the completion of the study. Consequently, data was collected from employee records six months and one year after the commencement of the study, in the form of total number of days sickness absence. It would also be possible, if required, to follow the same group of subjects throughout the course of their training to obtain further data on sickness absence.

## INDEPENDENT VARIABLES

From the literature search a number of psycho-social factors (the independent variables) were identified as being associated with high stress levels in human subjects. It was decided that the most important ones described in the literature should be included in the present study. The selected independent variables were categorised into the following three major groups:-

a) Environmental variables.

b) Personal variables.

c) Measures of Emotional Distress.

(For copies of all the measures used see Appendix One).

***a) Environmental Variables***

**Life Events:-**

The Social Readjustment Rating Scale (SRRS)-Holmes and Rahe (1967)

The SRRS is a 43 item self report schedule of recent life events, referring to changes that may occur in a person's domestic or work situation, including changes in

personal or interpersonal relationships and habits, essentially changes for which some readjustment is necessary on the part of the person.

Scoring is by two methods. Firstly, the actual number of life events and secondly, the magnitude of life change. In the second method, each life event is given a particular weighting and the total score is calculated as the sum of all the individual ratings.

Normative data is available. Holmes and Medusa (1974) found the mean score for the population in their study was 29.1 life change units .Holmes and Rahe (1967) identified the following cut-off points:-

A score of 150-199 points = mild and increases likelihood of illness by 40%.
A score of 200-299 points = moderate and increases likelihood of illness by 50%.
A score of 300 points and above = major and increases likelihood of illness by 80%

The schedule has been demonstrated to predict both minor illnesses such as colds, backache, cuts, bruises, stomach aches (Holmes and Holmes1970) and major onsets such as myocardial infarction (Rahe and Paasikivi; Theorell and Rahe 1971), indicating that psychological factors may play a significant role in the whole gamut of illness.

The Combined Hassles and Uplifts Scale (H and U)-Lazarus R.S. and Folkman S.(1989)

Whilst the SRRS tends to focus upon life events over the long term (previous six months) and also upon major life changes, the H and U scale focuses upon 'everyday encounters', which they call 'hassles' and 'uplifts' over a shorter time span(Lazarus and Folkman 1984;1987). Lazarus and Folkman (1989) described what they considered to be the advantages of their scale over other life event scales in the H and U user manual. In particular they describe what they consider to be a number of advantages of their scale over other life event scales. Earlier versions define stress solely in terms of the adaptational demands made upon the individual by life changes, regardless of whether they are positive or negative. Recent research has indicated that negative changes outweigh positive ones in producing distress and dysfunction. Earlier versions also focus upon major life changes rather than everyday recurrent demands over a shorter time span. These everyday demands have been called by Lazarus and Folkman (1987, 1989) 'hassles and uplifts'. The H and U scale addresses some of the shortcomings of earlier measures and Lazarus and Folkman (1989) described what they considered to be

the advantages of their scale over other life event scales in the H and U user manual.

The H and U scale consists of three independent scales. These are the 'daily hassles scale', the 'uplifts' scale and the 'combined hassles and uplifts' scale. The 53 item combined H and U scale was used in the present study. Scoring is by two methods. Firstly there is the frequency method, which simply adds up the number of hassles and uplifts endorsed by the individual without regard to severity and secondly there is the severity method, which is the mean rating of all the items endorsed.

Lazarus and Folkman (1989) present data which demonstrates good construct validity of the hassles portion of the scale as a measure of psychological stress and the test-retest reliability of frequency scores is +0.79, suggesting scores have both 'trait' and 'state' characteristics. They also present some normative data for an adult population. The mean number of hassles per day is 12.45 (S.D. 7.66) and mean severity of hassles is 1.34 (S.D.0.26).

**Measures of behavioural change associated with Psycho-social Stressors and Immune Responsiveness:-**

Behavioural changes such as change in diet, activity, exercise levels and sleep pattern are often linked to negative psychological states such as depression and anxiety. Indeed, they are usually included in psychosocial assessments (e.g. BDI, SRRS and GHQ). This does not exclude the possibility however, that such changes could occur in the absence of any psychosocial stressors.

Change in nutrition (Bistrian et al 1975), activity and exercise levels (Eskola 1978; Targan 1981) and sleep (Palmblad et al 1979), have been found to influence lymphocyte functioning with self-starvation, physical inactivity and insomnia all affecting the immune system functioning detrimentally.

It was decided to monitor any changes in sleeping habits, eating pattern and activity levels for the six month duration of the study, independently of other life change items listed in Social Readjustment Rating Scale (Holmes and Rahe 1967).

Shift patterns have also been found to influence the immune system (Nakano et al 1982 ). This was controlled for at the design stage of this study by selecting subjects with similar shift patterns.

**Intake and type of Training**

The type of training undertaken, whether it be Registered Mental Nurse (RMN) or Registered General Nurse (RGN) training may reflect different work experiences and expose subjects to different types of environmental stressors. Similarly, different intakes of student nurses may have different experiences and also variations in terms of group cohesiveness and supports experienced. It was thus considered important to include these potential environmental variables in the study.

***b) Personal Variables***

Personality:-

The Jenkin's Activity Schedule (JAS-form C)-Jenkins C.D., Zyzanski S.J. and Rosenman R.H. 1979)

The JAS form C is a self-report multiple choice questionnaire of 52 items designed to measure the stress related 'Type A' behaviour pattern. It is also found to be strongly associated with the risk of coronary heart disease. This coronary prone behaviour pattern is an overt behavioural syndrome, or style of living, characterised by extreme competitiveness, striving for achievement, aggressiveness, impatience, haste, restlessness, and feelings of being challenged by responsibility and pressure of time.

The JAS consists of four subscales. These are 'Type A behaviour' (Type A), 'speed and impatience' (factor S), 'job involvement' (factor J), and 'hard-driving and competitive' (factor H). The questionnaire takes approximately 15-20 minutes to complete.

The JAS has been demonstrated to be reliable (internal consistency ranging from 0.73 to 0.85 over the four scales) and valid (high agreement with interview ratings) as an assessment tool (JAS manual 1979). The test-retest reliability of between 0.60 and 0.70 over retest intervals of four years indicate that it is a stable 'trait' measure. The JAS has also been found to have some predictive validity in that those with higher JAS scores are more likely to sustain heart attacks. (JAS manual pages14-16). There are British norms for the adult population (Jenkins et al 1979).

The Short Type A Questionnaire-Fontana D. (1989)

The JAS is particularly time consuming to complete, score and interpret, so it was decided to include another much shorter questionnaire to assess its reliability and validity for future use as an instrument for measuring Type A behaviour by comparing it to the JAS.

The shortened Type A questionnaire consists of only 16 questions, to which the subject has to simply respond with a 'yes' or a 'no'. Each 'yes' response corresponds to 1 point. The maximum score is thus 16 and a higher score equates with a greater prevalence of Type A behaviours. There are currently no norms available for this questionnaire.

Cognitive Appraisal:-

Lazarus and Folkman (1984;1987) emphasise the role of cognitive appraisal in the stress and coping process. The following assessments measure the extent of negative beliefs, attitudes and characteristic ways of thinking about oneself, others and the world in general, which are associated with raised levels of psychological distress and poorer coping.

Dysfunctional Attitude Scale (DAS)-Weissman and Beck (1978)

This 40 item self rating scale was developed to assess the underlying assumptions and beliefs that constitute 'schemas' by which individuals construe their life experiences. There are two forms of the scale, DAS form A and DAS form B. Form A is used in this study. Form A uses a Likert style rating scale from 1 to 7, where 1= least dysfunctional and 7= most dysfunctional. The DAS score is the sum of all the items.

The norms for the non-depressed general population is a mean of 119.4 (SD 27.2), taken from Weissman (1979). For major depressives the norms are a mean of 147.45 (SD not given), taken from Silverman et al (1984). The internal consistency of the DAS is 0.90 and test-retest reliability is 0.84 (Dobson and Breiter 1983; Hammen and Krantz 1985), suggesting that it is a 'trait' measure with considerable stability over time. The DAS also correlates significantly (r=0.47) with the Beck Depression Inventory (Weissman and Beck 1978).

The Automatic Thoughts Questionnaire Revised(ATQ-R)- Kendall P.C., Howard B.L. and Hays C. (1989).

The ATQ-R is a revised 40 item version of the original 30 item ATQ questionnaire devised by Hollon and Kendall (1980). Subjects are asked to indicate on a scale of 1 (not at all) to 5 (all the time) how frequently the listed thoughts have occurred to them in the past week. There are two ways of scoring the ATQ-R, firstly valency measures and secondly, frequency measures. Frequency measures are used in this study, using the procedure outlined by Kendall et al (1989). The norms for the ATQ-R are taken from a cross-validation study by Kendall et al(1989). A psychologically healthy 'internal dialogue' is considered to be a ratio of 0.62 to 0.38 of positive to negative thinking.

The split-half reliability of the original 30 item ATQ is .97 and Cronbach's alpha of internal consistency is 0.96, both significant at the 0.001 level, demonstrating sufficient reliability (Hollon and Kendall 1980). In the ATQ-R the Cronbach's alpha correlation coefficient for the 10 non-negative items is 0.90, demonstrating sufficient reliability for the non-negative items.

Correlations between the ATQ, Beck Depression Inventory (BDI) and Minnesota Multiphasic Personality Inventory (MMPI) depression subscale (MMPI-D) are all statistically significant ($p<0.01$). It also differentiates between depressed and non-depressed groups (Harrell and Ryon 1983). The ATQ-R also discriminates between clinical groups (Kendall et al 1989). It is thus a reliable and valid assessment tool.

Self Esteem

Culture Free Self Esteem Inventory (CFSEI) - James Battle (1980).

The CFSEI is a self completed questionnaire which measures the perception that individuals have of their own 'self-worth'. There are three versions for adults (form AD), children (form A) and large-scale screening (form B). The version used in this study was the adult version (form AD) which contains 40 items with three subscales for 'general' (8 items), 'social' (16 items) and 'personal' (8 items) self esteem, plus a 'lie/ defensiveness' scale (8 items). Items are divided into two groups, those indicating high self esteem and those indicating low self esteem. The individual checks each item and

responds with either a 'yes' or a 'no'.

The SEI test-retest reliability is 0.81, indicating considerable stability over time. The internal consistency of the four subscales are for general (0.78), social (0.57), personal (0.72) and the lie/defensiveness scale(0.54). The SEI correlates favourably with the BDI and the MMPI (Battle 1980a). Scoring is as indicated in the manual (Battle 1980).

Coping Style

The Sense of Coherence Questionnaire (SOCQ)-Aaron Antonovsky (1987).

The 'Sense of Coherence' concept was originally formulated by Antnovsky in 1979 and the SOCQ was devised in1987. It is essentially a measure of 'coping style'. The SOCQ consists of a longer and a shorter version. The shorter 29 item scale version was used in this study. It consists of three sub-scales:-

1. Comprehensibility relates to the degree to which things make 'cognitive sense' and that things are ordered, consistent and predictable.
2. Manageability relates to the sense that whatever happens, one will cope and retain some control over events.
3. Meaningfulness relates to the extent to which something gives life meaning to the extent that one wants to invest in it and cares about what goes on.

The SOCQ demonstrates a statistically significant correlation with similar concepts such as the 'Hardiness' concept (Kobasa 1979) and with the 'Internal-External Locus of Control' measure (Rotter 1966). Antonovsky (1987) states that the SOCQ score consistently and significantly correlates with a wide range of 'illness' measures.

A summary of 11 studies using the scale demonstrates a high level of internal consistency (Chronbach's alpha ranging from 0.84 to 0.93) and gives support for the scale's validity (Antonovsky 1987). International comparisons of the normative data for healthworkers shows considerable consistency.

History of Psychological/Psychiatric Problems

Another important variable to look at when assessing subjects' current levels of emotional distress and coping style, was to look at their history of psychiatric/ psychological problems. Medical records available to the Occupational Health Service provided a readily available source of data. It was thus possible to ascertain whether or not subjects in the study had ever previously suffered from psychological or psychiatric problems. Given this information, it would be possible to establish whether or not a history of mental health problems is associated with current stress levels, immune responsiveness and ultimately sickness absence amongst the subjects in this study.

Personal Physical Characteristics and Habits

Whilst the method of sample selection attempts to minimise the variance accounted for by personal physical characteristics, it was not possible to control for these variables completely. Sex, age and marital status variables were included. There is also some evidence that smoking can have an immuno suppressive effect on the immune response and so this variable was also included.

*c) **Measures of Emotional Distress**:-*

The Hospital Anxiety and Depression (HAD) Scale-Zigmond A.S.and Snaith R.P. (1983)

This is a self assessment scale for detecting the presence and severity of anxiety and depressive states in non-psychiatric populations. It consists of seven anxiety items and seven depression items. Scoring is on a four point scale from no symptomatology (0) to severe symptomatology (3). The maximum possible score for either scale is thus 21. The cut-off point is 8 to 10, below 8 demonstrating an absence of symptoms and above 10 demonstrating presence of symptomatology .

The reliability of the two scales is high, the internal consistency for anxiety being +0.76 to +0.41:$p<0.01$ and depression +0.60 to +0.30 $p<0.02$. The validity of the two scales is also high, with correlations between subscale scores and ratings from psychiatric interviews being +0.70 for depression and +0.74 for anxiety, both significant at $p<0.001$ level (Zigmond and Snaith 1983 ). Thus, the HAD scale is presented as a reliable instrument for screening for clinically significant anxiety and depression in the

general population and also as a valid measure of severity of mood disorders.

The General Health Questionnaire (GHQ)-Goldberg D.and Williams P.(1988)

The GHQ is a self-administered screening test aimed at detecting mental health problems in non-psychiatric settings (e.g. primary care) and in the general population. There are four versions of the GHQ. They are the GHQ 60; GHQ 30; GHQ 28 and the GHQ 12. The choice of which questionnaire is used depends on the time available to complete them and the literacy of the subjects being screened. The GHQ 28, which is generally chosen for research purposes, was the one used in this study. The GHQ method of scoring was used, as described in the GHQ manual and the threshold for 'caseness' was defined as any score greater than 5.

The GHQ demonstrates high reliability (split half+0.95; Cronbach's Alpha values range from +0.82 to +0.93). Also, the GHQ demonstrates high validity. The results of 22 studies indicate a high correlation of +0.70 between scores on the GHQ and diagnostic interviews (Goldberg and Williams 1988). Previous studies of groups of Health Workers have been conducted. Vachon (1978) found that amongst palliative care nurses, 56% scored above 5 on the GHQ 30. Parkes (1980) found that 22% of student nurses scored above 12 on the GHQ 60. Firth-Cozens (1987) doing a study of House Physicians found 50% scoring above 5 on the GHQ 30 during their Houseman year.

Occupational Stress

Maslach Burnout Inventory (MBI)-Maslach C. and Jackson S.E. (1981)

The MBI measures the consequences of chronic stress associated with working in continuous face to face contact with clients, such as in human service professions (e.g. healthworkers, social workers, police force). This emotional draining is termed 'burnout'. It is a syndrome of emotional exhaustion, depersonalisation and reduced personal accomplishment and the three subscales of the MBI measure these aspect of burnout. They are:-

1. Emotional Exhaustion (EE) - when the worker no longer feels able to give of him/her self at a psychological level.

2. Depersonalisation (DP) - the development of negative, cynical attitudes and feelings about one's clients (Wills 1978).

3. Personal Accomplishment (PA) -the tendency to evaluate oneself more negatively,

particularly in regard to one's work with clients.

Subjects are asked to rate how often they experience a range of symptoms of burnout (22 items in total) on a 0 to 6 scale, ranging from 'never' (0) to 'everyday' (6). The three subscale scores are derived from this scale as described in the MBI manual (1981). Subjects are then allocated to one of three categories i.e. high, moderate or low degree of burnout, according to their profile on the three subscales. Normative data is available for healthworkers, namely physicians and nurses (Maslach and Jackson 1981). Maslach and Jackson (1981) provide substantial evidence for the reliability (Cronbach's alpha 0.90 for EE, 0.79 for DP and 0.71 for PA) and validity (correlations with observer ratings, dimensions of the job experience and with personal outcomes ) of the MBI.

## PROCEDURE

### 1. Ethical Approval

Ethical approval was granted by 'Tees Health' Medical Ethics Committee. (see Appendix Two).

### 2. Recruitment Procedure

a) The initial proposal for the project was discussed in the first instance with the Nurse Tutors who would be involved, since their support of the project was considered crucial to its success. Consequently, their support and approval for the project was obtained.

b) Individual tutors responsible for all the new intakes of student nurses over the time period between July 1992 and July 1993, were contacted directly at the 'Teesside and Durham College of Health' and a convenient date and time was allocated on the student nurses' induction week timetable, to allow the researcher to present the proposal to prospective participants in the study.

c) A talk was given by the researcher, during which the research proposal was introduced to all new intakes of student nurses over the one year duration of the study. The talk consisted of detailed information on the aims and procedures involved in the study. Any queries about it were answered.

## 3. Admission Procedure

a) Fully informed written consent to participate in the study was obtained from those volunteers who were eligible i.e. those who had not previously already had a course of hepatitis B vaccinations and who expressed a wish to be included (see Appendix Three).

b) All participants were assured that any information given would remain totally confidential to the research team, which consisted of the research co-ordinator, a registered general nurse and an administrative assistant.

c) The fact that subjects were included in this study did not in any way exclude them from making use of the Occupational Health facilities available to all employees. However, it was decide that if anyone involved in the study did refer themselves to the staff Psychology and Counselling Service, such intervention may modify stress levels and affect the results obtained. Thus, any student nurse using the service would be excluded from the study. However, in the event this did not occur.

## 4. The Course of Vaccinations

Hepatitis B vaccinations (V1, V2 and V3) consisting of 20 micrograms per ml of surface antigen (HBsAg ) injected into the deltoid muscle of the left arm were administered by a qualified state registered nurse at times zero (T0), one (T1) and six (T3) months (see Table Four below ). Before each injection was administered, the vials of vaccine were checked to ensure that they were of the same make (Engerix B) and batch number and each vial was shaken before use as advised in the instructions.

**Table Four:** 'Study Design in Diagrammatic Form'

| Points in time (T) | T0<br>0 months | T1<br>1 month | T 2<br>3½ months | T3<br>6 months | T4<br>7 months |
|---|---|---|---|---|---|
| Course of vaccinations (v) | V1 | V 2 | / | V3 | / |
| Psychological Assessment Booklets (A) | A1 | A 2 | A3 | A 4 | / |
| Blood Test (blood titre) levels (B) | / | / | / | / | B1 |

## 5. The Timing of Psychological Assessment Booklets

a) The dates and times for the administration of the psychological assessment booklets ( A1, A2, A3 and A4 ) were as far as possible arranged to coincide with the times of the vaccinations. This was not possible on every occasion however, since there were four assessment booklets and only three vaccinations to be administered over the six month duration of the study. Therefore, a separate time for the administration of booklet three (A3) had to be arranged.

b) Immediately after the vaccination (V1) was administered at the commencement of the study (T0), assessment booklet one (A1) was given to the subject to complete. This procedure was repeated at T1 and T3. The procedure at T2 was slightly different in that only the assessment booklet (A3) was given at this time. T2 was as far as possible placed midway between T1 and T3 in terms of timing, to ensure that the time-sampling technique used would be 'representative' of the whole six month time span of the study (if T2 had not been included there would have been a five month period during which no psychological assessment was

being applied and this of course would have been unacceptable).

c) Timing of Psychological Assessments - it was not appropriate to administer all the assessments on each occasion. Some measures were assessed as being more stable over time, for example, 'trait' rather than 'state' measures such as the JAS Type A personality measure (test-retest reliability between 0.60 and 0.70 over intervals of up to four years), the DAS (test-retest reliability of 0.84), the SEI (test-retest reliability 0.81) and the SOCQ (test-retest reliability of 0.54 over a two year period). Other measures such as the SRRS is designed to focus on the previous six months and so it is only necessary to include it once for every six months covered. Some measures such as the MBI are clearly only appropriate after some time in employment. In conclusion, the content of each booklet was a carefully considered process, not a random one. The measures included in each of the psychological assessment booklets are listed in Table Five below and copies of each psychological assessment can be found in Appendix One.

**Table Five:** 'Timing of Assessments'
(Tick = included in Assessment Booklet)

| BOOKLET | ONE | TWO | THREE | FOUR |
|---|---|---|---|---|
| MEASURE | | | | |
| HAD | ✓ | ✓ | ✓ | ✓ |
| GHQ | ✓ | ✓ | ✓ | ✓ |
| H & U | ✓ | ✓ | ✓ | ✓ |
| SRRS | ✓ | | | ✓ |
| DAS | ✓ | | ✓ | |
| MBI | | ✓ | ✓ | ✓ |
| CFSEI | | ✓ | | ✓ |
| ATQ-R | | | ✓ | ✓ |
| SOCQ | | | ✓ | |
| JAS | | | | ✓ |
| Short Type A | | ✓ | ✓ | |

**6. Serological Testing**

a) One month after the course of vaccinations and assessments was completed, a sample of blood (B1) was taken from each subject by a qualified nurse and sent to the Microbiology laboratory at South Cleveland Hospital for serological testing.

b) A few weeks after this, the results of the blood test were sent back to the Occupational Health Department.

7. The above procedures were repeated for each new intake of student nurses between July 1992 and July 1993.

8. Sickness absence data was collected for each group one year after the commencement of the study from records available through the nursing administration department of Durham and Teesside College of Health.

9. Information relating to any history of psychological or psychiatric problems, the results of pre-employment screening medicals, results of hepatitis B titre levels, rubella sensitivity testing, other physical measures required (e.g. body mass index) and biographical data (e.g. date of birth, age, sex, marital status) were available/ retrievable from the medical casenotes stored in the Occupational Health Department.

10. The assessment booklets were scored and the raw data obtained from the psychological measures used, together with the measures of behavioural change, results of serological tests for hepatitis B titre levels and rubella sensitivity, sickness absence and other relevant physiological measures were coded for computer analysis.

**Statistical Analyses**

The following statistical analyses were carried out using the SPSS.PC for Windows 3.1 statistical package:-

1. Frequencies and descriptive statistics to establish the normality of the distributions of data.

2. Correlations of all variables to identify the set of dependent and independent variables which are significantly correlated using Pearson's correlation coefficient critical significance level of 0.05.

3. Chi square on all frequency data

4. Independent samples two tailed T-tests on the dependent variables using the median split method of assigning to groups conducted on a set of independent variables using 0.05 as the critical significance level.

5. Stepwise multiple linear regression analysis to:-

   a) develop equations that summarise the relationship between the dependent variables (titres and sickness) and a set of personal and environmental variables.

   b) to assign relative importance to each independent variable and identify those which best predict the occurrence of psychological distress, antibody titre levels and sickness absence. An alpha of 0.05 was established as the critical level of statistical significance for this purpose, although it was recognised that some authors (e.g. Tabachnick and Fidell 1989) have suggested a less stringent level of an alpha of 0.1 for model testing.

6. Further statistical analyses as considered appropriate.

# RESULTS

## SUBJECT RESPONSE RATE

A total of 71 student nurses were recruited over a one year period. Of these, 61 (86%) met the eligibility criteria outlined in the method section of this study. All G1 subjects gave their informed consent in writing to participate in the study (100%). Of those entering the study, 54 (88.5%) completed all four questionnaire booklets and provided a blood sample at the end of the study for laboratory analysis. There was a relatively small dropout rate of 7 subjects (11.5%).

**Table Six: SUBJECT CHARACTERISTICS**

| | |
|---|---|
| SEX | 47 female (87%); 7 male (13%) |
| AGE | Average age of females 23 years<br>Average age of males 24 years<br>Overall mean age 23 years<br>Age range 18-41 years |
| MARITAL STATUS | 41 single (76%); 11 married (20%)<br>2 separated or divorced (4%) |
| HISTORY OF MENTAL HEALTH PROBLEMS | 53 had no history (98%)<br>1 had been treated for mild depression following a bereavement (2%) |
| CURRENT PHYSICAL HEALTH | 100% of subjects had passed a pre-employment Medical in the two weeks prior to the commencement of the study |
| WEIGHT | 100% of subjects had a body mass index (BMI) within the normal range (within + 25% of ideal BMI) |
| TYPE OF TRAINING | 38 were doing Registered General Nursing (RGN) Training (70%); 16 were doing Registered Mental Nursing (RMN) Training (30%) |

## DESCRIPTIVE STATISTICS

The data obtained were checked using the 'frequencies' subcommand of the SPSS.PC statistics package to establish how many cases fell into the various categories and checking for any missing data. The data were then analysed to establish whether or not they approximated a normal distribution before doing any further analyses. This was done by visually presenting the distribution of scores in the form of normal p-p plots (see Appendix Four).

The results obtained from the descriptive statistics indicated that the scores approximated a normal distribution. Sample size used in the study (N=54) exceeded the minimum number derived from a power analysis equation (i.e. N=51); see Appendix Five) required to make the statistical analyses meaningful (P. Narins 1994).

One extreme 'outlier' was identified in the sickness absence variable (>+3 standard deviations above the mean). This particular case had a total of 125 days sickness absence over the first year compared to a mean of 5.1 (S.D. 5.8) days. If this case had been included in the analyses it would have undoubtedly have confounded the results obtained. Consequently, it was deleted from the analyses (i.e. N=53 for sickness absence). The validity of deleting outlying cases can be enhanced if one can convincingly argue that the outlying case was not a member of the population under study to begin with (Tabachnick and Fidell 1989). This particular subject had been on long term sick as a consequence of an operation for a dislocated kneecap sustained in an accident. Thus, it was considered valid to exclude this case from the analyses.

**Table Seven:** **COMPARISON OF MEAN SCORES ON PSYCHOSOCIAL VARIABLES WITH NORMATIVE DATA**

( Overall means of repeated measures )

| VARIABLE | PRESENT STUDY | NORMATIVE COMPARISON |
|---|---|---|
| Automatic Thoughts Questionnaire - Revised | 0.69 +ve to 0.31 -ve | = NORMAL RANGE<br>0.62 +ve to 0.38 -ve<br>Kendall et al (1989) |
| Daily Hassels and Uplifts (Hassles Subscale) | Number = 18.39 (SD 9.49)<br>Seventy = 1.47 9SD 0.37) | = NORMAL RANGE<br>Number = 12.45 (SD 7.66)<br>Seventy = 1.34 (SD 0.26)<br>Lazarus & Folkman (1989) |
| Hospital Anxiety and Depression Scale Anxiety Subscale | 5.81 (SD 2.80) | = NOT CLINICALLY ANXIOUS |
| Hospital Anxiety and Depression Subscale | 1.97 (SD 1.77) | = NON-DEPRESSED<br>Zigmond & Snaith (1983) |
| General Health Questionnaire | 2.24 (SD 2.94) | = NORMAL<br>(cut off point > 5)<br>Goldberg & Williams (1988) |
| Maslach Burnout Inventory:- | | Normative data for health workers:- |
| Depersonalisation Subscale | 2.76 (SD 2.97) | <5 = LOW |
| Emotional Exhaustion Subscale | 10.30 (SD 7.03) | <18 = LOW |
| Personal Accomplishment Subscale | 35.50 (SD 7.83) | 34-39 = AVERAGE<br>overall profile = low<br>Maslach & Jackson (1981) |
| Culture Free Self-esteem Inventory:- | | |
| General self-esteem | 13.18 (SD 2.84) | = HIGH |
| Personal self-esteem | 05.18 (SD 2.07) | = AVERAGE |
| Social self-esteem | 07.06 (SD 0.77) | = HIGH |
| Total self-esteem | 25.40 (SD 5.01) | =AVERAGE |
| Lie-defensiveness scale | 05.95 (SD 1.44) | = NORMAL<br>Battle (1980a) |

| VARIABLE | PRESENT STUDY | NORMATIVE COMPARISON |
|---|---|---|
| Social readjustment Rating Scale - life change units: | | |
| a) In 6 months prior to study Taken at Time 0 | 184.57 (SD 95.99) | = MILD (150-199)Increased likelihood of illness by 40% |
| b) Over 6 months of the study Taken at Time 3 | 232.57 (SD 127.78) | = MODERATE (200-299) Increased likelihood by 50% Holmes & Rage (1967) |
| Dysfunctional Attitudes Scales | 107.54 (SD 22.59) | = NORMAL RANGE 119.4 (SD 27.2) Weissman (1979) |
| Sense of Coherence Questionnaire (total) | 141.37 (22.59) | = NORMAL RANGE 148.63 (SD 17.5) Antonovsky (1987) |
| Jenkins Activity Schedule - Type A measure: | | Converted to percentile ranks (Normal range = 25-75 ile) |
| a) Broad Type A | 30th % ile | = NORMAL RANGE |
| b) Hard Driving & Competitiveness Subscale | 18th % ile | = LOW |
| c) Speed and Impatience subscale | 24th % ile | = LOW |
| d) Job Involvement | 49th % ile | = NORMAL RANGE Jenkins et al (1979) |

Some variables were also excluded from the analysis, since the data obtained was not suitable for statistical analyses. These included the data on rubella sensitivity tests, where 100% of subjects showed a rubella +ve response and smoking where 46 subjects (85%) were non-smokers.

## RESULTS OF THE ANALYSES OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STRESSORS, THE IMMUNE RESPONSE AND SICKNESS ABSENCE

The results are presented in three sections relating to the two independent variables (antibody titres and sickness absence) and other relevant findings:-

### 1. ANTIBODY TITRES

### ANTIBODY TITRES AND MEASURES OF EMOTIONAL DISTRESS:-

#### a) DEPRESSION

**Correlations:-**

The most commonly used measure of a linear (straight line) association between two variables is Pearson's Product Moment Correlation Coefficient (R). In the present study Pearson's 'R' indicated a statistically significant ($p<0.05$) negative correlation between depression at the commencement of the study (Time 0) and blood antibody titre levels ($R = -.31$, $p = 0.023$, $N = 54$).

**Independent Samples Two tailed T-test:-**

The results of an independent samples two-tailed T-test showed that the 'high' depression group (mean = 3.4) at Time 0 (at the commencement of the study) had significantly lower antibody titre levels (mean = 510) than the 'low' depression group (mean = 0.8) with mean titre levels of 757, using the median split method ($t = 2.52$, $p = 0.015$, $df = 52$). Levine's test for equality of variances indicated that the variances of the two groups were equal.

**Factorial Analysis of Variance:-**

A simple between subjects factorial analysis of variance was conducted using antibody titre level as the dependent variable and depression (at Time 0) and emotional exhaustion (at Time 1) as the factors. The results of this analysis indicated that there was an interaction between depression and emotional exhaustion ($F = 4.50$, $p = 0.039$, $df = 1,53$)

**comparison of means**

| Emotional Exhaustion (at Time 1) | Depression (time 0) Low | Depression (time 0) High |
|---|---|---|
| Low | 723.6 | 712.3 |
| High | 778.1 | 414.1 |

**Planned Comparisons**

When a difference between groups has been found, one usually wants to get some idea about where those differences lie. Where an "a priori" hypothesis has not been made an unplanned, or 'post-hoc' comparison would need to be carried out to find out which combination of means are different from each other. Post hoc comparisons such as the Scheffe or Bonferroni are commonly used. However, in the present study a priori hypotheses have been made which predict explicitly where the differences will lie. For such planned comparisons, less conservative comparisons such as the least significant difference (LSD) comparison can be used. The LSD test uses t-tests to perform all the pairwise comparisons between group means.

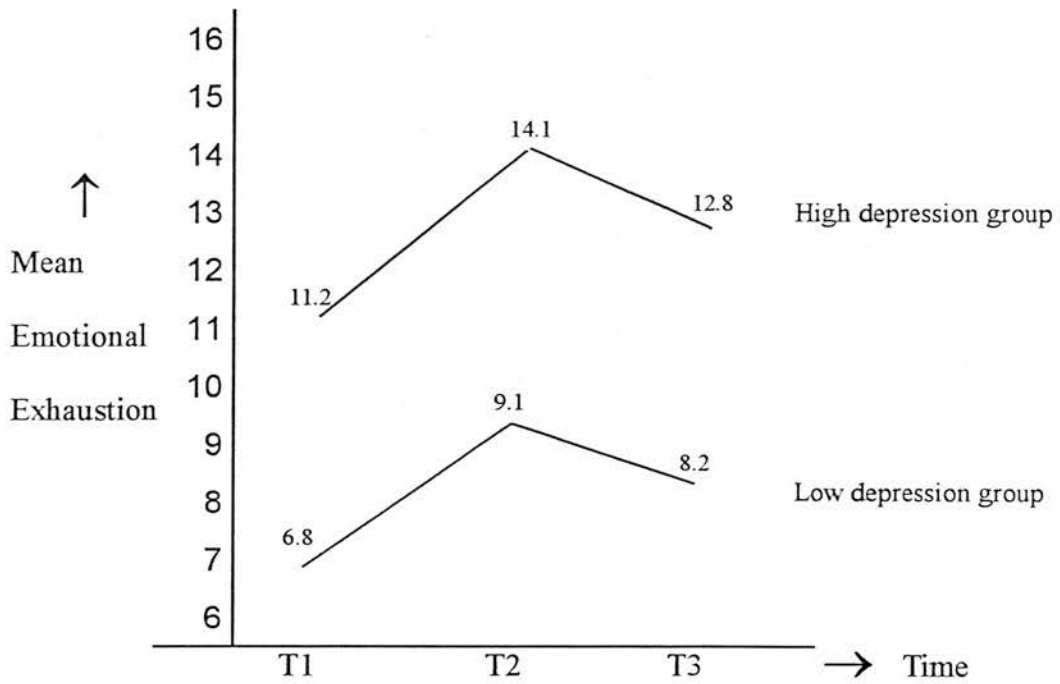
In the present study an LSD test showed specifically that there was a significant difference between the high depression/high emotional exhaustion and the low depression/high emotional exhaustion conditions ($p < 0.05$).

Repeated Measures Analysis of Variance

When there are more than two variables to be compared from the same

case and the data are normally distributed or the sample size is large, it is appropriate to use a repeated measures analysis of variance. Thus, in the present study it was possible to compare the same subjects scores at different points in time using the repeated measures design. In some factorial analysis of variance one or more IV's may be measured between subjects, while one or more IV's are measured within subjects. These are known as mixed between - within subjects analyses of variance, otherwise known as a repeated measures analysis of variance.

In the present study depression (at time O) was measured between subjects and emotional exhaustion was measured within subjects. The results indicated a significant difference between the high v low depression groups and emotional exhaustion ($F = 6.49$; $P = 0.014$; $df = 1, 52$).




b) **SOMATIC SYMPTOMS**

Using Pearson's Product Moment Correlation Coefficient (R) a significant positive correlation was found between somatic symptoms of stress (as measured by subscale A of the GHQ 28) at the commencement of the study (time O) and blood antibody titre levels ($R = +.28$; $p = 0.038$, $N=54$).

The results of a two-tailed T-test showed that the group 'high' on somatic

symptoms (mean = 2.7) of stress at time 0 (using the median split method) had significantly higher antibody titre levels (mean = 816) than the group low (mean = 0.0) on somatic symptoms with a titre level of 581 ($t = 2.33$; $p=0.027$; $df = 27$) Levine's test for equality of variances indicated that the variances between the two groups were not equal, so the t value under the separate variances estimate was used.

The results of a simple factorial design analysis of variance indicated that there was an interaction between anxiety and somatic symptoms at time 0. ($F = 4.84$; $p = 0.033$; $df = 1,53$).

**comparison of means**

| | | Somatic Symptoms (at Time 0) | |
|---|---|---|---|
| | | Low | High |
| Anxiety (time 0) | Low | 669.9 | 565.5 |
| | High | 456.8 | 927.9 |

A least significant difference (LSD) test showed specifically that there was a significant difference between the high somatic/high anxiety and the low somatic/ high anxiety conditions ($p < 0.05$).

## c) PERSONALITY AND COPING STYLE

The results of a simple factorial design analysis of variance indicated that there was an interaction between personality type and the manageability subscale of the SOCQ ($F = 4.79$; $p = 0.033$; $df = 1,53$).

comparison of means

| Manageability Subscale(SOCQ) | Type A (Broad Measure) Low | Type A (Broad Measure) High |
|---|---|---|
| Low | 458.3 | 805.1 |
| High | 665.6 | 574.8 |

An LSD test showed specifically that there was a significant difference between the high type A/low manageability and the low type A/low manageability conditions ($p < 0.05$)

## VARIABLES PREDICTING TITRE LEVELS:-

### Multiple Regression Analysis

A procedure known as multiple regression analysis was used. This statistical technique allows one to assess the relationship between one dependent variable (DV) and several independent variables (IV's). In the present study hepatitis B blood antibody levels formed the DV (i.e. outcome variable) and those variables already documented in the results section as being significantly associated with antibody titre levels formed the IV's (i.e. predictor or causal variables). The aim of this regression analysis was to find an equation which represents the best prediction of the dependent variable (titre levels) from the several independent variables.

There are three major types of regression, namely standard, hierarchical and statistical regression. There are three versions of statistical regression namely forward selection, backward selection and stepwise regression (which is a compromise of the first two procedures). Standard and hierarchical regression are useful for model testing, whereas stepwise regression is most useful for model building and eliminating variables that are clearly superfluous in order to tighten up future research. Generally, stepwise regression is considered a controversial procedure, since the order of entry of variables is based solely upon statistical criteria, rather than logical or theoretical considerations and the meaning or interpretation of variables is not taken into account (Tabachnick and Fidell 1989).

In the present study it was decided to use the stepwise regression procedure in preference to other types of regression analysis, on the basis that the aim of this analysis was to build a model which is best able to predict antibody titre levels and ultimately establish if this model complies with the hypotheses outlined in the introductory section of this study, relating to the logic of causal order (Davis 1985).

It was first necessary to test whether the multiple regression model was appropriate to use with the data. To establish this, a check for the violation of the assumptions of linearity, homogeneity of variance and normality was conducted. Examination of the normal p-p plots of residuals demonstrated that these assumptions were met (see Appendix Four).

In order to include some of the independent variables in the regression equation, it was necessary to adjust for the known interaction effects already reported in this results section. (An interaction effect exists when the effects of one variable are influenced by scores on another variable). One way to adjust for interaction effects is to change the two or more independent variables that are interacting with each other into a 'composite' of these variables and to include this in the equation as a new independent variable, as well as its individual components (i.e. the original independent variables before the new composite one was created). If the beta coefficient is significant, then this indicates that its variables have a combined effect as well as their separate effects. This new variable is created by multiplying the two or more interacting variables together (Hedderson 1987; Tabachnick and Fidell 1989).

In the present study the results of the simple factorial design analysis of variance has demonstrated interactions between personality and manageability; anxiety and somatic symptoms of stress; depression and emotional exhaustion. These three pairs of interacting independent variables were thus changed into three new composite variables using the multiplication method described above and given new names which appropriately described the interation.. Thus:-

$$*\text{Personality} \times \frac{1}{\text{manageability}} = \text{psychological vulnerability}$$

$$\text{Anxiety} \times \text{emotional exhaustion} = \text{hyper-reactivity}$$

$$\text{Depression} \times \text{emotional exhaustion} = \text{hypo-reactivity}$$

The three new composite variables above were included in the stepwise

regression analysis, as well as the original individual components.

*Note: The inverse (i.e. $\frac{1}{\text{manageability}}$) was multiplied by personality to form the new composite variable 'psychological vulnerability', since multiplying a positive and a negative score without doing this would neutralise the effects of any interaction.

The following results were obtained using the stepwise multiple regression procedure:-

| Independent Variable | B | SE(B) | β | t | p |
|---|---|---|---|---|---|
| Hyper-reactivity | 9.78 | 3.71 | 0.311 | 2.64 | ** |
| Hypo-reactivity | -7.68 | 1.98 | -0.543 | -3.89 | *** |
| Manageability | -15.31 | 6.28 | -0.341 | -2.44 | ** |

* = sig. at 0.05 level of significance

** = sig. at 0.01 level of significance

*** = sig. at 0.001 level of significance

$R^2 = .551$ Adjusted $R^2 = .261$ $F = 7.25$ **p = 0.0004**

The results of the stepwise procedure indicate that the composite variables 'hyper-reactivity' and 'hypo-reactivity' and the individual variable of 'manageability' have an additive effect in predicting antibody titre levels. Jointly, the three variables account for 26% of the variance in titre level scores. Independently, hypo-reactivity appears to be the key mediating variable accounting for 11% of the variance, with hyper-reactivity accounting for 8% and manageability 7% of the variance respectively. The creation of

the composite variables from the sets of interacting independent variables improves the prediction of antibody titre levels, compared to their individual components except for the personality x manageability interaction, where manageability appears to be more predictive than the interaction of the two variables.

It is recommended when doing stepwise regression analysis to do a 'two halves' analysis. This essentially involves randomly allocating cases in the sample into two halves and doing separate analyses on each half. Only those independent variables which hold over the two analyses are included in the equation (Tabachnick and Fidell 1989). This was done for the sample in the present study and all the above variables were found to hold over both analyses (see Appendix Six).

## 2. SICKNESS ABSENCE

Sickness absences data in terms of the total number of days sickness during the six month duration of the study and over a one year period from the commencement of the study (corresponding to the six months of the study plus the six month following the completion of the study or 'follow-up period') was collected. ( Range = 0 to 26 days).

### a) SICKNESS ABSENCE AND ANTIBODY TITRE LEVELS:-

The results of a two-tailed T-test comparing high v low sickness absence groups over one year (using median split method) indicated that the 'high sickness' group (mean=9.2) had significantly lower antibody titre scores (mean = 530) than the low sickness group (mean = 0.8) with a mean titre level of 728 ($t = 1.96$, $p = 0.05$, $df = 51$) Levine's test for equality and variances indicated that the variances of the two groups were equal.

## SICKNESS ABSENCE AND EMOTIONAL DISTRESS:-

### b) ANXIETY

The results of a Pearsons Correlation Coeficient (R, indicated that sickness absence over the six months of the study was positively correlated with anxiety at Time 0 ($R = +0.32$, $p<0.05$).

The results of a two-tailed T-test comparing high v low anxiety groups at Time 0 indicated that the 'high' anxiety group at Time 0 (mean = 9.0) had significantly more sickness absence at six months (mean = 3.7days) compared to the 'low' anxiety group (mean = 3.0) with a mean of 1.1 days sickness absence ($t = -2.85$, $p = 0.08$, $df = 31.88$). Levine's test for equality of variances indicated that the variances of the two groups were not equal, so the t value under the separate variances estimate was used.

A similar finding was found after one year, where the 'high' anxiety group (mean = 9.0) at Time 0 had significantly more sickness absence (mean = 6.7 days) than the 'low' anxiety group (mean = 3.0) with a mean of 3.5 days sickness absence ($t = -2.04$, $p = 0.046$, $df = 41.01$). Levine's test for equality of variances indicated that the variances of these two groups were not equal, so the t value under the separate variances estimate was used.

c) EMOTIONAL EXHAUSTION

The results of a Pearson's 'R' indicated that sickness absence was correlated positively with emotional exhaustion at Time 1, at both six months ($R = +0.33$, $p<.05$, $N = 54$) and one year ($R = + 0.28$, $p < 0.05$, $N = 54$).

The results of an independent samples two-tailed T-test comparing 'high' (mean = 13.7) and 'low' (mean = 5.0) emotional exhaustion groups at Time 1, indicated that the high emotional exhaustion group had significantly more sickness absence (mean =6.9 days) after one year than the low emotional exhaustion group with a mean of 3.6 days sickness absence ($t = -2.02$, $p = 0.05$, $df = 35.33$). Levine's test for equality of variances indicated that the variances of the two groups were not equal, so the t value under the separate variances estimate was used.

**VARIABLES PREDICTING SICKNESS ABSENCE:-**

The following results were obtained using the stepwise multiple regression procedure outlined earlier in the results section.

| Independent Variable | B | SE(B) | β | t | p |
|---|---|---|---|---|---|
| Hypo-reactivity (depression at Time 0 x emotional exhaustion time 1) | 0.063 | 0.029 | 0.289 | 2.15 | * |

* = sig at 0.05 level of significance

$R^2 = .08$ Adjusted $R^2 = .065$ $F = 4.63$ **$p = 0.036$**

The results of the stepwise procedure indicates that the composite variable 'hypo-reactivity' predicts sickness absence after one year. This variable accounts for 6.5% of the variance in the number of days sickness absence after one year.

## 3. OTHER RELEVANT FINDINGS

### LIFE EVENTS:-

#### Life Events and Personality

The results of a Pearson Correlation Coefficient indicated that there was a statistically significant positive correlation between personality (Type A Broad Measure) and the number of life events reported over the six months prior to the commencement of the study ($R = +0.31$, $p = 0.021$, $N = 54$).

More specifically, a significant positive correlation was found between 'speed and impatience (factor's' on the Jenkins Activity Schedule) and the number of life events reported in the six months prior to the commencement of the study ($R = +0.37$, $p = 0.006$, $N = 54$).

The results of a two-tailed T-test comparing 'high' (mean = 9.5), versus 'low' (mean = 3.6) number of reported life events (in the six months prior to the commencement of the study) groups showed that the 'high' reported number of life events group were significantly higher on factor's' (speed and impatience subscale of the JAS) with a mean of 33.5 life events, than the 'low' reported number of life events group which had a mean of 16.5 life events ($t = 2.89$, $p = 0.006$, $df = 42.0$) Levine's test of equality of variances indicated that the variance of the two groups were not equal, so the t value under the separate variances estimate was used.

#### Life Events and Coping

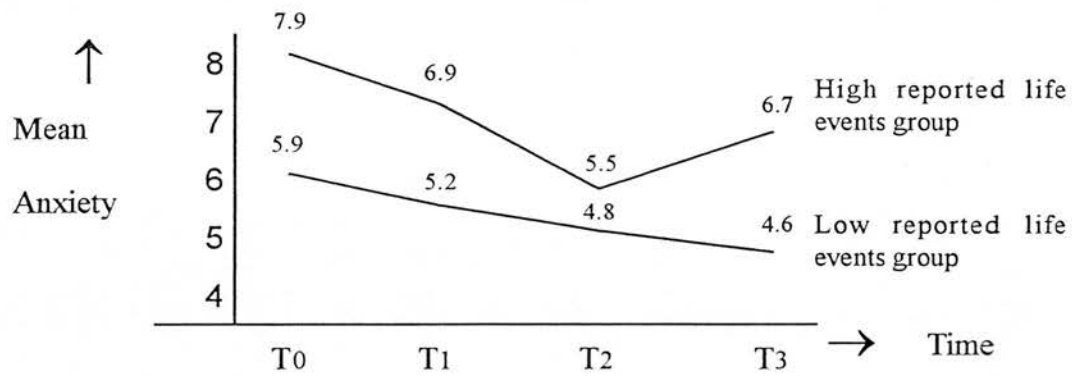
The results of a Pearson Correlation Coefficient indicated that there was a statistically significant negative correlation between the number of life events reported in the six months prior to the commencement of the study and coping style, as measured by the total sense of coherence scores ($R = -.35$, $p = 0.01$, $N = 54$).

**Life Events and Emotional Distress**

A repeated meseaures design analyses of variance indicated a significant difference between high v low reported life events groups (in the six months prior to the commencement of the study) on the following measures of emotional distress:-

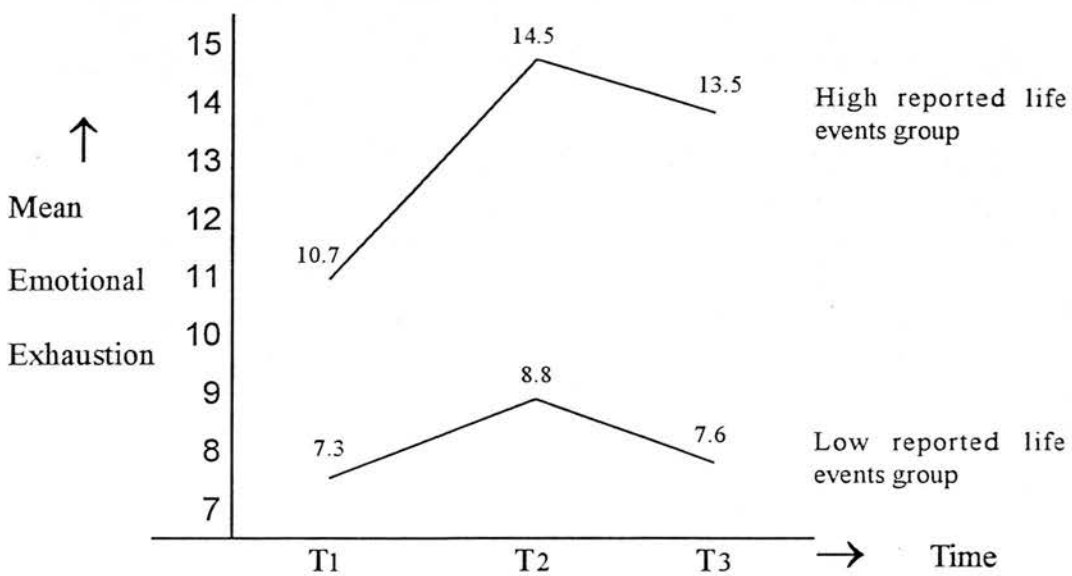
**Life events and anxiety:-**

(F = 4.67, p = 0.035, df = 1, 52)




**Life Events and Emotional Exhaustion:-**

(F = 4.32, p = 0.043, df = 1,52)



## PERSONALITY

### Personality and Coping Style:-

A significant negative correlation was found between factor 's' (speed and impatience subscale of the JAS) and the manageability subscale of the sense of coherence questionnaire (R = -0.42, p = 0.001, N = 54).

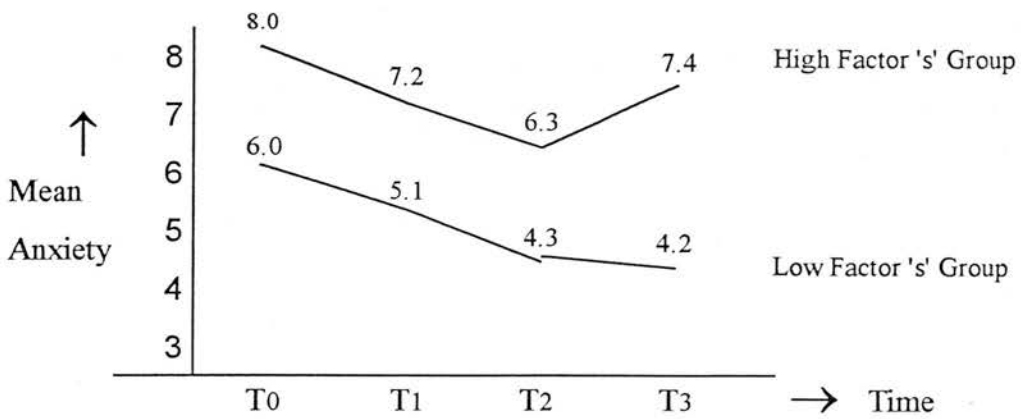
The results of a two-tailed T-test comparing 'high' (mean = 44.6), versus 'low' (mean = 8.8) factor 's' subjects using medium split method) showed that 'high' factor 's' subjects scored significantly lower on the manageability subscale (t = 3.28, p = 0.002, df = 52) and the meaningfulness subscale (t = 2.39, p = 0.02, df = 52) of the sense of Coherence Questionnaire than low factor 's' subjects. Levine's test for equality of variances indicated that the variances between the two groups were equal.

### Personality and Measures of Emotional Distress:-

A significant between groups difference was found on a repeated measures analysis of variance when high v low factor 's' (speed and impatience subscale of the JAS) were compared on the following measures of emotional distress:-

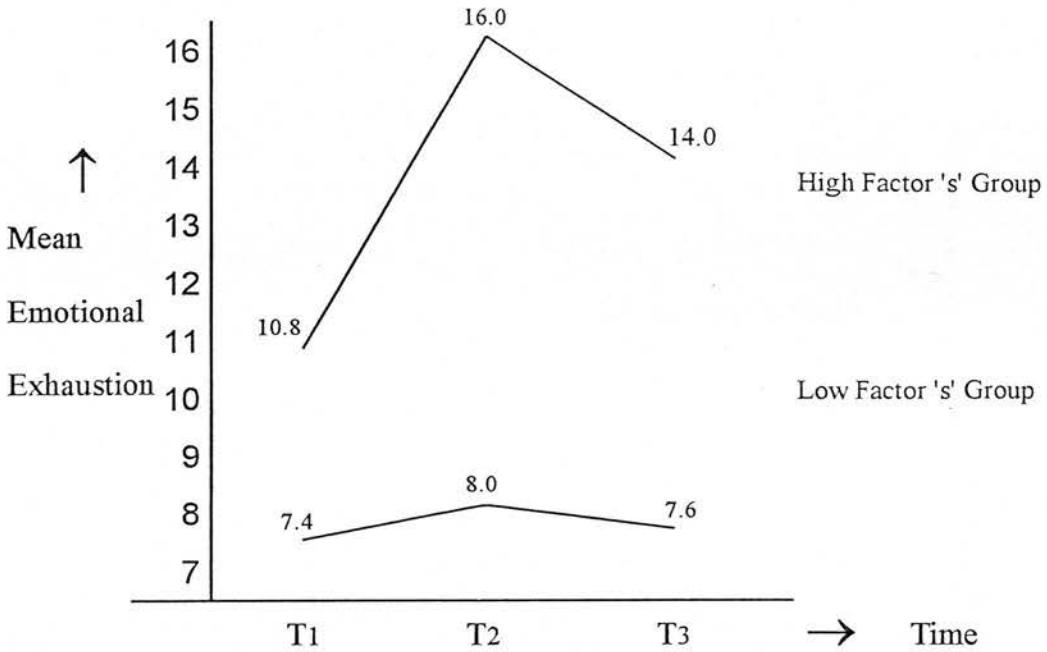
**Personality and anxiety**

(F = 10.40, p = 0.002, Df = 1, 52)



**Personality and Emotional Exhaustion**

(F = 11.14, p = 0.002, df = 1, 52)




**COPING STYLE**

Correlation matrix of Coping Style by measures of emotional distress:- (N = 54)

| VARIABLES | Anxiety (Time 0) | Emotional Exhaustion (Time 1) |
|---|---|---|
| SOCQ TOTAL | r = - 0.63 (p < 0.001) | r = -0.61 (p < 0.001) |
| Manageability subscale | r = 0.57 (p < 0.001) | r = -0.59 (p < 0.001) |
| Meaningfulness Subscale | r = 0.58 (p < 0.001) | r = - 0.53 (p < 0.001) |
| Comprehensibility Subscale | r = 0.56 (p < 0.001) | r = -0.51 (p < 0.001) |

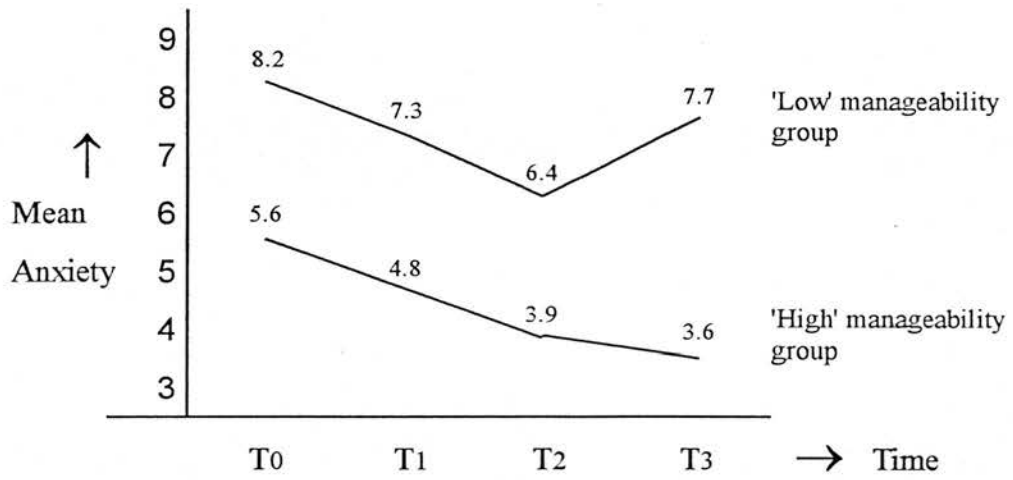
Briefly summarised the table indicates that both measures of emotional distress (anxiety and emotional exhaustion) have a high negative correlation with all the subscales of the sense of Coherence Questionnaire and with the overall measure of Sense of Coherence. Put more specifically poorer coping (low sense of coherence) is significantly associated with high distress levels.

Manageability and Emotional Distress:-

Repeated measures analyses of variance showed significant between groups differences when comparing high v low manageability groups (median split method) and the following measures of emotional distress:-

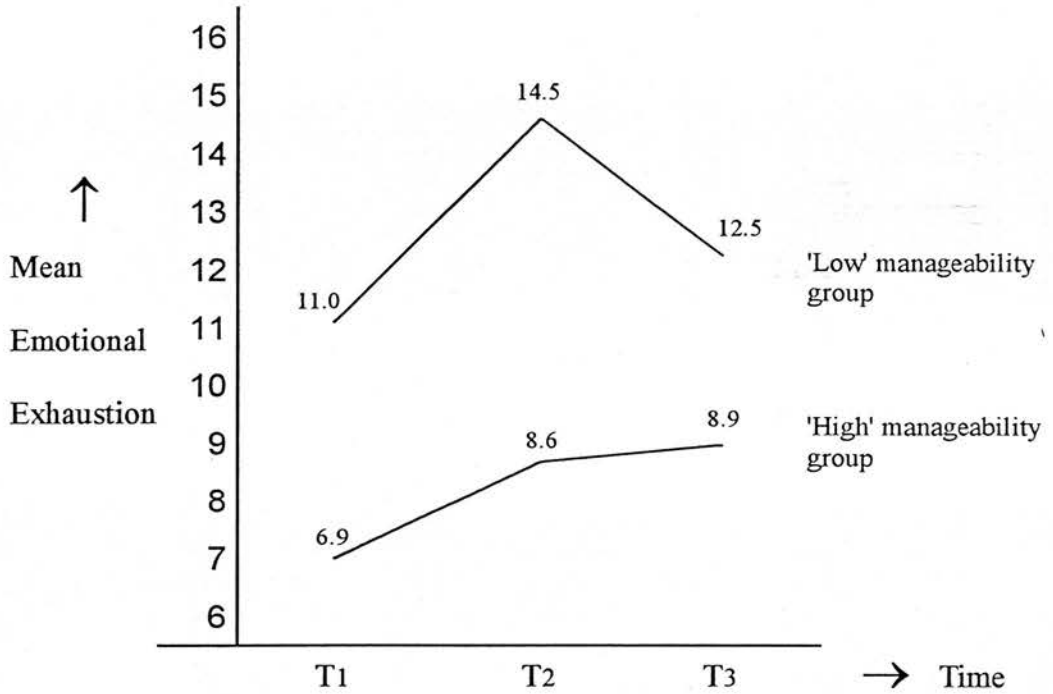
Manageability and anxiety

($F = 18.96$, $p = 0.000$, $df = 1, 52$)



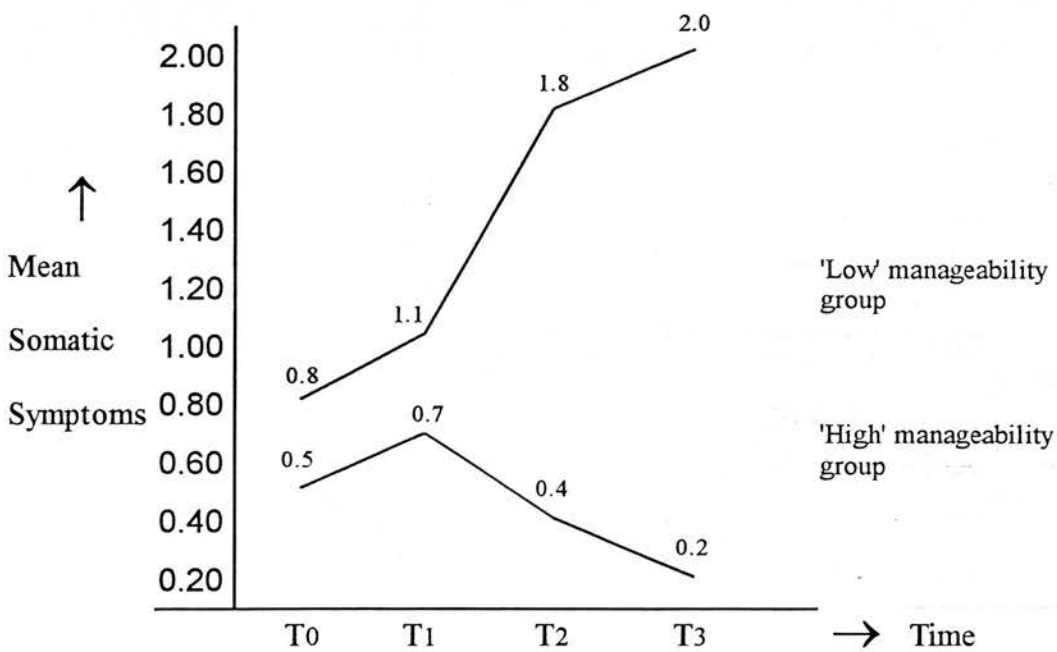
Manageability and Emotional Exhaustion

(F = 5.89, p = 0.019; df = 1, 52)



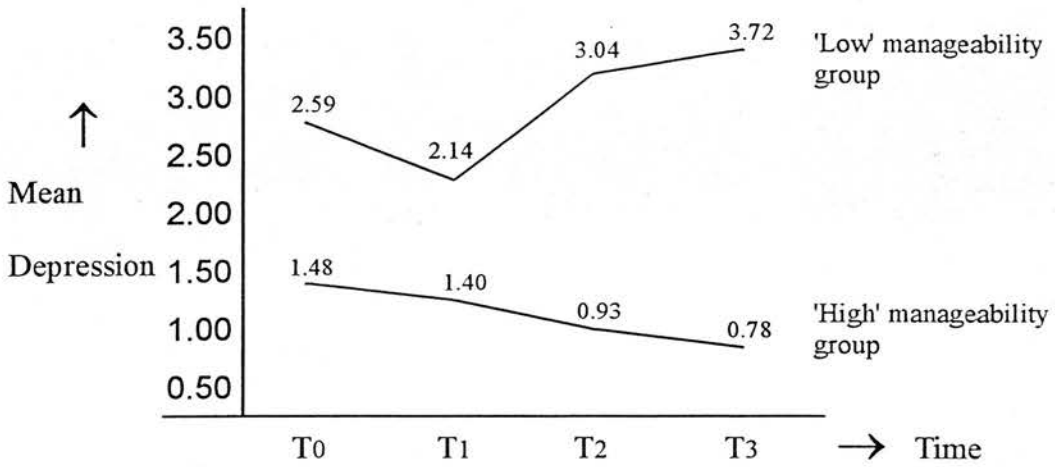

Manageability and Somatic Symptoms

(F = 11.25, p = 0.001, df = 1, 52)



Manageability and Depression

(F = 14.03, p = 0.000, df = 1, 52)



# DISCUSSION

## RESPONSE RATE

88.5% (N = 54) of the subjects entering the study completed all parts of it. This was considered an exceptionally high response rate when compared to some other questionnaire surveys carried out amongst nursing staff (e.g. Everest, Richards and Hanrahan 1979; Bergmann et al 1977). The good response rate was achieved by nurturing the support and fully informed consent of not only the Medical Ethics Committee but also the nurse tutors and students from the very outset of the study, through presentations of the research protocol and discussions with all groups involved in the study. The tutors in the school of nursing made time available within the nurses' study blocks to carry out the research, thus ensuring that all the subjects were 'on site' at the same time. It was possible to monitor the whereabouts of any subject at any time through the student nurse allocations officer. Also, it is a compulsory condition of employment in the National Health Service, that any employee having direct contact with patients must have a course of Hepatitis B vaccinations. Dropouts from the study were through failure to complete the psychological questionnaire booklets rather than not being vaccinated, (except for one subject who became pregnant and consequently stopped the course of vaccination).

## SUBJECT CHARACTERISTICS

From the subject characteristics reported in the results section, variations in antibody titre scores due to physiological variables were minimised. No statistically significant differences in titre scores were found on the variables of age (range 18-41 years), sex (81% female), physical fitness (all had passed a pre-employment medical on the two weeks prior to commencing employment) obesity (all within 25% of ideal Body Mass Index), measures of behavioural change (i.e. diet, activity levels, exercise or sleep pattern) or circadian variations (testing carried out at a similar time of day for all subjects).

With respect to psychosocial variables, none of the subjects had any history of psychiatric illness, none had experienced a change in marital status (76% single), all had commenced new employment (nurse training), a homogenous socio-economic group

## SUMMARY TABLE OF HYPOTHESES AND RESULTS

**Hypothesis One: "Life Events are neutral"**
***Results obtained that support this hypothesis:***

Results indicate that relationship between emotional distress and life events is moderated by personality and coping factors (see hypotheses two and three below).

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**Hypothesis Two: "Personality is a moderating factor between life events and emotional distress"**
***Results obtained that support this hypothesis:***

1. Pearson Correlation Coefficient - positive correlation between Type A (broad measure) personality and number of life events supported in six months prior to commencement of the study ($R = +0.31$, $p = 0.02$, $N = 54$).

2. Pearson 'R' indicates a positive correlation between 'factor S' (Jenkins Activity Schedule) and number of life events reported in six months prior to commencement of the study ($R = +0.37$, $p = 0.006$, $N = 54$.)

3. Independent Samples two-tailed T-test indicated high number of life events group (over six months prior to commencement of study) were significantly higher on 'factor S' than low number of life events group ($t = 2.89$, $p = 0.006$, $df = 42.0$).

4. Repeated measures analysis of variance indicated that the high 'factor S' group had significantly higher levels of anxiety ($F = 10.40$, $p = 0.002$, $df = 1,52$) and emotional exhaustion ($F = 18.96$, $p = 0.001$, $df = 1,52$) than the low 'factor S' group.

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**Hypothesis Three: "Coping style is a moderating factor between life events and emotional distress"**
***Results obtained that support this hypothesis:***

1. Poor coping (as a trait measured by the sense of coherence scale total score) showed a significant negative correlation with the number of life events reported in the six months prior to the commencement of the study ($R = -0..35$, $p = 0.01$, $N = 54$)

2. Sense of coherence total score) showed significant negative correlation with anxiety at Time O ($R = +0.63$, $p = <0.001$, $N = 54$) and emotional exhaustion at Time 1 ($R = -0.61$, $p = <0.001$, $N = 54$).

3. Repeated measures analysis of variance indicated the low manageability (sense of coherence subscale) group was associated with significantly higher emotional exhaustion ($F = 5.89$, $p = 0.019$, $df = 1,52$) somatic symptoms ($F = 11.25$, $p = 0.001$, $df = 1,52$), anxiety ($F = 18.96$, $p = 0.001$, $df = 1,52$) and depression ($F = 14.03$, $p = 0.001$, $df = 1,52$)

**<u>Hypothesis Four</u>: "Personality and Coping factors work in an interactive way"**
***Results obtained that support this hypothesis:***

1. Significant negative correlation between 'factor S' (speed and impotence subscale of the Jenkins Activity Scale) and manageability subscale of sense of coherence questionnaire
(R = -0.42, p = 0.001, N = 54).

2. Independent two-tailed T-test indicated that high 'factor S' group scored significantly lower on the manageability subscale of sense of coherence questionnaire
(t = 2.39, p = 0.02, df = 52)

3. A simple factorial design analysis of variance indicated there was an interaction between personality Type and the manageability subscale of the sense of coherence questionnaire and raised antibody titre levels (F = 4.78, p = 0.033, df = 1,53). An LSD test showed specifically that there was significant difference between the high Type A/low manageability and the low Type A/low manageability conditions ($p < 0.05$)

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**<u>Hypothesis Five</u>: "Emotional Distress is the mediating variable through which life events, personality and coping influence the immune system"**
***Results obtained that support this hypothesis:***

1. A Correlation indicated that there was a significant negative association between depression at Time O and antibody titre levels (R = -.0.31, p = 0.023, N = 54)

2. A positive correlation was found between somatic symptoms of stress (subscale of the GHQ) at time O and antibody titre levels
(R = +0.28, p = 0.038, N = 54).

3. An Independent Samples two-tailed T-test showed that the high depression group (time O) had significantly lower antibody levels than the low depression group (t = 2.52, p = 0.015, df = 52).

4. An Independent Samples two-tailed T-test showed that the high somatic symptoms group at time 0 had significantly higher titre levels than the low somatic symptoms group (t = 2.33, p = 0.027, df = 27).

5. A simple between subjects factorial analysis of variance indicated that there was an interaction between depression (at time O) and emotional exhaustion (at Time 1) and lowered antibody levels (F = 4.50, p = 0.039, df = 1,53). An LSD test indicated a significant difference between the high depression / high emotional exhaustion and low depression / high emotional exhaustion conditions ($p<0.05$).

6. The results of a simple between subjects analysis of variance indicated that there was an interaction between anxiety and somatic symptoms (at Time O) and raised antibody levels (F - 4.84, p = 0.033, df = 1,53). An LSD test showed specifically that there was a significant difference between the high somatic / high anxiety and low somatic / high anxiety conditions ($p<0.05$).

## Hypothesis Five Continued

7. Stepwise Multiple Regression Analysis indicated that the composite variables 'hyper-reactivity' and 'hypo-reactivity' and the individual variable of 'manageability' have an additive effect in predicting antibody titre levels. Jointly they account for 26% of variance in titre level scores. Independently, hypo-reactivity accounts for 11%, hyper-reactivity 8% and manageability 7% of the variance respectively.

## Hypothesis Six: "Subtle psychological changes in response to every day stressors are associated with sickness behaviour"

***Results obtained that support this hypothesis:***

1. Pearson's correlation coefficient indicated a positive correlation between sickness absence over the six months of the study and anxiety at Time O ($R = +0.32$, $p<0.05$, $N = 53$) and a positive correlation with emotional exhaustion (at Time 1) at both six months ($R = +0.33$, $p< 0.05$, $N = 53$) and one year ($R = +0.28$, $p<0.05$, $N = 53$).

2. Independent samples two-tailed T-tests indicated that the high anxiety group (Time O) had significantly more sickness absence over one year than the low anxiety group ($t = 2.04$, $p = 0.046$, $df = 41.01$).

3. Independent samples two-tailed T-test comparing high and low emotional exhaustion groups (at time 1) indicated that the high emotional exhaustion group had significantly more sickness absence over one year than the low emotional exhaustion group ($t = 2.02$, $p = 0.05$, $df = 35.33$).

4. A Stepwise multiple regression analysis indicated that the composite variable 'hypo-reactivity' predicts sickness absence after one year. This variable accounts for 6.5% of the variance in the number of days sickness absence.

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## Hypothesis Seven: "There is an association between sickness behaviour and the immune response"

***Results obtained that support this hypothesis:***

1. An Independent samples two-tailed T-test comparing high and low sickness absence groups indicated that the high sickness absence group had significantly lower antibody titres than the low sickness group over one year ($t = 1.96$, $p = 0.05$, $df = 51$).

**<u>Hypothesis Eight</u>: "The results obtained will comply with the sequence of events predicted by the rules of causal logic" (Davis 1985)**
***Results obtained that support this hypothesis:***

The results obtained do comply with the predicted sequence.

(i.e. occupation and income), at the same stage in training, all had experienced shift work, started similar course work assignments and practical placements. Thus, to a large extent the variance in titre scores due to environmental variables was minimised.

The mean scores obtained on the measures of psychosocial stress (outlined in the method section of this study) were within the normal 'non-clinical' range when compared with the normative data. Thus, the subjects used in this study were representative of the normal, healthy (both mentally and physically) general population. The make-up of the subject population was representative of the student nurse population working in the National Health Service (being largely young, non-obese, physically and mentally healthy). Also, as far as possible, the variance in the titre scores due to the confounding effects of physiological, behavioural or environmental variables was minimised.

## DISCUSSION OF THE RESULTS IN RELATION TO THE AIMS AND HYPOTHESES OF THE STUDY

To recap, the areas of the present study were as follows:-

1. To carry out an empirical investigation of the relationship between psychosocial stresses and the immune response in humans, which takes into account the methodological considerations outlined in the introductory section of this study (pages 47 - 49).

2. Demonstrate that subtle psychological changes in response to every day stresses in the normal healthy population will influence the workings of the immune system and ultimately have pathological outcomes.

3. Construct a theoretical framework based upon the findings outlined in the literature search, which is also capable of explaining the results obtained in the present study.

AIM NUMBER ONE:-

An empirical investigation of the relationship between psychosocial stresses and the immune response in humans was successfully conducted. With respect to addressing the methodological considerations outlined in the introductory section (pages

(47-49), the present study was largely successful but was limited to working within existing resources and time constraints. No additional funding was made available to carry out the study and the investigator was restricted to fitting the research around a full-time job, which it was felt by the employers should take priority over the research.

a) The study was carefully designed. As far as possible it was prospective in design but it was not possible to be truly prospective within the limited resources available and as such only one blood sample was taken to measure antibody titres. The strength of this study could have been improved if three or four measures of antibody titres could have been taken over the six month period of the study but this was not possible. Also, it is unlikely that the Medical Ethics Committee of the Health Authority would have approved the study if additional invasive procedures were included in the research protocol, since it might be construed that student nurses were being used as 'human guinea pigs'.

b) The study was conducted over a longer time span than many of those outlined in the literature search. It made repeated measures of psychosocial variables over a six month period and further data on sickness absence was collected one year after the commencement of the study. In addition some retrospective data on life events in the six months prior to the study was collected. Thus, some of the data collected in the study related to an eighteen month time span.

c) The study attempted to control for the effects of a wide range of possible confounding variables. A number of physiological variables known to influence the immune response such as age, sex, obesity, physical fitness and circadian rhythms were all controlled for at the design stage. Also, environmental variables such as life changes including starting a new job, changes in supports, starting shift work, course work assignments, practical placements, as well as variables such as socio-economic status were controlled for at the design stage. Other variables such as measures of behavioural change (i.e. sleep, diet, activity levels and exercise) and personal habits such as smoking were monitored over the six months of the study and looked at during the data analysis stage of the study. No statistically significant differences in antibody titre levels between subjects were found on any of these variables.

d) The study made use of well-validated and reliable measures. A broad range of

well-known, tried and tested psychosocial measures used in mainstream psychological practice were used in this study. (A discussion of the validity and reliability of these measures is found in the method section of this study, pages 63 - 72).

The measures of immunity were also well validated and reliable. Since all subjects in this study were rubella positive it was not possible to do any further analyses using this measure. The measure of Hepatitis B antibody levels is an extremely sensitive one. The Hepatitis B vaccine is produced using the most up to date recombinant DNA technology and the measure of immune responsiveness used the enzyme linked immuno-assay technique.

e) The study attempted to clearly define concepts such as stress, stress and strain and provided overviews of the literature on stress and immunity which could be understood by those without a specific training as either a psychologist or an immunologist.

f) A broad range of psychological measures were included in the study. These were chosen in accordance with the findings of the literature search and aimed to address the complexity of the range of possible interactions involved. These included measures of environmental and personal characteristics, coping style and emotional distress and a clear rationale was given as to why these specific measures were chosen, in contrast to a number of studies in the literature review which appears to select one or two variables seemingly at random.

g) The sample size was large enough to make the study valid in a statistical sense. The largest NHS occupational group was chosen to ensure that sufficient numbers of subjects were obtained for the study and the design ensured that relatively few subjects were lost to the study. More subjects would have been desirable but this was not practically possible within the scope of this study. However, in view of the fact that a wide range of psychological measures were used and a repeated measures design was adopted, this compensated for the sample size to some degree.

AIM NUMBER TWO:-

The second aim of this study, namely to "demonstrate that subtle psychological changes in response to everyday stressors in the normal healthy population will influence the workings of the immune system and ultimately have pathological outcomes", has also been largely achieved. It has already been demonstrated in the section on 'subject characteristics' (page 78) that the population used in the study consisted of normal, healthy subjects who on all psychosocial measures scored within the normal 'non-clinical' range when compared to their respective normative reference groups. Thus in contrast to many previous studies outlined in the literature which focus on pathology and disease the present one studied normal, healthy subjects.

a) It was found that subtle psychological changes in response to everyday stressors in normal healthy subjects do indeed influence the workings of the immune system. Specifically, emotional 'states' have been demonstrated to be significantly associated with blood antibody titre levels to Hepatitis B vaccine (Hypothesis Five Supported). Furthermore, it appears from the results obtained, that different types of emotional states are associated with different effects on the immune system. All the measures of emotional distress identified as being significantly associated with the immune response to Hepatitis B vaccine were at "non-clinical" levels and yet significant relationships were still clearly detected.

The results indicated that the interaction between depressive affect (rather than depression per se, since clinical levels were not observed) and emotional exhaustion (Subscale of the Maslach Burnout Inventory) had an 'immune-suppressive' effect. The finding that there was a relationship between depressive affect and immune responsiveness was not surprising, since this is well documented in the literature on depression and immunity (for references to this see page 36). Although a repeated measures design was used, only the initial measures of depression and emotional exhaustion were significant. This suggests that the emotional state of the individual at the time of the first Hepatitis B vaccination is most predictive of the subsequent immune response.

It is hypothesised that the particular neuroendocrine mechanism underlying the above reaction is the Hypothalamic-Pituitary-Adreno-Cortical (HPAC) system described in the introduction (see page 9). This system is described as the

'conservation-withdrawal' system, is associated with chronic stress and is thought to occur when threats are perceived as overwhelming and the individual is not coping (Henry and Stephens 1977). Depression is a common feature of this response (Gibbons 1964; Gitlin and Gerner 1986). Under conditions of successful coping the HPAC system is suppressed (Levine, Weinberg and Brett 1979) but when the individual is not coping, adrenocorticotrophic hormone (ACTH) and corticosteriods (cortisol in humans) are released. Raised cortisol levels are associated with immune suppression (Henry and Stephens 1977).

Perhaps the more surprising (and less well-documented) finding from the present study was that the interaction between anxiety and somatic symptoms of stress (as measured by the General Health Questionnaire 28 item version subscale) was associated with an "immune-enhancing" effect. However, at an intuitive level, it does not seem unreasonable that a state of raised physiological arousal is accompanied by an increase in blood antibodies at least in the short term. It is hypothesised that the neuroendocrine mechanism underlying this reaction is the 'Sympathetic-Adrenal-Medullary' (SAM) system. This system is associated with acute stressful states such as fear, anger and excitement (Amkraut and Solomon 1975) and results in an increase in the levels of Catecholamines (epinephrine and norepirephrine) into the blood stream. There is evidence that increased levels of catecholamines an enhance the primary antibody response to a stressful stimulus (see pages 17-18 for references).

Similarly, as for depression and emotional exhaustion, only the initial measures of anxiety and somatic symptoms of stress taken at the time of the first Hepatitis B vaccination (i.e. the subjects' first contact with the vaccine), were associated with the immune response, providing further support for the view that it is the emotional state of the individual at the time of the first contact with the vaccine that is most predictive of the immune response.

The results of a stepwise multiple regression analysis indicated that the composite variables labelled 'hyper-reactivity' (anxiety x somatic symptoms of stress), 'hypo-reactivity' (depression x emotional exhaustion) and the 'manageability' (control) variable (subscale of the Sense of Coherence Questionnaire), were the three variables predicting antibody titre levels (jointly accounting for 26% of the variance).

The finding that "manageability", which is conceptually similar to Rotter's 'locus of Control' (1966) and Kobasa's 'hardiness' concept is associated with immune responsiveness is again consistent with the literature. Coping ability has been demonstrated to be related to the immune response, such that better coping is associated with greater immune responsiveness (Roessler et al 1979; Locke, Hurst and Heisel 1978). In the present study, low perceived control (a dimension of coping) is predictive of lowered blood antibody titre levels.

One possible way in which coping may effect the immune response is through physiological mechanisms (Elliott 1979). Where an individual appraises that a situation has potential for 'mastery' it is perceived as a "challenge" (Lazarus 1966) and an attempt is made to gain mastery over it by a process of 'dominant challenged control', which leads to activation of the SAM, raising catecholamines and immune enhancement. However, where the individual perceives they have little or no control (a state known as 'subordinate loss of control'), the HPAC System is activated, raising ACTH and cortisol levels and consequently suppressing of the immune response. The conclusion reached here is that different levels of personal control are differentially associated with catecholamine and cortisol secretion and these have differential effects on the immune system (Frankenhaeuser and Johansson 1986).

Fisher (1986) in her 'cognitive control model' (see page 45) attempts to integrate the control dimension' with the physiological mechanisms described above. In particular raised catecholamines are associated with raised anxiety (effort distress) and an increase in somatic symptoms. (These variables are the very ones identified in the present study under the composite variable 'hyper-reactivity'). With repeated failure to control a passive state of helplessness and depression develops (similar to the 'hypo-reactivity' variable identified in the present study).

Also in the present study, the interaction of personality and control was found to be associated with raised blood antibody levels. Specifically, being a Type A individual ('broad measure' subscale of the Jenkins Activity Schedule) in a situation of low perceived control (manageability) is associated with raised Hepatitis B antibody titre levels. This may at first sight appear to contradict the findings already discussed above on control and coping. However, on closer analysis the

findings remain consistent with the literature. Type A personalities appear to be motivated by an intense need to assert and maintain control over their environment (Lazarus 1971; Glass 1977, 1983; Matthews and Glass 1984; Strube and Werner 1985). Thus in Fisher's terms they experience more 'effort distress' in situations of challenged control than non-Type A individuals (Fisher 1986). Thus, raised levels of catecholamines are released and this has immuno-enhancing effects. Glass (1977) identifies this as the first stage in a two-stage model. The first one is where a Type A individual is placed in a situation of brief exposure to uncontrollable stress and is characterised by what Glass terms 'hyper-responsiveness' (a state of exaggerated physiological arousal). However, with prolonged exposure to uncontrollable events Glass describes the onset of a condition known as 'hypo-responsiveness' (a state of reduced physiological arousal, despondency and depression). This second state is similar to that described by Seligman as 'learned helplessness' (Seligman 1975). Thus, it can be seen that the findings of the present study can be readily understood if this "two stage" model is employed. The interaction of personality and control is explained within such a framework.

In conclusion, subtle psychological changes in response to everyday stressors in normal healthy subjects do influence the workings of the immune system. Some physiological mechanisms have been proposed to explain how this might take place.

b) The present study also supports the hypothesis that subtle psychological changes in response to everyday stressors in the normal population are associated with pathological outcomes (Hypothesis number six supported). Not only is the composite variable 'hypo-reactivity' (depression x emotional exhaustion) predictive of lowered blood antibody titre levels but it is also predicture of higher sickness absence over a one year period. This is also supported by the finding that higher sickness absence is associated with lower blood antibody titre levels. (Hypothesis number seven supported)

AIM NUMBER THREE:-

The third aim of the present study was to "construct a theoretical framework based upon the findings outlined in the literature search, which is also capable of explaining the results in the present study". An attempt to do so is presented in the following pages of the discussion, with further reference to the hypotheses outlined in the introduction to this study (pages 56 - 58).

a) The role of 'life events'

The results indicated that there was an association between the number of life events reported and the level of emotional distress experienced. Specifically, a higher number of reported life events was associated with higher levels of anxiety and more emotional exhaustion (on the Maslach Burnout Inventory). These associations do not necessarily indicate a direct causal relationship and the findings remain consistent with the hypotheses if it can be demonstrated that the relationship between life events and emotional distress is moderated by personality and coping factors (see hypotheses two and three below). The conclusion reached is that life events are a necessary but in isolation not sufficient to influence an individual's emotional state or the workings of the immune system (Hypothesis number one supported).

b) The role of Personality and Coping (vulnerability factors):-

The results suggest that personality factors do play a moderating role between life events and emotional distress (Hypothesis number two supported). Specifically, those scoring high on Type "A" behaviour generally and in particular those 'scoring' highly on the 'speed and impatience' subscale of the Jenkins Activity Schedule (JAS), a measure of one aspect of Type A behaviour, reported significantly more stressful life events than those low on the JAS subscale. The results also indicate that individuals scoring highly on the speed and impatience subscale of the JAS show greater physiological reactivity to stressful life events than low type A individuals. In particular they scored more highly on reported anxiety and experienced higher levels of emotional exhaustion.

These findings, that certain Type A personality characteristics are associated with both a greater number of reported life events and high levels of emotional

distress, add weight to the hypothesis that personality acts as a moderating variable between life events and emotional distress. It also explains the statistically significant association between the number of stressful life events reported and the level of emotional distress experienced (see hypothesis number one above).

The results show that those who report themselves to be poor copers report significantly more stressful life events than good copers (Hypothesis number three supported). Also, an individual's perception of coping is associated with the amount of emotional distress experienced. Specifically, those who perceive themselves to be 'poor copers' experienced significantly higher levels of anxiety, depression and emotional exhaustion than good copers.

The finding that those who perceive themselves as poor copers report a greater number of life events and higher levels of distress, supports the hypothesis that coping factors as well as personality act as a moderating variable between life events and emotional distress. In particular, those individuals who perceive themselves to have little control over stressful life events experience higher levels of anxiety, somatic symptoms emotional exhaustion and depression than those who perceive themselves to have control over life events.

Also, a significant negative association between personality and "perceived control" (manageability) over stressful life events was found. Subjects scoring highly on the 'speed and impatience' subscale of the JAS perceived themselves to have significantly less control over stressful life events than those scoring low on this subscale of the JAS.

Note: The finding that poor copers experience more distress would be tautological if one defined both as 'state' measures. However , in the context of this study, the measure of coping used (i.e. the sense of coherence questionnaire - Antonovsky 1987 ) was a relatively stable 'trait' measure.

## TOWARDS A WORKABLE MODEL OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STRESSORS AND THE IMMUNE RESPONSE:-

From the literature search presented in the introduction combined with the findings of the present study an attempt to build a testable theoretical framework has been made:-

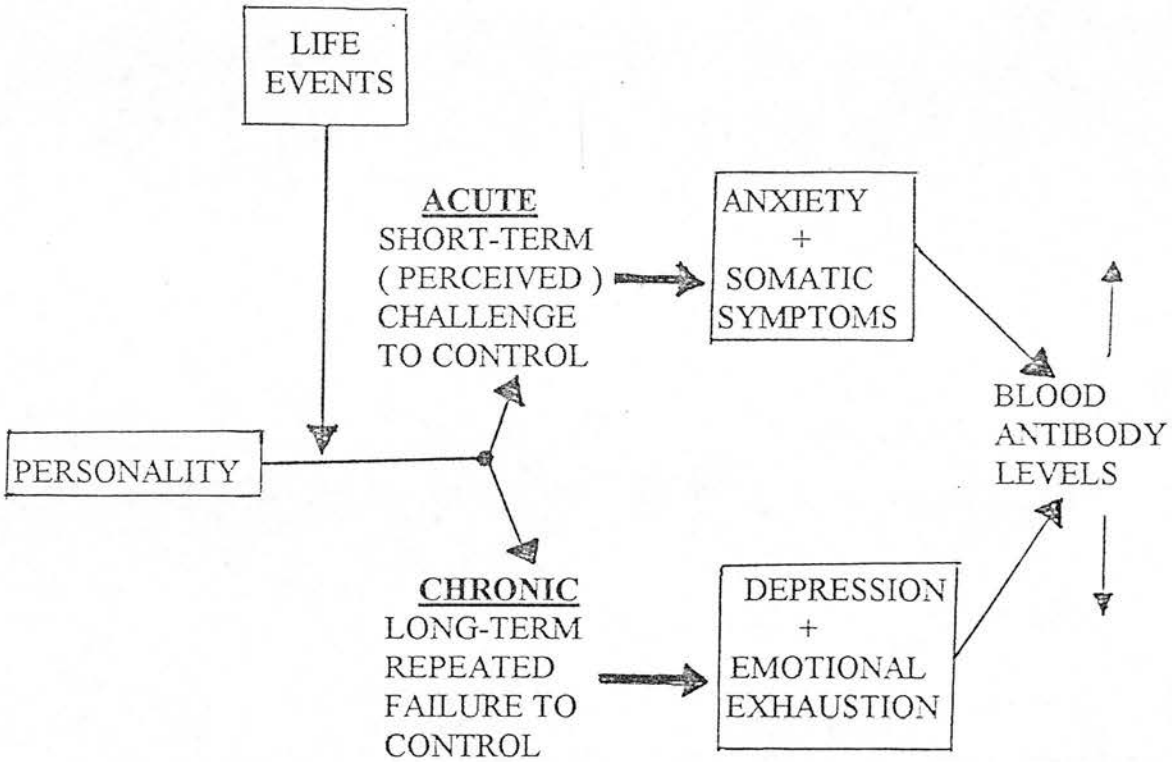
1. Type A individuals in situations of low perceived control over life events display an exaggerated physiological arousal response and commence a relentless struggle to gain/regain control. Associated with this is increased Sympathetic - Adrenal Medullary activity, with associated raised catecholamine activity and increased blood antibody levels.

2. If the individual is successful in gaining/regaining control, bodily systems return to normal.

3. An individual will continue to engage in the struggle for control as long as they perceive there is some chance of gaining/regaining control. (i.e. it is perceived as challenging).

4. The findings of the literature search, together with the present results, suggest that with repeated failure to control (or indeed in situations that are objectively uncontrollable), the Type A individual will eventually 'give up'. In so doing, they display an exaggerated state of reduced physiological arousal (compared to Type B individuals) and associated with this activation of the 'Hypothalamic-Pituitary-Adreno-Cortical system', with raised corticosteroid activity and consequently lowered blood antibody levels:-

Figure Nine: **A PROPOSED MODEL OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STRESSORS AND BLOOD ANTIBODY TITRE RESPONSE IN HUMANS**




The above model complies with the sequence of events predicted by the rules of causal logic (Davis 1985) outlined in the introduction (Hypothesis number eight supported).

Of the three previous studies found in the literature which make use of the antibody response to Hepatitis B vaccine to explore the relationship between stress and the immune response in humans (Jabaaij 1992; Glaser et al 1992; Petry et al 1991), two of the studies (Jabaaij 1992; Glaser et al 1992) demonstrated that psychosocial stress affects the immune response in a negative direction and the results of the third (Petry et al 1992) found that psychosocial stress affects the immune response in a positive direction. These apparently contradictory findings can be explained by the above model, in terms of acute and chronic reactions to psychosocial stresses.

The literature (e.g. Fisher 1986) also identifies two groups of illnesses which can be readily explained by the above model. The first group are "somatic illnesses" Fisher (1986) states that "any process which increases the persistence, frequency or intensity of arousal caused by the struggle for control is likely to increase the risk of ill-health" (page 240). She suggests that this occurs as a result of the strain being placed upon the various physiological systems of the body causing structural damage, if the struggle for control becomes prolonged or chronic. The increased risk of system malfunction via the process of 'somatisation' can lead to somatic type complaints such as raised blood pressure, damage to coronary arteries, gastric complaints, ulcers, muscular aches and pains and headaches. Fisher calls raised anxiety levels in this context 'effort distress' and associated with this in the present study is a raised level of blood antibodies.

The second group of illnesses Fisher (1986) says can occur when the individual repeatedly fails to gain control and eventually gives up the struggle for control. Fisher calls this 'distress without effort'. Whilst the first group (somatic illnesses) are associated with the Sympathetic Adrenal Medullary system, this second group is associated with the Hypothalamic-Pituitary-Adrenal-Cortical system and raised cortisol levels in humans. Raised cortisol increases the individual's susceptibility to a whole range of immuno-incompetence type illnesses such as colds, infections, viruses, skin complaints and allergies and is associated in the present study with reduced levels of blood antibodies.

# CONCLUSIONS

The Aims and Hypotheses outlined in the introduction have on the whole been supported. The following conclusions may be drawn from the results obtained:-

1. States of Emotional Distress are associated with immunological changes. Specifically the interaction of anxiety and somatic symptoms has IMMUNO-ENHANCING effects. The interaction of depressed affect and emotional exhaustion has an IMMUNO-SUPPRESSIVE effect and is also associated with more sickness absence. This is supported by the finding that higher sickness absence is associated with lower antibody levels.

2. The interaction of a Type A individual in a situation of low perceived control is associated with RAISED antibody levels, whereas low perceived control on its own is predictive of LOWERED antibody levels.

3. Life events are necessary but (on their own) not sufficient to influence an individual's emotional state or immune functioning.

4. Personality and Coping style (psychological vulnerability factors) act as moderator variables between life events and emotional distress. Specifically, an individual scoring higher on Type A behaviour is significantly more likely to report a greater number of stressful life events and experience more emotional distress in response to them, than a Type B personality. Low perceived control is also associated with a greater number of stressful life events reported and higher levels of emotional distress experienced.

In summary, the results of this study at first inspection may appear to be contradictory, in that states of emotional distress are shown to be associated with both LOWERED AND RAISED blood antibody titre levels. However, these findings can be explained by the fact that Type A individuals in situations of low perceived control exhibit different responses to acute and chronic stresses. Glass (1977) presents evidence to suggest that with brief exposure to uncontrollable stress, an acute state of 'hyper-responsiveness' is activated. However, with prolonged exposure to uncontrollable stress the individual moves into a chronic state of 'hypo-responsiveness'. The former is associated

with increased physiological arousal and the latter with decreased physiological arousal. This 'two phase' model explains 'the apparent contradiction in the results.

There is further evidence to support this explanation of the results. There are possible 'neuroendocrinal mechanisms underlying these processes (O'Leary 1990; Henry and Stephens 1977). O'Leary (1990) provides evidence to suggest that 'acute emotional states' activate the "Sympathetic - Adrenal - Medullary System", which is accompanied by the release of catecholamines (epinephrine and nonepinephrine) into the blood stream. Catacholamines act to redistribute lymphocytes out of areas of storage and into the circulating blood stream. Thus, a state of acute physiological arousal can be associated with increased blood antibody levels.

With prolonged exposure to objectively uncontrollable stress Type A's reach a state of 'hypo-responsiveness' (Glass 1977). Henry and Stephens (1977) suggest a possible neuroendocrinal mechanism for this process. When stressors are appraised as 'overwhelming', as for Type A individuals who have repeatedly failed to control the situation, Sympathetic Adrenal Medullary System activity ceases and the "Hypothalamic - Pituitary - Adrenocortical - System" is activated (sometimes known as the 'conservation - withdrawal system). Activation of this system often accompanies chronic stress as well as clinical depression (Gibbons 1964; Gitlin and Gerner 1986). As a consequence adrenocortico-trophic hormone (ACTH) and corticosteroids (cortisol in humans) are released. Cortisol has a primarily 'immuno-suppressive' effect, resulting in the reduction of lymphocyte numbers in the blood stream. Thus, the body becomes more susceptible to illnesses like colds, viruses, allergies, and opportunistic infections etc. This mechanism would explain the findings of the present study, that the presence of depression and emotional exhaustion are associated with lowered blood antibody levels and also with increased sickness absence.

## IMPLICATIONS OF THIS RESEARCH

1. The findings are suggestive of a 'disease prone' personality type. It appears that Type A individuals with their strong need to control their environment and who are more 'reactive' may also be more prone to both somatic and immuno-incompetence type illnesses in situations of low perceived control, or objectively uncontrollable situations, than Type B individuals.

2. Whilst psychosocial stresses may not directly cause diseases, they may create the necessary pre-conditions for disease processes to take hold.

3. Psychological therapies may have a significant part to contribute in improving physical as well as mental health. Any therapy which brings about a reduced or distress free state (according to the model outlined above) will restore a state of equilibrium' to the emotional and physiological processes which ultimately lead to ill health. Behavioural therapies such as relaxation training and systematic desensitisation for phobias act by reducing anxiety levels. Cognitive therapy may act by developing the individuals coping skills such as problem solving and increasing their perception of being in control, which will consequently reduce emotional distress and reduce the likelihood of physical illnesses resulting. Type A behavioural modification may also have beneficial effects on physical health by acting earlier in the causal sequence of events by reducing 'reactivity' to environmental stressors and the overwhelming desire to control them.

## SOME SUGGESTIONS FOR FUTURE RESEARCH:

a) Establish the 'generalisability' of the results of the present study by replicating it with subject populations other than student nurses.

b) More detailed information about the relationship between psychosocial stresses and the immune response could be obtained by introducing repeated and multiple measures of the immune response over the whole time span of the study, using a larger sample size of subjects.

c) Further explore the potential of psychological therapies to have beneficial effects on physical as well as mental health.

d) Further explore the hypotheses that 'hyper-responsiveness and immuno-enhancement are associated with more somatic illness and that 'hypo-responsiveness and immunosuppression' are associated with more immuno-incompetence type illness. This could be empirically tested in a fairly straight forward way by monitoring into which category of illness (i.e. somatic or immuno-incompetency) people who become sick fall.

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# APPENDICES

# APPENDIX ONE

## PSYCHOLOGICAL ASSESSMENTS USED

# FRONT SHEET

PERSONAL DETAILS:-

Please complete ALL sections on the first assessment. For subsequent assessments complete only your NAME and DATE OF BIRTH. (Only complete other sections when there has been a change of some kind e.g. change of address or tutor).

SURNAME: .....

FIRST NAME: .....

DATE OF BIRTH: .....

MARITAL STATUS: .....

ADDRESS: .....

.....

.....

TELEPHONE NUMBER: .....

CONTACT ADDRESS: .....

.....

.....

PERSONAL TUTOR: .....

DO NOT COMPLETE THIS PART (FOR ADMINISTRATION PURPOSES ONLY)

SUBJECT CODE NUMBER ALLOCATED:-

## a) ENVIRONMENTAL VARIABLES

# THE SOCIAL READJUSTMENT RATING SCALE

**(Holmes & Rahe 1967)**

## QUESTIONNAIRE NUMBER TWO

Read through the list below and tick the lifestyle changes you have experienced in the last EIGHT MONTHS:-

Death of a partner

Divorce

Separation from partner

Jail sentence or being institutionalised

Death of a close member of family

Illness or injury

Marriage

Loss of job

Reconciliation with marriage partner

Retirement

Health problems of close member of family

Pregnancy

Sex problems

Addition to family

Major changes at work

Changes in financial status

Death of friend

Changes in line of work

Changes in number of disagreements with partner

Large mortgage taken out

Mortgage or loan foreclosed

Responsibility change

Child leaves home

In law problems

Personal achievement realised

Partner starts of stops work

Starting a new school

Leaving school

Changes in living conditions

Changes in personal habits

Trouble with employer

Change in working hours

Change in residence

Change in recreation

Change in church/spiritual activities

Change in social activities

Small mortgage taken out

Change in sleeping habits

Change in number of family get-togethers

Major change in eating pattern

Holiday

Christmas

Minor violation of law

# THE COMBINED HASSLES AND UPLIFTS SCALE

**(Lazarus & Folkman 1989)**

## QUESTIONNAIRE NUMBER THREE

Directions

HASSLES are irritants - things that annoy or bother you; they can make you upset or angry.
UPLIFTS are events that make you feel good; they can make you joyful, glad, or satisfied. Some hassles and uplifts occur on a fairly regular basis and others are relatively rare. Some have only a slight effect, others have a strong effect.
When you respond to the items you must have a specific time period in mind. Please indicate the time period you will be thinking about:

Past month

Past week

Yesterday

Today

Other

This questionnaire lists things that can be hassles and uplifts in day to day life. During a given time period, some of these things will have been a hassle, some will have been an uplift. Others will have been both a hassle and an uplift.

Please think about how much of a hassle and how much of an uplift each item was for you in the time period shown above. Please indicate on the left-hand side of the page (under "HASSLES") how much of a hassle the item was by circling the appropriate number. Then indicate on the right-hand side of the page (under "UPLIFTS") how much of an uplift it was for you by circling the appropriate number.

Remember, circle one number on the left-hand side of the page and one on the right-hand side of the page for each item.

Please circle one number on both sides

| HASSLES | | UPLIFTS |
|---|---|---|
| How much of a hassle was this for you? | | How much of an uplift was this for you? |
| 0 = none or not applicable<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal | | 0 = None or not applica<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal |
| 0 1 2 3 | 1. Your child(ren) | 0 1 2 3 |
| 0 1 2 3 | 2. Your parents of parents in law | 0 1 2 3 |
| 0 1 2 3 | 3. Other relative(s) | 0 1 2 3 |
| 0 1 2 3 | 4. Your spouse | 0 1 2 3 |
| 0 1 2 3 | 5. Time spent with family | 0 1 2 3 |
| 0 1 2 3 | 6. Health or well-being of a family member | 0 1 2 3 |
| 0 1 2 3 | 7. Sex | 0 1 2 3 |
| 0 1 2 3 | 8. Intimacy | 0 1 2 3 |
| 0 1 2 3 | 9. Family related obligations | 0 1 2 3 |
| 0 1 2 3 | 10. Your friend(s) | 0 1 2 3 |
| 0 1 2 3 | 11. Fellow workers | 0 1 2 3 |
| 0 1 2 3 | 12. Clients,customers,patients etc. | 0 1 2 3 |
| 0 1 2 3 | 13. Your supervisor or employer | 0 1 2 3 |
| 0 1 2 3 | 14. The nature of your work | 0 1 2 3 |
| 0 1 2 3 | 15. Your work load | 0 1 2 3 |
| 0 1 2 3 | 16. Your job security | 0 1 2 3 |
| 0 1 2 3 | 17. Meeting deadlines or goals on the job | 0 1 2 3 |
| 0 1 2 3 | 18. Enough money for necessities (food, clothing, housing, health care, taxes, insurance, etc) | 0 1 2 3 |
| 0 1 2 3 | 19. Enough money for education | 0 1 2 3 |
| 0 1 2 3 | 20. Enough money for emergencies | 0 1 2 3 |
| 0 1 2 3 | 21. Enough money for extras (entertainment, recreation, vacations, etc.) | 0 1 2 3 |
| 0 1 2 3 | 22. Financial care for someone who doesn't live with you | 0 1 2 3 |
| 0 1 2 3 | 23. Investments | 0 1 2 3 |
| 0 1 2 3 | 24. Your smoking | 0 1 2 3 |
| 0 1 2 3 | 25. Your drinking | 0 1 2 3 |

Please circle one number on both sides

| HASSLES | | | | | | UPLIFTS | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| How much of a hassle was this for you? | | | | | | How much of an uplift was this for you? | | | | |
| 0 = none or not applicable<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal | | | | | | 0 = None or not applica<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal | | | | |
| 0 | 1 | 2 | 3 | 26. | Effects of drugs and medications | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 27. | Your physical appearance | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 28. | Time alone | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 29. | Exercise(s) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 30. | Your medical care | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 31. | Your health | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 32. | Your physical abilities | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 33. | The weather | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 34. | News events | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 35. | Your environment (quality of air, noise level, greenery etc) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 36. | Political or social issues | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 37. | Your neighbourhood (Neighbours setting) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 38. | Conserving (gas, electricity water, gasoline, etc.) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 39. | Pets | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 40. | Cooking | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 41. | Housework | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 42. | Home repairs | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 43. | Yardwork | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 44. | Car maintenance | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 45. | Taking care of paperwork(paying bills, filling out forms etc.) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 46. | Home entertainment (TV, music, reading, etc.) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 47. | Amount of free time | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 48. | Recreation and entertainment outside the home (movies, sports, eating out, walking etc.) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 49. | Eating (at home) | 0 | 1 | 2 | 3 | |
| 0 | 1 | 2 | 3 | 50. | Church or community organisations | 0 | 1 | 2 | 3 | |

Please circle one number on both sides

| HASSLES | | UPLIFTS |
|---|---|---|
| How much of a hassle was this for you? | | How much of an uplift was this for you? |
| 0 = none or not applicable<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal | | 0 = None or not applicab<br>1 = Somewhat<br>2 = Quite a bit<br>3 = A great deal |
| 0 1 2 3 | 51. Legal matters | 0 1 2 3 |
| 0 1 2 3 | 52. Being organised | 0 1 2 3 |
| 0 1 2 3 | 53. Social commitments | 0 1 2 3 |

## b) PERSONAL VARIABLES

**JENKINS ACTIVITY SCHEDULE**

**(Jenkins, Zyzanski and Rosenman 1979)**

## QUESTIONNAIRE NUMBER 5

This questionnaire asks questions about aspects of behaviour that have been found helpful in medical diagnosis. Each person is different, so there are no "right" or "wrong" answers.

For each question choose the answer that is true for you. Tick only one answer for each question. If you change your mind delete the old mark completely.

1. Do you ever have trouble finding time to get your hair cut or styled?

   a Never
   b Occasionally
   c Almost always.

2. How often does your job "stir you into action"?

   a Less often than most people's jobs
   b About average
   c More than most people's jobs

3. Is your everyday life filled mostly by

   a problems needing a solution?
   b challenges needing to be met?
   c a rather predictable routine of events?
   d not enough things to keep me interested or busy?

4. Some people live a calm, predictable life. Others often find themselves facing unexpected changes, frequent interruptions, inconveniences or "things going wrong". How often are you faced with these minor (or major) annoyances or frustrations?

   a Several times a day
   b About once a day
   c A few times a week
   d Once a week
   e Once a month or less

5. When you are under pressure or stress, what do you usually do?

   a Do something about it immediately
   b Plan carefully before taking any action

6. Ordinarily, how rapidly do you eat?

   a I'm usually the first one finished
   b I eat a little faster than average
   c I eat at about the same speed as most people
   d I eat more slowly than most people

7. Has your spouse or a friend ever told you that you eat too fast?

   a Yes, often
   b Yes, once or twice
   c No, never

8. How often do you find yourself doing more than one thing at a time, such as working while eating, reading while dressing, or figuring out problems while driving?

   a I do two things at once whenever practical
   b I do this only when I'm short of time
   c I rarely or never do more than one thing at a time.

9. When you listen to someone talking, and this person takes too long to come to to the point, how often do you feel like hurrying the person along?

   a Frequently
   b Occasionally
   c Almost never

10. How often do you actually "put words in the person's mouth" in order to speed things up?

    a Frequently
    b Occasionally
    c Almost never

11. If you tell your spouse or a friend that you will meet somewhere at a definite time, how often do you arrive late?

    a Once in a while
    b Rarely
    c I am never late

12. How often do you find yourself hurrying to get places even when there is plenty of time?

    a Frequently
    b Occasionally
    c Almost never

13. Suppose you are to meet someone at a public place (street corned, building lobby, restaurant) and the other person is already 10 minutes late. What will you do?

    a Sit and wait
    b Walk about while waiting
    c Usually carry some reading matter or writing paper so I can get something done while waiting.

14. When you have to "wait in line" at a restaurant, a store, or the post office, what do you do?

a Accept it calmly
b Feel impatient but not show it
c Feel so impatient that someone watching can till i am restless
d Refuse to wait in line and find ways to avoid such delays

15. When you play games with young children about 10 years old (or when you did so in past years) how often do you purposely let them win?

a Most of the time
b Half the time
c Only occasionally
d Never

16. When you were younger, did most people consider you to be

a definitely hard-driving and competitive?
b probably hard-driving and competitive?
c probably more relaxed and easygoing?
d definitely more relaxed and easygoing?

17. Nowadays, do you consider yourself to be

a definitely hard-driving and competitive?
b probably hard-driving and competitive?
c probably more relaxed and easygoing?
d definitely more relaxed and easygoing?

18. Would you spouse (or closest friend) rate you as

a definitely hard-driving and competitive?
b probably hard-driving and competitive?
c probably more relaxed and easygoing?
d definitely more relaxed and easygoing?

19. Would your spouse (or closest friend) rate your general level of activity as

a too slow - should be more active?
b about average - busy much of the time?
c too active - should slow down?

20. Would people you know well agree that you take your work too seriously?

a Definitely yes
b Probably yes
c Probably no
d Definitely no

21. Would people you know well agree that you have less energy than most people?

a Definitely yes
b Probably yes
c Probably no
d Definitely no

22. Would people you know well agree that you tend to get irritated easily?

a Definitely yes
b Probably yes
c Probably no
d Definitely no

23. Would people who know you well agree that you tend to do most things in a hurry?

a Definitely yes
b Probably yes
c Probably no
d Definitely no.

24. Would people who know you well agree that you enjoy a "contest" (competition) and try hard to win?

a Definitely yes
b Probably yes
c Probably no
d Definitely no

25. How was your temper when you were younger?

a Fiery and hard to control
b Strong but controllable
c No problem
d I almost never got angry

26. How is your temper nowadays?

a Fiery and hard to control
b Strong but controllable
c No problem
d I almost never got angry

27. When you are in the midst of doing a job and someone (not your boss) interrupts you, how do you usually feel inside?

a I feel O.K. because I work better after an occasional break
b I feel only mildly annoyed
c I really feel irritated because most such interruptions are unnecessary

28. How often are there deadlines on you job?

a Daily or more often
b Weekly
c Monthly or less often
d Never

29. These deadlines usually carry

a minor pressure because of their routine nature
b considerable pressure, since delay would upset my entire work group
c Deadlines never occur on my job

30. Do you ever set deadlines or quotas for yourself at work or at home?

a No
b Yes, but only occasionally
c Yes, once a week or more

31. When you have to work against a deadline, what is the quality of your work?

a Better
b Worse
c The same (Pressure makes no difference)

32. At work, do you ever keep two jobs moving forward at the same time by shifting back and forth rapidly from one to the other?

a No, never
b Yes, but only in emergencies
c Yes, regularly

33. Are you content to remain at your present job level for the next five years?

a Yes
b No, I want to advance
c Definitely no; I strive to advance and would be dissatisfied if not promoted in that length of time.

34 If you had your choice, which would you rather get?

a A small increase in pay **without** a promotion to a higher level job
b A promotion to a higher level job **without** an increase in pay

35. In the past three years, have you ever taken less than your allotted number of vacation days?

a Yes
b No
c My type of job does not provide regular vacations

36. In the last three years, how has your personal yearly income changed?

a It has remained the same or gone down
b It has gone up slightly (as a result of cost-of-living increases or automatic raises based on years of service).
c It has gone up considerably

37. How often do you bring your work home with you at night, or study materials related to your job?

a Rarely or never
b Once a week or less
c More than once a week

38. How often do you go to your place of work when you are not expected to be there (such as nights or weekends)?

a It is not possible on my job
b Rarely or never
c Occasionally (less than once a week)
d Once a week or more

39. When you find yourself getting tired on the job, what do you usually do?

a Slow down for a while until my strength comes back
b Keep pushing myself at the same pace in spite of the tiredness

40. When you are in a group, how often do the other people look to you for leadership?

a Rarely
b About as often as they look to others
c More often than they look to others

41. How often do you make yourself written lists to help you remember what needs to be done?

a Never
b Occasionally
c Frequently

For questions 42 - 46 compare yourself with the average worker in your present occupation and mark the most accurate description.

42. In amount of effort you put forth I give

a much more effort
b a little more effort
c a little less effort
d much less effort

43. In sense of responsibility, I am

a much more responsible
b a little more responsible
c a little less responsible
d much less responsible

44. I find it necessary to hurry

a much more of the time
b a little more of the time
c a little less of the time
d much less of the time

45. In being precise (careful about detail), I am

a much more precise
b a little more precise
c a little less precise
d much less precise

46. I approach life in general

a much more seriously
b a little more seriously
c a little less seriously
d much less seriously

For questions 47 - 49, compare your present work with your work setting five years ago. if you have not been working for five years, compare your present job with your first job.

47. I have worked more hours per week

a at my present job
b five years ago
c cannot decide

48. I carried more responsibility

a at my present job
b five years ago
c cannot decide

49 I was considered to be at a higher level (in prestige or social position)

a at my present job
b five years ago
c cannot decide

50. How many different job titles have you held in the last 10 years? (Be sure to count shifts in kinds of work, shifts to new employers and shifts up and down within a firm).

a 0 - 1
b 2
c 3
d 4
e 5 or more

51. How much schooling did you receive?

a 0 - 4 years
b 5 - 8 years
c Some high school
d Graduated from high school
e Trade school or business college
f Some college (including junior college)
g Graduated from four year college
h Post-graduate work at college or university

52 When you were in school were you an office of any group, such as a student council, glee club, 4-H club, sorority or fraternity, or captain of an athletic team?

a No
b Yes, I held one such position
c Yes, I held two or more such positions

NOW GO ON TO QUESTIONNAIRE NUMBER 6

**SHORT TYPE A QUESTIONNAIRE**

**(Fontana 1989)**

## QUESTIONNAIRE NUMBER 4

PLEASE INDICATE BY ANSWERING YES OR NO WHICH TYPES OF BEHAVIOUR GENERALLY DESCRIBES YOU:-

1. Do you characteristically do several things at once (e.g. telephoning, holding a conversation, jotting notes on a pad and swivelling back and forth on your chair all at the same time)?

2. Do you feel guilty when relaxing as if there's always something else you should be doing?

3. Are you quickly bored when other people are talking? Do you find yourself wanting to interrupt or finish their sentences for them, or in some way get them to hurry up?

4. Do you try to steer conversations towards your own interests, instead of wanting to hear about those of others?

5. Are you usually anxious when engaged in a task to get it finished so that you can get on to the next job?

6. Are you unobservant when it comes to anything that isn't immediately connected with what you're actually doing?

7. Do you prefer to HAVE rather than BE (i.e. to experience your possessions rather than to experience yourself)?

8. Do you do most things (eating, talking, walking) at top speed?

9. Do you find people like yourself challenging and people who dawdle infuriating?

10. Are you physically tense and assertive?

11. Are you more interested in winning than simply in taking part and enjoying yourself?

12. Do you find it hard to laugh at yourself?

13. Do you find it hard to delegate?

14. Do you find it almost impossible to attend meetings without speaking up?

15. Do you prefer activity holidays to dreamy, relaxing ones?

16. Do you push those for whom you're responsible (children, subordinate, partner) to try to achieve your own standards. without showing much interest in what they really want out of life?

# THE DYSFUNCTIONAL ATTITUDE SCALE

**(Weissman and Beck 1978)**

## QUESTIONNAIRE NUMBER FOUR

This inventory lists different attitudes or beliefs which people sometimes hold. Read each statement carefully and decide how much you agree or disagree with the statement.

For each of the attitudes, show your answer by placing a tick ( ✓ ) under the column that best describes how you think. Be sure to choose only one answer for each attitude. because people are different, there is no right answer or wrong answer to these statements.

To decide whether a given attitude is typical of your way of looking at things, simply keep in mind what you are like most of the time.

EXAMPLE

| | Totally agree | Agree very much | Agree slightly | Neutral | Disagree slightly | Disagree very much | Totally disagree | |
|---|---|---|---|---|---|---|---|---|
| 1. Most people are OK once you get to know them | | | | | | | | |

Look at the example above. to show how much a sentence describes you attitude, you can check any point from "totally agree" to "totally disagree". In the above example, the checkmark at "agree slightly" indicates that this statement is somewhat typical of the attitudes held by the person completing the inventory.

Remember that your answer should describe the way you think most of the time.

Now turn the page and begin.

| Attitudes | Totally agree | Agree very much | Agree slightly | Neutral | Disagree slightly | Disagree very much | Totally disagree |
|---|---|---|---|---|---|---|---|
| Remember, answer each statement according to the way you think **most of the time.** | | | | | | | |
| 1 It is difficult to be happy unless one is good-looking, intelligent, rich and creative | | | | | | | |
| 2 Happiness is more a matter of my attitude towards myself than the way other people feel about me | | | | | | | |
| 3 People will probably think loss of me if I make a mistake | | | | | | | |
| 4 If I do not do well all the time, people will not respect me | | | | | | | |
| 5 Taking even a small risk is foolish because the loss is likely to be a disaster | | | | | | | |
| 6 It is possible to gain another person's respect without being especially talented at anything | | | | | | | |
| 7 I cannot be happy unless most people I know admire me | | | | | | | |
| 8 If a person asks for help, it is a sign of weakness | | | | | | | |
| 9 If I do not do as well as other people it means I am an inferior human being | | | | | | | |
| 10 If I fail at my work, then I am a failure as a person | | | | | | | |
| 11 If you cannot do something well, there is little point in doing it at all | | | | | | | |
| 12 Making mistakes is fine because I can learn from them | | | | | | | |
| 13 If someone disagrees with me, it probably indicates he does not like me | | | | | | | |
| 14 If I fail partly, it is as bad as being a complete failure | | | | | | | |

| | Totally agree | Agree very much | Agree slightly | Neutral | Disagree slightly | Disagree very much | Totally disagree |
|---|---|---|---|---|---|---|---|
| 15 If other people know what you are really like, they will think less of you | | | | | | | |
| 16 I am nothing if a person I love doesn't love me | | | | | | | |
| 17 One can get pleasure from an activity regardless of the end result | | | | | | | |
| 18 People should have a reasonable likelihood of success before undertaking anything | | | | | | | |
| 19 My value as a person depends greatly on what others think of me | | | | | | | |
| 20 If I don't set the highest standards for myself, I am likely to end up a second rate person | | | | | | | |
| 21 If I am to be a worthwhile person, I must be truly outstanding in at least one major respect | | | | | | | |
| 22 People who have good ideas are more worthy than those who do not | | | | | | | |
| 23 I should be upset if I made a mistake | | | | | | | |
| 24 My own opinions of myself are more important than other's opinions of me | | | | | | | |
| 25 To be a good, moral, worthwhile person, I must help everyone who needs it. | | | | | | | |
| 26 If I ask a question, it makes me look inferior. | | | | | | | |
| 27 It is awful to be disapproved of by people important to you | | | | | | | |
| 28 If you don't have other people to lean on, you are bound to be sad | | | | | | | |
| 29 I can reach important goals without slave driving myself | | | | | | | |
| 30 It is possible for a person to be scolded and not get upset | | | | | | | |

| Attitudes | Totally agree | Agree very much | Agree slightly | Neutral | Disagree slightly | Disagree very much | Totally disagree |
|---|---|---|---|---|---|---|---|
| 31 I cannot trust other people because they might be cruel to me | | | | | | | |
| 32 If others dislike you, you cannot be happy | | | | | | | |
| 33 It is best to give up your own interests in order to please other people. | | | | | | | |
| 34 My happiness depends more on other people than it does on me | | | | | | | |
| 35 I do not need the approval of other people in order to be happy | | | | | | | |
| 36 If a person avoids problems, the problems tend to go away | | | | | | | |
| 37 I can be happy even if I miss out on many of the good things in life | | | | | | | |
| 38 What other people think about me is very important | | | | | | | |
| 39 Being isolated from others is bound to lead to unhappiness | | | | | | | |
| 40 I can find happiness without being loved by another person | | | | | | | |

# AUTOMATIC THOUGHTS QUESTIONNAIRE REVISED

**(Kendall, Howard and Hayes 1981)**

## QUESTIONNAIRE NUMBER 6

INSTRUCTIONS

Listed below are a variety of thoughts that pop into people's heads. Please read each thought and indicate how frequently, if at all, the thought occurred to you over the last week. Please read each item carefully and circle the appropriate answers on the answer sheet in the following fashion:

1 = not at all
2 = sometimes
3 = moderately often
4 = often
5 = all the time

| RESPONSE | THOUGHTS |
|---|---|
| 1 2 3 4 5 | 1. I feel like I'm up against the world |
| 1 2 3 4 5 | 2. I'm no good |
| 1 2 3 4 5 | 3. I'm proud of myself |
| 1 2 3 4 5 | 4. Why can't I ever succeed |

REMEMBER, each sentence that you read is a THOUGHT that you may have had often, less frequently or not at all. Tell us how often over the LAST WEEK you have had each of the thoughts.

| | |
|---|---|
| 1 2 3 4 5 | 5. No one understands me. |
| 1 2 3 4 5 | 6. I've let people down |
| 1 2 3 4 5 | 7. I feel fine |
| 1 2 3 4 5 | 8. I don't think I can go on |
| 1 2 3 4 5 | 9. I wish I were a better person |
| 1 2 3 4 5 | 10. No matter what happens, I know I'll make it |
| 1 2 3 4 5 | 11. I'm so weak |
| 1 2 3 4 5 | 12. My life's not going the way I want it to |
| 1 2 3 4 5 | 13. I can accomplish anything |
| 1 2 3 4 5 | 14. I'm so disappointed in myself |
| 1 2 3 4 5 | 15. Nothing feels good anymore |
| 1 2 3 4 5 | 16. I feel good |
| 1 2 3 4 5 | 17. I can't stand this anymore |
| 1 2 3 4 5 | 18. I can't get started |
| 1 2 3 4 5 | 19. What's wrong with me? |
| 1 2 3 4 5 | 20. I'm warm and comfortable |
| 1 2 3 4 5 | 21. I wish I were somewhere else |
| 1 2 3 4 5 | 22. I can't get things together |
| 1 2 3 4 5 | 23. I hate myself |
| 1 2 3 4 5 | 24. I feel confident I can do anything I set my mind to |

1 = not at all
2 = sometimes
3 = moderately often
4 = often
5 = all the time

| | | | | | | |
|---|---|---|---|---|---|---|
| 1 | 2 | 3 | 4 | 5 | 25. | I'm worthless |
| 1 | 2 | 3 | 4 | 5 | 26. | Wish I could just disappear |
| 1 | 2 | 3 | 4 | 5 | 27. | What's the matter with me? |
| 1 | 2 | 3 | 4 | 5 | 28. | I feel very happy |
| 1 | 2 | 3 | 4 | 5 | 29. | I'm a loser |
| 1 | 2 | 3 | 4 | 5 | 30. | My life is a mess |
| 1 | 2 | 3 | 4 | 5 | 31. | I'm a failure |
| 1 | 2 | 3 | 4 | 5 | 32. | This is super! |
| 1 | 2 | 3 | 4 | 5 | 33. | I'll never make it |
| 1 | 2 | 3 | 4 | 5 | 34. | I feel so helpless |
| 1 | 2 | 3 | 4 | 5 | 35. | Something has to change |
| 1 | 2 | 3 | 4 | 5 | 36. | There must be something wrong with me |
| 1 | 2 | 3 | 4 | 5 | 37. | I'm luckier than most people |
| 1 | 2 | 3 | 4 | 5 | 38. | My future is bleak |
| 1 | 2 | 3 | 4 | 5 | 39. | It's just not worth it |
| 1 | 2 | 3 | 4 | 5 | 40. | I can't finish anything |

# CULTURE FREE SELF-ESTEEM INVENTORY

**(Battle 1980)**

## QUESTIONNAIRE NUMBER 6

DIRECTIONS:

Please mark each question in the following way: If the question describes how you usually feel make a tick mark ( ✓ ) in the "yes" column. If the question does not describe how you usually feel make a tick mark ( ✓ ) in the "no" column. Please tick only one column (either "yes" or "no") for each of the 40 questions. This is not a test and there is not "right" or "wrong" answers.

| | | Yes | No |
|---|---|---|---|
| 1. | Do you have only a few friends ..... | | |
| 2. | Are you happy most of the time ..... | | |
| 3. | Can you do most thing as well as others .. | | |
| 4. | Do you like everyone you know ..... | | |
| 5. | Do you spend most of your free time at home ..... | | |
| 6. | Do you like being a male/female..... | | |
| 7. | Do most people you know like you ..... | | |
| 8. | Are you usually successful when you attempt important tasks or assignments.... | | |
| 9. | Have you ever taken anything that did not belong to you .... | | |
| 10. | Are you as intelligent as most people ... | | |
| 11. | Do you feel your are as important as most people ... | | |
| 12. | Are you easily depressed ..... | | |
| 13. | Would you change many things about yourself if you could ..... | | |
| 14. | Do you always tell the truth ..... | | |
| 15. | Are you as nice looking as most people .. | | |

| | Yes | No |
|---|---|---|
| 16. Do may people dislike you ..... | | |
| 17. Are you usually tens or anxious ..... | | |
| 18. Are you lacking ins elf confidence ..... | | |
| 19. Do you gossip at times ..... | | |
| 20. Do you often feel that you are no good at all ..... | | |
| 21. Are you as strong and healthy as most people ..... | | |
| 22. Are your feelings easily hurt ..... | | |
| 23. Is it difficult for you to express your views of feelings ..... | | |
| 24. Do you ever get angry ..... | | |
| 25. Do you often feel ashamed of yourself ... | | |
| 26. Are other people generally more successful than you are ..... | | |
| 27. Do you feel uneasy much of the time without knowing why ..... | | |
| 28. Would you like to be as happy as others appear to be ..... | | |
| 29. Are you ever shy ..... | | |
| 30. Are you a failure ..... | | |
| 31. Do people like your ideas ..... | | |
| 32. Is it hard for you to meet new people ... | | |
| 33. Do you ever lie ..... | | |
| 34. Are you often upset about something ..... | | |
| 35. Do most people respect your views ..... | | |

| | Yes | No |
|---|---|---|
| 36. Are you more sensitive than most people . | | |
| 37. Are you as happy as most people ..... | | |
| 38. Are you ever sad ..... | | |
| 39. Are you definitely lacking in initiative. | | |
| 40. Do you worry a lot ..... | | |

THE END

THANK YOU FOR YOUR CO-OPERATION

# SENSE OF COHERENCE QUESTIONNAIRE

**(Antonovsky 1987)**

## QUESTIONNAIRE NUMBER 8

Here is a series of questions relating to various aspects of our lives. Each question has seven possible answers. Please mark the number which expresses your answer with the numbers 1 and 7 being the extreme answers. If the words under 1 are right for you circle 1; if the words under 7 are right for you circle 7. If you feel differently, circle the number which best expresses your feeling. Please give only one answer to each question.

1. When you talk to people, do you have the feeling that they don't understand you?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| Never have this feeling | | | | | | always have this feeling |

2. In the past, when you had to do something which depended upon co-operation with others, did you have the feeling that it:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| surely would not get done | | | | | | surely would get done |

3. Think of the people with whom you come into contact daily, aside from the ones to whom you feel closest. How well do you know most of them?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| you feel that they're strangers | | | | | | you know them very well |

4. Do you have the feeling that you don't really care about what goes on around you?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very seldom or never | | | | | | very often |

5. Has it happened in the past that you were surprised by the behaviour of people whom you thought you knew well?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| never happened | | | | | | always happened |

6. Has it happened that people whom you counted on disappointed you ?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| never happened | | | | | | always happened |

7. Life is:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| full of interest | | | | | | completely routine |

8. Until now you life has had:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| no clear goals or purpose at all | | | | | | very clear goals and purpose |

9. Do you have the feeling that you're being treated unfairly?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

10. In the past ten years your life has been

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| full of changes without your knowing what will happen next | | | | | | completely consistent and clear |

11. Most of the things you do in the future will probably be:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| completely fascinating | | | | | | deadly boring |

12. Do you have the feeling that you are in an unfamiliar situation and don't know what to do?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

13. What best describes how you see life:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| one can always find a solution to painful things in life | | | | | | there is no solution to painful things in life |

14. When you face a difficult problem, the choice of a solution is:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| feel how good it is to be alive | | | | | | ask yourself why you exist at all |

15. When you face a difficult problem, the choice of a solution is:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| always confusing and hard to find | | | | | | always completely clear |

16. Doing the things you do every day is

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| a source of deep pleasure and satisfaction | | | | | | a source of pain and boredom |

17. Your life in the future will probably be:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| full of changes without your knowing what will happen next | | | | | | completely consistent and clear |

18. When something unpleasant happened in the past you tendency was:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| "to eat yourself up" about it | | | | | | to say "ok that's that I have to live with it" and go on |

19. Do you have very mixed up feelings and ideas?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

20. When you do something that gives you a good feeling

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| it's certain that you'll go on feeling good | | | | | | it certain that something will happen to spoil the feeling |

21. Does it happen that you have feelings inside you would rather not feel?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

22. You anticipate that your personal life in the future will be:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| totally without meaning or purpose | | | | | | full of meaning and purpose |

23. Do you thing that there will always be people whom you'll be able to count on in the future?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| you're certain there will be | | | | | | you doubt there will be |

24. Does it happen that you have the feeling that you don't know exactly what's about to happen?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

25. Many people even those with a strong character sometimes feel like sad sacks (losers) in certain situations. How often have you felt this way in the past?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| never | | | | | | very often |

26. When something happened, have you generally found that:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| you over estimated or under-estimated its importance | | | | | | you saw things in the right proportion |

27. When you think of difficulties you are likely to face in important aspects of your life, do you have the feeling that:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| you will always succeed in over coming the difficulties | | | | | | you won't succeed in over coming the diffic-ulties |

28. How often do you have the feeling that there's little meaning in the things you do in your daily life?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

29. How often do you have feelings that you're not sure you can keep under control?

| 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|
| very often | | | | | | very seldom or never |

THE END

THANK YOU FOR YOUR CO-OPERATION

## c) MEASURES OF EMOTIONAL DISTRESS

# THE HOSPITAL ANXIETY AND DEPRESSION SCALE

**(Zigmond & Snaith 1983)**

# QUESTIONNAIRE NUMBER 1

Do not take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought ouT response.

I feel tense or "wound up":

- Most of the time
- A lot of the time
- From time to time, occasionally
- Not at all

I still enjoy the thing I used to enjoy:

- Definitely as much
- Not quite so much
- Only a little
- Hardly at all

I get a sort of frightened feeling as if something awful is about to happen:

- Very definitely and quite badly
- Yes, but not too badly
- A little, but it does not worry me
- Not at all

I can laugh and see the funny side of things:

- As much as I always could
- Not quite so much now
- Definitely not so much now
- Not at all

Worrying thoughts go through my mind:

- A great deal of the time
- A lot of the time
- From time to time but not too often
- Occasionally

I feel cheerful:

Not at all
Not often
Sometimes
Most of the time

I can sit at ease and feel relaxed:

Definitely
Usually
Not often
Not at all

I feel as if I am slowed down:

Nearly all the time
Very often
Sometimes
Not at all

I get a sort of frightened feeling like "butterflies" in the stomach:

Not at all
Occasionally
Quite often
Very often

I have lost interest in my appearance:

Definitely
I don't take so much care as I should
I may not take quite as much care
I take just as much care as ever

I feel restless as if I have to be on the move:

Very much indeed
Quite a lot
Not very much
Not at all

I look forward with enjoyment to things:

As much as ever I did
Rather less that I used to
Definitely less than I used to
Hardly at all

I get sudden feelings of panic:

Very often indeed
Quite often
Not very often
Not at all

I can enjoy a good book or radio or T.V. programme:

Often
Sometimes
Not often
Very seldom

NOW COMPLETE QUESTIONNAIRE NUMBER TWO.

**THE GENERAL HEALTH QUESTIONNAIRE (28 item version)**

**(Goldberg and Williams 1988)**

QUESTIONNAIRE NUMBER 5

Please read carefully:

We should like to know if you have had any medical complaints and how your health has been in general, over the past few weeks. Please answer ALL the questions on the following pages simply by underlining the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Thank you very much for your co-operation.

---

HAVE YOU RECENTLY

| | | | | |
|---|---|---|---|---|
| A1 - been feeling perfectly well and in good health? | Better than usual | Same as usual | Worse than usual | Much worse than usual |
| A2 - been feeling in need of a good tonic? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| A3 - been feeling run down and out of sorts? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| A4 - felt that you are ill? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| A5 - been getting any pains in your head? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| A6 - been getting a feeling of tightness or pressure in your head? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| A7 - been having hot and cold spells? | Not at all | No more than usual | Rather more than usual | Much more than usual |

HAVE YOU RECENTLY

| | | | | |
|---|---|---|---|---|
| B1 - lost much sleep over worry? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B2 - had difficulty in staying asleep once you are off? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B3 - felt constantly under strain? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B4 - been getting edgy and bad-tempered? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B5 - been getting scared or panicky for no good reason? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B6 - found everything getting o top of you? | Not at all | No more than usual | Rather more than usual | Much more than usual |
| B7 - been feeling nervous and strung up all the time? | Not at all | No more than usual | Rather more than usual | Much more than usual |

---

| | | | | |
|---|---|---|---|---|
| C1 - been managing to keep yourself busy and occupied? | More so than usual | Same as usual | Rather less than usual | Much less than usual |
| C2 - been taking longer over the things you do? | Quicker than usual | Same as usual | Longer than usual | Much longer than usual |
| C3 - felt on the whole you were doing things well? | Better than usual | About the same | Less well than usual | Much less well |
| C4 - been satisfied with the way you've carried | More satisfied | About same as usual | Less satisfied than usual | Much less satisfied |
| C5 - felt that you are playing a useful part in things? | More so than usual | Same as usual | Less useful than usual | Much less useful |
| C6 - felt capable of making decision about things? | More so than usual | Same as usual | Less so than usual | Much less capable |
| C7 - been able to enjoy your normal day to day activities? | More so than usual | Same as usual | Less so than usual | Much less than usual |

HAVE YOU RECENTLY

| | | | | |
|---|---|---|---|---|
| D1 - been thinking of yourself as a worthless person? | Not at all | No more than usual | Rather more than usual | Much more than usua |
| D2 - felt that life is entirely hopeless? | Not at all | No more than usual | Rather more than usual | Much more than usua |
| D3 - felt that life isn't worth living? | Not at all | No more than usual | Rather more than usual | Much more than usua |
| D4 - thought of the possibility that you might make away with yourself? | definitely not | I don't think so | Has crossed my mind | Definitel have |
| D5 - found at times you couldn't do anything | Not at all | No more than usual | Rather more than usual | Much more than usua |
| D6 - found yourself wishing you were dead and away from it all? | Not at all | No more than usual | Rather more than usual | Much more than usua |
| D7 - found that the idea of taking your own life | Definitely not | I don't think so | Has crossed my mind | Definitel has |

A [ ] B [ ] C [ ] D [ ] TOTAL [ ]

THE END

THANK YOU FOR YOUR CO-OPERATION

# MASLACH BURNOUT INVENTORY

**(Maslach and Jackson 1981)**

## QUESTIONNAIRE NUMBER 5

DIRECTIONS:

Please indicate how often you experience the following:

---

HOW OFTEN :

0 = Never
1 = A few times a year or less
2 = Once a month or less
3 = A few times a month
4 = Once a week
5 = A few times a week
6 = Every day

| HOW OFTEN 0 - 6 | Statements: |
|---|---|
| 1. | I feel emotionally drained away from work |
| 2. | I feel used up at the end of the workday. |
| 3. | I feel fatigued when I get up in the morning and have to face another day on the job. |
| 4. | I can easily understand how my recipients feel about things. |
| 5. | I feel I treat some recipients as if they were impersonal objects. |
| 6. | Working with people all day is really a strain on me. |
| 7. | I deal very effectively with the problems of my recipients. |
| 8. | I feel burned out from my work. |
| 9. | I feel I'm positively influencing other people's lives through my work. |
| 10. | I've become more callous toward people since I took this job. |
| 11. | I worry that this job is hardening me emotionally. |
| 12. | I feel very energetic. |

HOW OFTEN:
0 - 6

13. I feel frustrated by my job.

14. I feel I'm working too hard on my job.

15. I don't really care what happens to some recipients.

16. Working with people directly puts too much stress on me.

17. I can easily create a relaxed atmosphere with my recipients.

18. I feel exhilarated after working closely with my recipients.

19. I have accomplished many worthwhile things in this job.

20. I feel like I'm at the end of my rope.

21. In my work, I deal with emotional problems very calmly.

22. I feel recipients blame me for some of their problems.

---

Administrative use only:

| | cat. | | cat. | | cat. |
|---|---|---|---|---|---|
| EE: | _____ _____ | DP: | _____ _____ | PA: | _____ _____ |

# APPENDIX TWO

## 'ETHICAL APPROVAL'

SOUTH TEES HEALTH

District Offices
Poole Hospital
Nunthorpe, Middlesbrough
Cleveland TS7 0NJ
Telephone: Middlesbrough 320000
Fax: (0642) 324176

PKN/LH

31 July 1992

Mr M R Bamber
Occupational Health Department
South Cleveland Hospital
Marton Road
Middlesbrough

Dear Mr Bamber

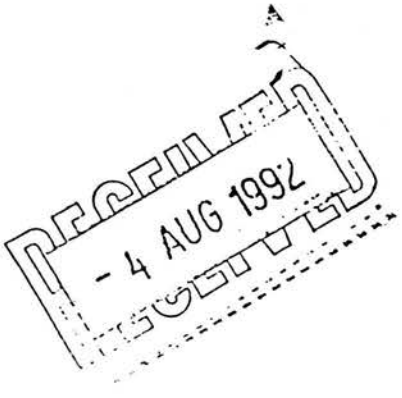
92/47 - Negative psychological states and the immune system

The above project was considered at the meeting of the Ethics Committee held on 30 July 1992. Members of the Ethics Committee considered this to be a well designed study that should produce interesting findings. There were no ethical reservations and we are happy for you to proceed.

I would be grateful if you would agree to provide a progress report when I write to you again in about a year.

Yours sincerely

P K Newman
Chairman
Ethics Committee



# APPENDIX THREE

## "WRITTEN CONSENT FORMS"

SOUTH TEES HEALTH AUTHORITY OCCUPATIONAL HEALTH SERVICE

RESEARCH PROJECT

"NEGATIVE PSYCHOLOGICAL STATES AND THE IMMUNE SYSTEM"

CONSENT FORM

NAME: .....

ADDRESS: .....

The above mentioned research has been fully explained and is understood by me and I hereby give my informed consent to participate in the said research.

SIGNED: .....

DATE: .....

In the presence of:-

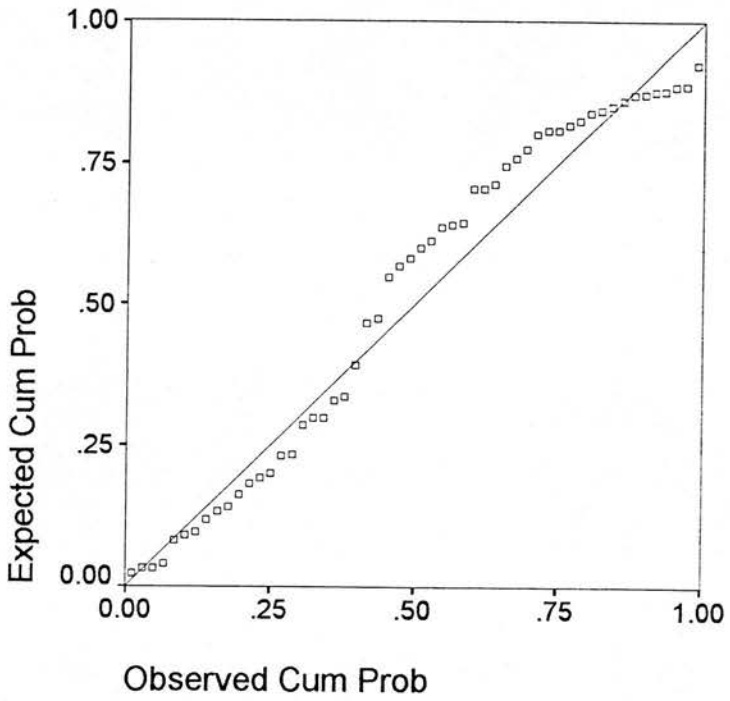
SIGNED: .....
Responsible Investigator

DATE: .....

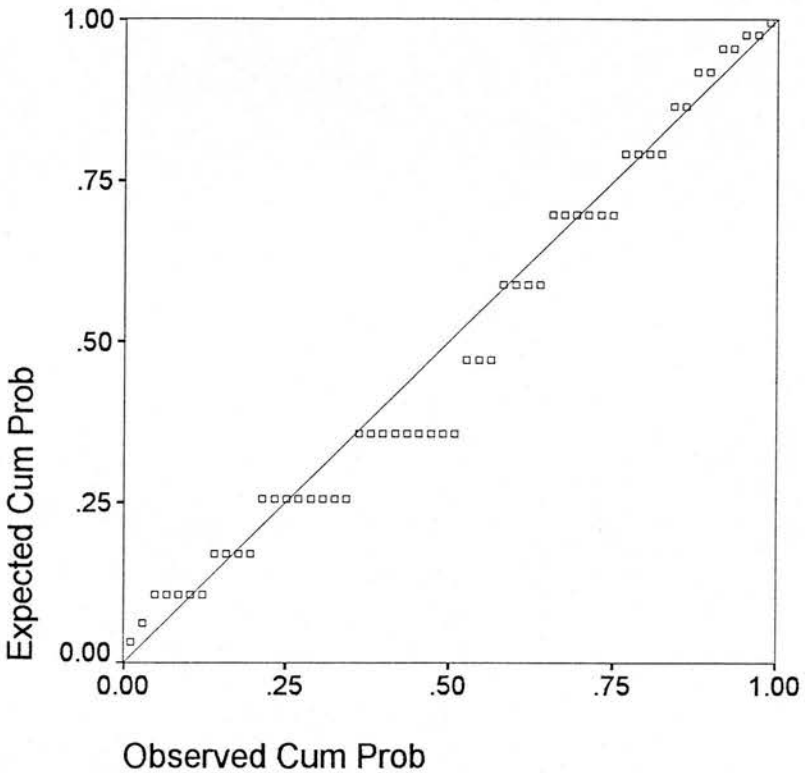
# APPENDIX FOUR

## "NORMAL P-P PLOTS"

## 1. HEPATITIS B ANTIBODY TITRE SCORES

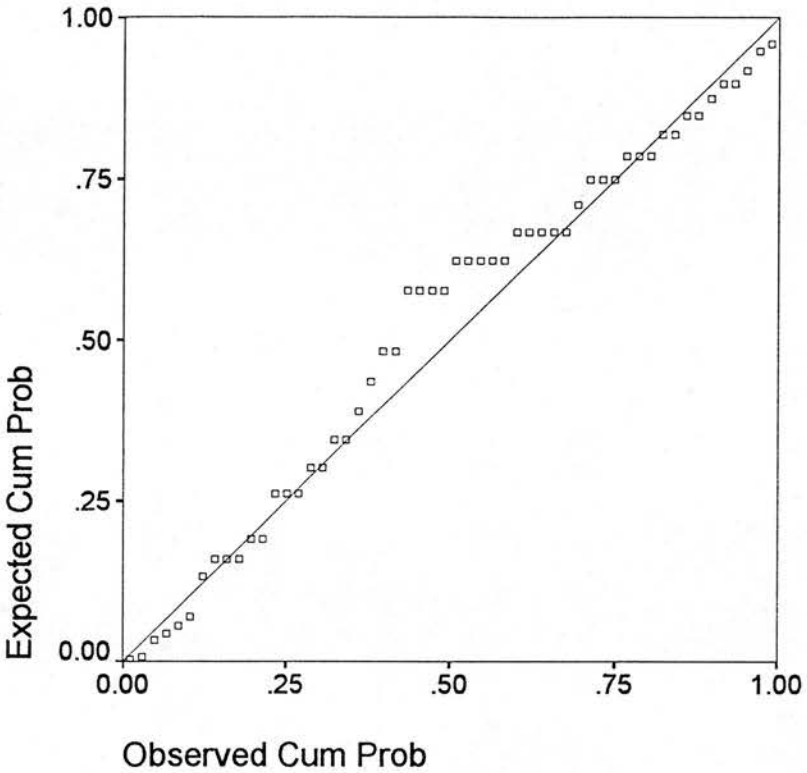


## 2. NUMBER OF LIFE EVENTS IN THE SIX MONTHS LEADING UP TO THE COMMENCEMENT OF THE STUDY

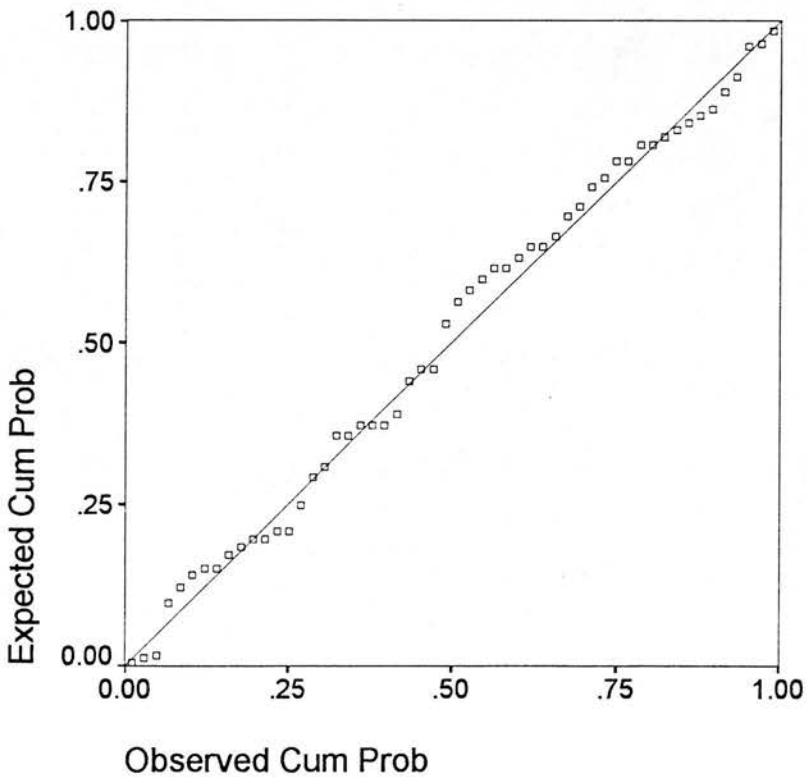


## 3. SENSE OF COHERENCE

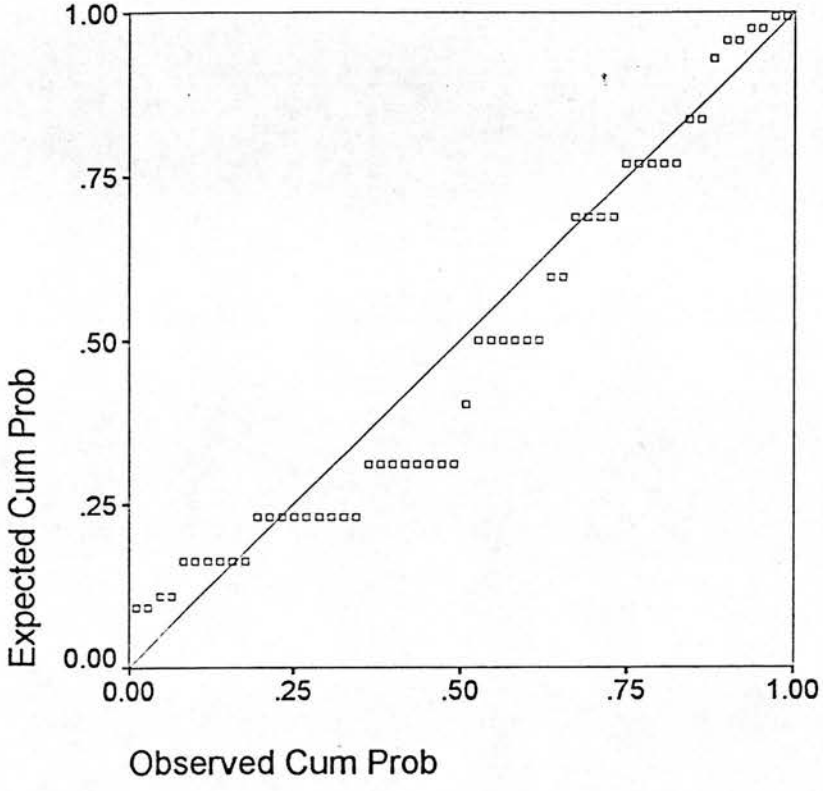
### a) TOTAL SCORES




### b) MANAGEABILITY SUBSCALE SCORES

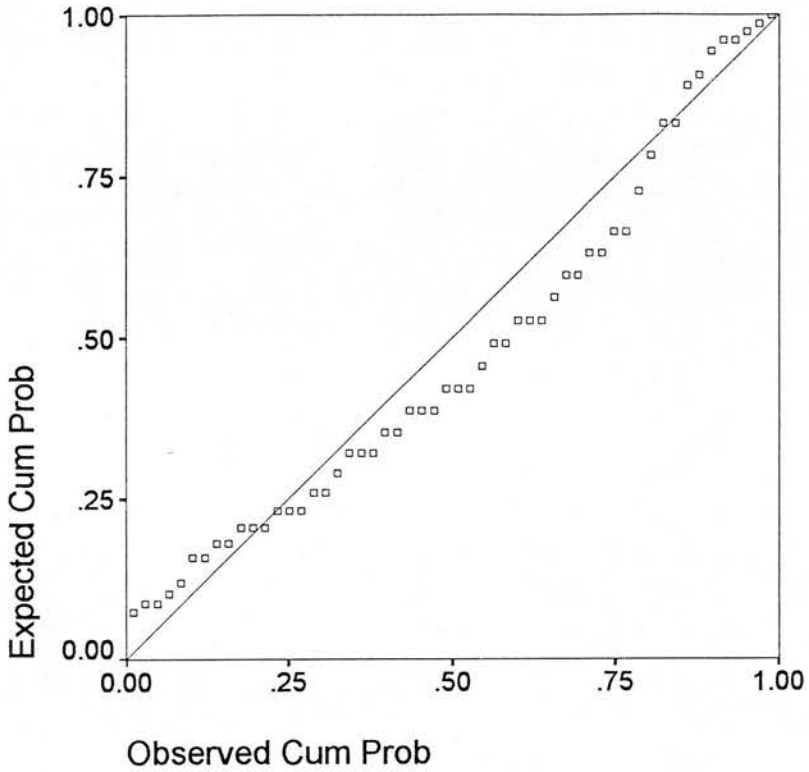


## 4. JENKINS ACTIVITY SCHEDULE 'BROAD TYPE A' SCORES

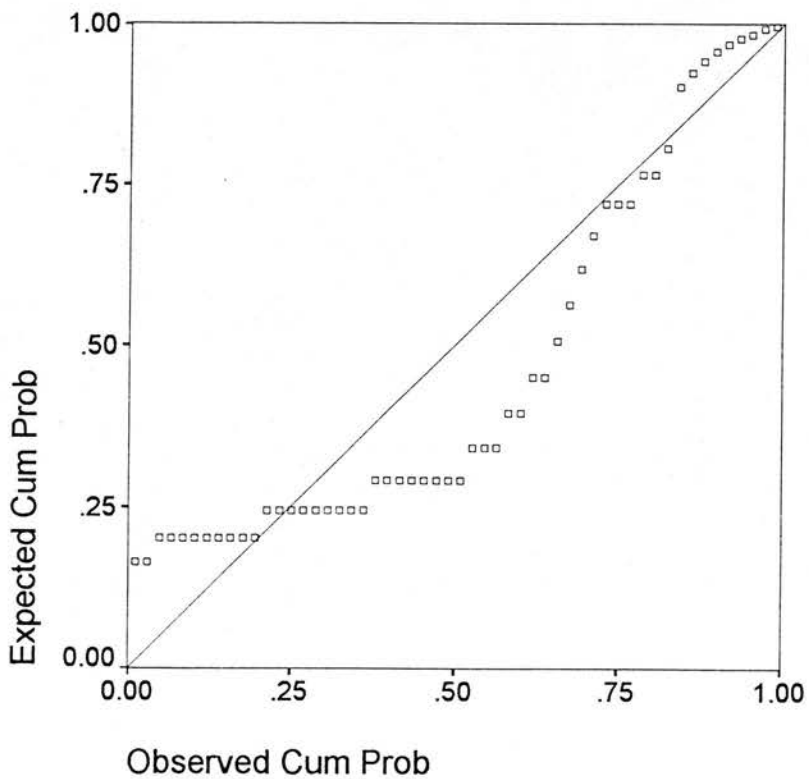


## 5. HOSPITAL ANXIETY AND DEPRESSION SCALE

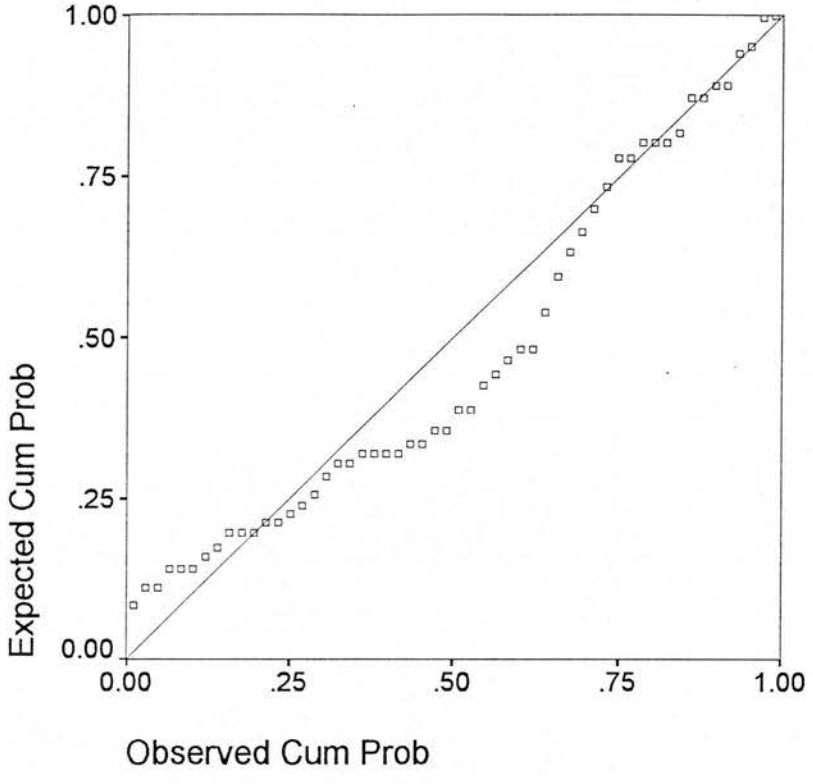
### a) ANXIETY SUBSCALE (mean scores)




### b) DEPRESSION SUBSCALE (mean scores)

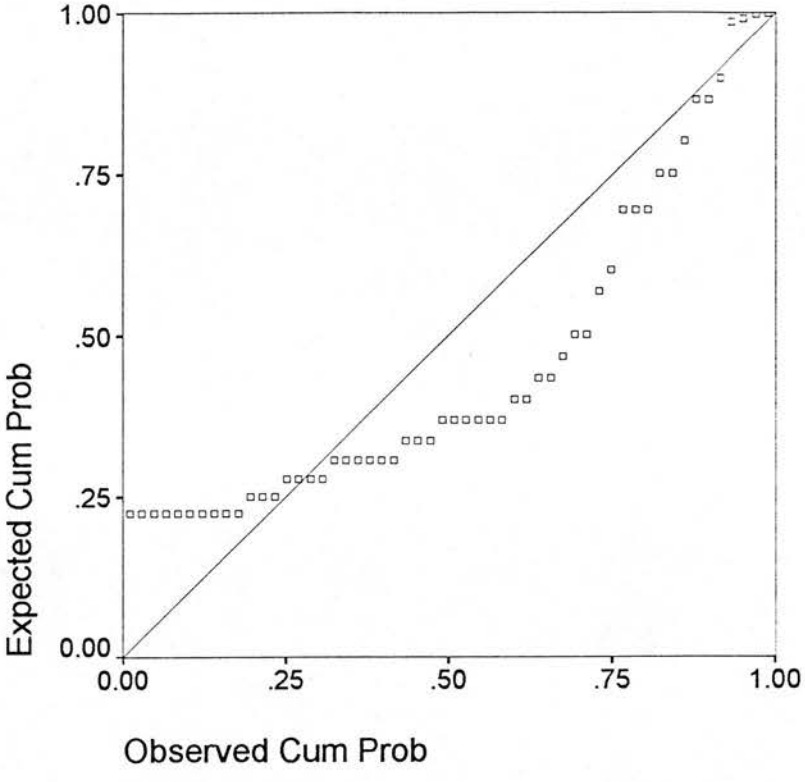


## 6. MASLACH BURNOUT INVENTORY EMOTIONAL EXHAUSTION SUBSCALE (mean scores)

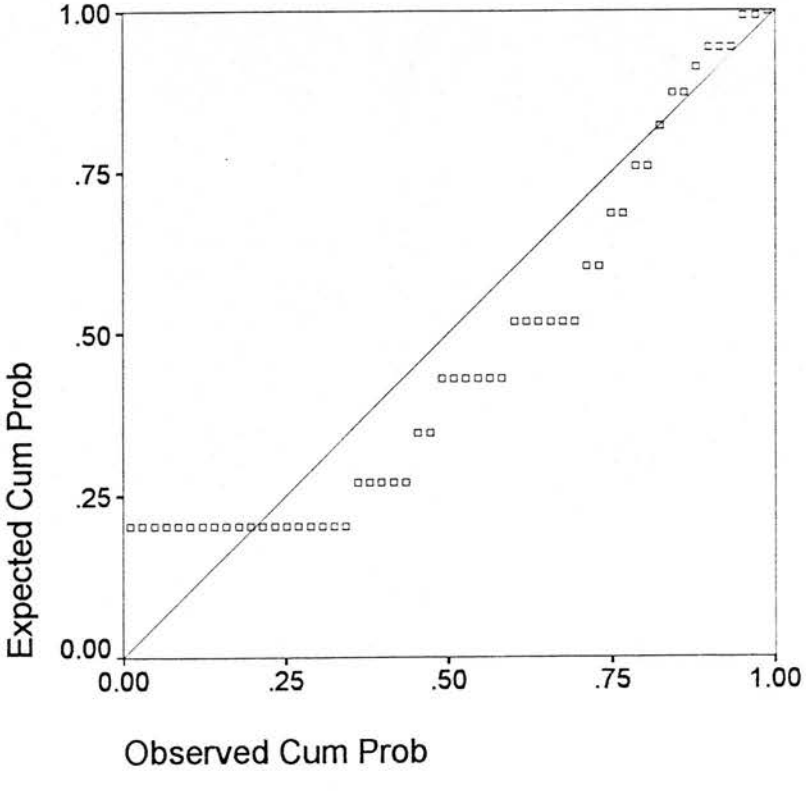


## 7. GENERAL HEALTH QUESTIONNAIRE

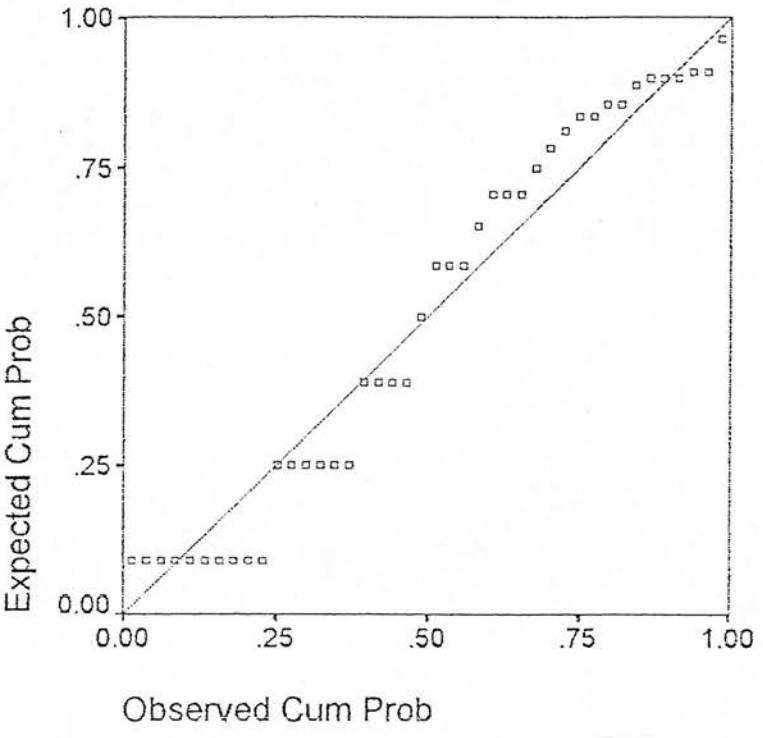
### a) OVERALL MEAN SCORES




### b) SOMATIC SYMPTOMS SUBSCALE (mean scores)



## 8. NUMBER OF DAYS SICKNESS ABSENCE OVER A ONE YEAR PERIOD



# APPENDIX FIVE

## "SAMPLE SIZE"

## FORMULA TO ESTABLISH APPROPRIATE SURVEY

**SAMPLE SIZE:-**

1.

$$\frac{\left(\begin{matrix}\text{Proportion high}\\ \text{antibody titres}\end{matrix}\right)\quad\left(\begin{matrix}\text{Proportion low}\\ \text{antibody titres}\end{matrix}\right)}{\text{Standard Error}^2} = N$$

2.

$$\frac{(.51)\ (.49)}{0.07^2} = N$$

3.

$$\frac{0.25}{0.0049} = 51$$

4. 51 = An adequate sample size in this study.

**Present Study N = 54**

(Source: Narins 1994)

# APPENDIX SIX

## "TWO HALVES ANALYSIS"

## "TWO HALVES ANALYSIS"

### a) GROUP ONE (N = 27)

* * * * M U L T I P L E R E G R E S S I O N * * * *

Listwise Deletion of Missing Data

Equation Number 1 Dependent Variable.. TITRE HEPATITIS B

Block Number 1. Method: Enter ANXBYSOM EEXBYDEP SOCQMA

Variable(s) Entered on Step Number
1.. SOCQMA SENSE OF COHERENCE QUESTIONAIRE MANAGEAB
2.. ANXBYSOM had1a multiplied by ghq1a
3.. EEXBYDEP mbieel multiplied by had1d

| | |
|---|---|
| Multiple R | .62357 |
| R Square | .38884 |
| Adjusted R Square | .30912 |
| Standard Error | 328.63456 |

Analysis of Variance

| | DF | Sum of Squares | Mean Square |
|---|---|---|---|
| Regression | 3 | 1580395.12710 | 526798.37570 |
| Residual | 23 | 2484015.53957 | 108000.67563 |

F = 4.87773 Signif F = .0091

---------- Variables in the Equation ----------

| Variable | B | SE B | Beta | T | Sig T |
|---|---|---|---|---|---|
| ANXBYSOM | 10.883101 | 4.067939 | .436848 | 2.675 | .0135 |
| EEXBYDEP | -5.464873 | 2.332651 | -.460771 | -2.343 | .0282 |
| SOCQMA | -18.303625 | 8.345779 | -.431278 | -2.193 | .0387 |
| (Constant) | 1567.773671 | 463.046330 | | 3.386 | .0025 |

**b) <u>GROUP TWO</u> (N = 27)**

* * * * M U L T I P L E R E G R E S S I O N * * * *

Listwise Deletion of Missing Data

Equation Number 1 Dependent Variable.. TITRE HEPATITIS B

Block Number 1. Method: Enter ANXBYSOM EEXBYDEP SOCQMA

Variable(s) Entered on Step Number
1.. SOCQMA SENSE OF COHERENCE QUESTIONAIRE MANAGEAB
2.. ANXBYSOM hadla multiplied by ghqla
3.. EEXBYDEP mbieel multiplied by hadld

| | |
|---|---|
| Multiple R | .62304 |
| R Square | .38818 |
| Adjusted R Square | .30838 |
| Standard Error | 323.61267 |

Analysis of Variance

| | DF | Sum of Squares | Mean Square |
|---|---|---|---|
| Regression | 3 | 1528234.48174 | 509411.49391 |
| Residual | 23 | 2408678.70345 | 104725.16102 |

F = 4.86427 Signif F = .0092

---------- Variables in the Equation ----------

| Variable | B | SE B | Beta | T | Sig T |
|---|---|---|---|---|---|
| ANXBYSOM | 10.578841 | 4.006340 | .431456 | 2.641 | .0146 |
| EEXBYDEP | -5.516846 | 2.297403 | -.473480 | -2.401 | .0248 |
| SOCQMA | -17.714054 | 8.182547 | -.426853 | -2.165 | .0410 |
| (Constant) | 1551.107333 | 454.870029 | | 3.410 | .0024 |