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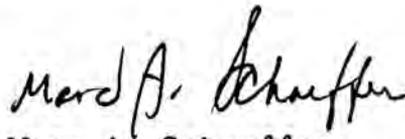
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ABSTRACT

Title of Dissertation: Measures of Self-report, Urinary Catecholamines, and Salivary Immunoglobulin-A in Victims of Chronic Stress

Marc A. Schaeffer, Doctor of Philosophy, 1985

Dissertation directed by: Andrew Baum, Ph.D., Department of Medical Psychology

The present investigation was conducted to examine relationships among self-reports of health, urinary catecholamines, and salivary immunoglobulin A (s-IgA) in victims of chronic stress. Previous research has identified markers of stress in samples of individuals living near the damaged nuclear power plant at Three Mile Island (TMI) and a group living adjacent to a toxic waste site in Delaware (DEL). Comparisons were made on demographically matched subjects from TMI, DEL, and a sample of controls from Frederick, Maryland.

Chronic stress consequences have been noted over 2 years after the TMI accident and eighteen months after DEL residents were informed of toxic waste threat. This study was not concerned with harmful exposure, but focused upon responses to environmental threat. It was hypothesized that TMI and DEL subjects relative to controls would exhibit increased self-report of symptoms, elevations in urinary catecholamines, and a reduction of s-IgA concentration. Since s-IgA protects against bacterial and viral invasion, it was thought that lowered immunoglobulin among TMI and DEL subjects would yield a possible explanation for enhanced susceptibility to infection in these

groups.

Data were collected fifty-eight months after the TMI accident and eighteen months after announcement of the toxic waste site in Delaware. Subjects completed questionnaires assessing health status. Specimens of urine and saliva, collected at a standardized time to control for circadian rhythm, were assayed by radioenzymatic COMT technique and single radialimmunodiffusion respectively.

Although TMI and DEL subjects reported more health problems and exhibited higher catecholamine concentrations relative to controls, the s-IgA measure was not distinguishable among the groups. Further, s-IgA level was not associated with catecholamine concentrations, but was positively correlated with elevated health complaints. In addition, increased health problems were correlated with elevations in catecholamine levels. While it is possible that s-IgA may not be sensitive to stress, it is also possible that stress intensity was insufficient to have impact. Although, elevations of symptom reporting and catecholamines were found in TMI and DEL subjects, these measures were not clinically significant. Nonetheless, the long term nature of these deviations from homeostasis could be cause for concern.

MEASURES OF SELF-REPORT, URINARY CATECHOLAMINES,
AND SALIVARY IMMUNOGLOBULIN-A
IN VICTIMS OF CHRONIC STRESS

by

Marc A. Schaeffer

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Introduction

A desperate disease requires a dangerous remedy....Guy Fawkes

Stress has received considerable attention as being a contributor to disease, yet the mechanism underlying this association remains unknown. However, a promising solution to this mystery points to immune system deficiencies as an important link in the stress-disease process. A common naive notion is that stress causes disease. More appropriately stated, stress enhances susceptibility to disease. Although stress may be necessary in order to disrupt health, it is generally not sufficient.

On an intuitive level, or through personal experience, it is possible to conceptualize behavioral, cognitive, and emotional factors that influence the body's defenses. The classical motherly declaration is for example, "if you do not get some rest, you are going to get sick." Moreover, phobic individuals respond to specific dreaded stimuli with a range of symptoms or physiological reactions. For example, individuals who are afraid to fly, often show signs of nausea, hives, fever, and heart palpitations when faced with having to fly. Similarly, it is not uncommon for a speech-anxious person to note debilitating symptoms including loss of voice prior to a public address. The relationship between a psychological state as anxiety, fear, grief, or even joy and the body's ability to resist infection,

allergies, or cancer leaves most scientists with a feeling of inadequacy of expressing the relationship. Simply knowing that the relationship exists is far from understanding the particulars in operation of the disease process or the ability to predict outcomes.

Researchers from several disciplines have joined together in attempting to explain the stress-disease process. It is no longer adequate to explore the psychosomatic aspects of disease without a broad knowledge encompassing psychology, physiology, neurology, and endocrinology. While psychologists have been studying the impact of individual's interactions with the environment, physiologists have been probing our neuronal and hormonal responses to human environmental interactions. Today our relationship with the environment is much more complex than it has ever been.

One major environmental problem concerns the use of nuclear power. The accident at Three Mile Island (TMI) in March, 1979, was an unprecedented event and continues to be a unique experience with technological disaster. The events of the accident itself, and subsequent developments related to radioactive contamination have created a tense environment for TMI residents. Researchers have provided evidence indicating that TMI residents have continued to feel threatened and stressed (Bromet, 1980a; 1980b; Baum, Gatchel, & Schaeffer, 1983). Another type of technological problem producing unrest similar to that noted at TMI, involves a group of Delaware residents who live adjacent to a chemical waste site (DEL). The size of the site and toxic nature of the chemical waste limits the feasibility for making the adjacent neighborhood a safe place to live. Data collected among those living near the toxic waste site has

indicated a response similar to that seen at TMI. If the TMI and Delaware residents are truly experiencing chronic stress, these samples of threatened individuals are a good group to study for stress-related problems. One problem worthy of investigation is the possibility of immune system deficiencies, particularly since TMI and DEL area residents have already displayed an elevation of health complaints (Schaeffer & Baum, 1982; Fleming & Baum, in preparation).

Although many investigators have examined immune system effects in laboratory environments, relatively few studies have been performed in the field. While most of these studies have related acute stress to immune response, the long-term nature of chronic stress is equally important. This proposal focuses on the relationship between chronic stress among DEL and TMI residents and the possibility of immune system suppression. Specifically, the levels of a salivary immunoglobulin will be compared among samples at TMI, DEL, and a control group.

At least two research groups (McClelland, Floor, Davidson, & Saron, 1980; Jemmott, Borysenko, Borysenko, McClelland, Chapman, Meyer, & Benson, 1983) have collected salivary immunoglobulin as an index of immune system function and have reported a relationship between stress and concentration of salivary immunoglobulin. Relying upon salivary immunoglobulin relative to other immune system measures is apparently relatively easy, non-invasive, and inexpensive. An attempt also will be made to link immune system suppression with disturbances of health. Since there is an abundance of research suggesting that catecholamines influence immune function, the relationship between immunoglobulin and catecholamines also will be examined.

Stress

The remedy is worse than the disease....Bacon

People often ruminate over their problems, worries, and concerns. Psychologists refer to these worries and concerns as stress. However, "stress" has become a banal catch-all to describe the stereotyped response to a variety of threatening stimuli. Further, stress has been used in so many different ways that its usage triggers a semantic nightmare. This section attempts to put some of the elements of what is known about stress in a coherent perspective. Stress is intricate, and it is also dynamic, so that it is continuously changing. Stress may be defined as a complex of emotional, mental, behavioral, and biological responses to the threat of being harmed or to loss of something valued. Thus, stress actually refers to a process that is not only specific, but also central to the relationship between people and their environments. The definition above and that which currently is known about stress comes from decades of research. In the early part of this century the study of stress focused primarily on physiological responses. For example, the laboratories of Cannon (e.g., Cannon, & de la Paz, 1911) and Selye (1936) were busy documenting physiological phenomena associated with stressful experiences. The study of stress however, has been moving from the purely physiological stance to one representing more of an interaction between physiology and psychology.

Selye's General Adaptation Syndrome. Hans Selye (1956) presented the first comprehensive influential model of stress which he

called the General Adaptation Syndrome (GAS). Selye observed that many stressors caused the same three consequences. This response triad included enlargement of the adrenal glands, involution of the thymus, and ulceration of the stomach. Selye found that not only did injection of impure extracts cause this to occur, but other stressors in the form of heat, cold, x-ray exposure, and exercise also could bring about the same triad of responses. Because a wide variety of stimuli could cause the same consequences, Selye concluded that the stress syndrome was nonspecific. That is, all stressors give rise to the same responses by the body. However, Selye's choice of the term nonspecific led many critics to attack his theory. Some studies have supported the notion of nonspecific stress responses and others have found different responses to different events (Baum, Singer, & Baum, 1981; Frankenhaeuser, 1978; Mason, 1975). Whether a stress response is the same for all stressful events remains unclear.

Selye described the GAS as a syndrome occurring in three separate stages. First, the alarm reaction is experienced as an organism becomes aware of the stressor and preparations to resist the stressor are made. When reserves are ready, the organism enters a stage of resistance, applying various coping mechanisms and usually achieving suitable adaptation. When adaptation is not achieved however, the organism experiences prolonged exposure to a stressor, and is at risk for irreversible damage or death in the final exhaustion stage. Adaptive reserves are depleted by long term conflict with stressors and resistance is no longer possible. The result of exhaustion is likely to be the onset of diseases of adaptation such as cardiovascular disorders, kidney disease, and arthritis.

The importance of the GAS is in its depiction of how stress can lead to exhaustion and resulting physiologic damage. Thus, Selye's model focused on a sequence of threat, biologic response, and recovery. Selye's notion of nonspecificity however, seems to ignore psychologic mechanisms in determining response to a stressor.

Psychobiological models of stress. A major development in stress research in the 25 years since Selye presented the GAS has been the integration of psychological mechanisms into what essentially remains a biological model. John Mason (1975) challenged Selye's stress model by arguing that the stress response is neither nonspecifically induced nor represented by a single syndrome and that psychological awareness of noxious events may be necessary for stress to occur. Using heat as a physical stressor, Mason demonstrated a lack of stress-like adrenal responses when perception and sensation of the stressor were eliminated. Another study (Symington, Currie, Curran, & Davidson, 1955) of two groups of dying patients also supports this idea. In this study one group was made up of patients who died after being unconscious (in a coma) and the other of patients who were conscious until death. Autopsies of the two groups revealed adrenal enlargement for the conscious group and no adrenal changes for the coma group.

Armed with data that distinguishes different patterns of responses associated with stressors varying in the degree of anger and fear, or uncertainty, Mason has suggested an element of specificity in stress responses. Earlier studies of emotion suggested that specific emotions lead to specific physiological reactions, but other studies have indicated a nonspecific emotion response (Ax, 1953; Maranon, 1924;

Schachter, 1957; Schachter & Singer, 1962). Mason (1975) was able to discriminate between uncertainty and challenge on the basis of hormonal profile. Where uncertainty produced increases in corticosteroids, norepinephrine, and epinephrine, challenge elicited only increases in norepinephrine and corticosteroids.

Still more support for a psychological component of stress comes from the laboratory of Marianne Frankenhaeuser and her colleagues. The Frankenhaeuser group has concentrated on measures of the catecholamines epinephrine and norepinephrine. These researchers have reported that the catecholamines affect emotional and cognitive functioning and that they are secreted in response to purely psychological events. In one study, increases in levels of epinephrine and norepinephrine were associated with decreasing amounts of control over electric shock (Frankenhaeuser & Risler, 1970), and in another, both understimulation (not having enough to do) and overstimulation (having too much to do) were associated with rises in epinephrine and norepinephrine levels (Frankenhaeuser, Nordheden, Myrsten, & Post, 1971).

Frankenhaeuser's work is important because it demonstrates the pervasive role of psychological factors in eliciting a primary physiological symptom of stress. This physiological response is in turn associated with psychological responses including emotionality and changes in cognitive ability. It also suggests a kind of nonspecificity similar to Selye's, though involving hormones other than corticosteroids. That is, the same reaction (elevations of the catecholamines epinephrine and norepinephrine, as well as cortisol) occurs in response to a variety of psychological events. The list of stressors that can trigger this response includes urban commuting, job

dissatisfaction, loss of control, conflict, taking examinations, noise anticipation of aversive events, and boredom (see Collins & Frankenhaeuser, 1978; Frankenhaeuser, 1972; 1977; 1978; Johansson, 1977; Lunberg & Frankenhaeuser, 1978; Singer, Lundberg, & Frankenhaeuser, 1978).

It would be misleading to give the impression that the study of stress dwells solely upon biological aspects as catecholamines and corticosteroids. Social and psychological variables have been studied to consider the overall pattern of stress responses. While the biological factors are important because they are responsible for much of what we feel or do under stress, psychological factors have been associated with underlying bodily changes including susceptibility to illness and disease.

Psychological stress. Lazarus and others have emphasized the psychological dimension of the stress concept. Of particular importance to Lazarus is the role of perception and cognitive appraisal in the stress response. He suggests for example, that unless we perceive a situation as threatening, we will not experience stress. If this concept of perception and appraisal is extended to Selye's work, the animals in those experiments must have sensed or been aware of the danger of Selye's stressors in order to respond in the manner of the GAS. Recall that the study of Symington et al. (1955) found that unconscious dying patients showed no evidence of stress (as measured by adrenal activity) relative to a group of patients who were conscious. Thus, two individuals exposed to the same situation may have totally different reactions based upon their subjective appraisal of the ongoing environmental events. Mason also found a reduction of stress

response when awareness of the stress was blocked.

Lazarus' laboratory provided support for the importance of appraisal in a series of experiments in which different groups of subjects were exposed to the same stressful film, but each film had a different sound track or different pretext for viewing. These different contexts manipulated appraisal of the films. For example in one study (Speisman, Lazarus, Mordkoff, & Davidson, 1964) three groups of subjects were shown the same film depicting primitive initiation rites that involved rather unpleasant and crude genital surgery. A different sound track accompanied each film. One group heard narration emphasizing pain, mutilation, and possible disease consequences (trauma condition); another group heard a script in which the pain and consequences were denied and the participants in the rites were represented as willing and happy (denial condition); and the third group heard a detached description of the rites from an anthropological perspective (intellectualization condition). Results indicated that stress responses were reduced for subjects in the denial and intellectualization conditions relative to the trauma condition. It was argued that the denial and intellectualization groups appraised the film's events as less threatening, while the audio track in the trauma condition emphasized those aspects of the film that were more likely to be stressful.

By pointing out that stressors can be psychological, Lazarus (1966) made the study of stress more complex and challenging. As with other aspects of behavior, psychological stressors cannot be measured directly. Instead, they must be inferred from responses or defined in terms of the situations in which they arise. It is worth noting

however, that an experience of extreme anxiety or any severe emotional upset usually leads to changes in behavior (see Rogers, Dubey, & Reich, 1979). With this concept in mind a certain caution must be taken in linking stress with psychological distress and particularly psychophysiological disorders.

The range of behaviors that people use to alleviate stress is broad. Drug taking, changes in diet, alterations in the sleep/wake cycle are just some of the means used in coping with stress. Thus, in talking about stress and how it produces somatic change, it is useful to clarify whether stress itself has produced change by direct physiological change or whether the change is indirect, a function of behavioral change which in turn has affected health or how people feel.

Lazarus has distinguished between two different types of coping. One type of coping addresses the situation or the problem. This form of coping involves an individual trying to manipulate or alter his or her relationship to a stressful situation through direct action. People may change a stressful situation, flee, or otherwise remove the physical presence of a stressor. Alternatively, people may seek information about a situation in order to understand problems better and predict future events. A second type of coping deals with emotional response to a situation. When it is either too difficult, too costly, or inappropriate to manage direct action, a form of palliative coping can be applied. Palliative techniques of adapting to a stressor involve reappraising the stressful situation by altering one's internal environment. Abusing drugs or alcohol, learning to relax, creating or using psychological defense mechanisms, and engaging in meditation are examples of this form of coping.

More recently, Lazarus and Launier (1978) have identified four modes of coping. Direct action is included, as is palliative coping. Information seeking is viewed as a separate approach, and doing nothing at all is also discussed as a way of coping with stress. Such a classification allows us to group a wide variety of different behaviors under common elements. Thus, someone who copes with a stressful event by thinking about its positive aspects may achieve the same thing as another person who denies or ignores the event.

Coping is an important determinant of the effects that stress may have. Both the way in which one copes and whether he/she is successful in reducing the threat or danger experienced affect what happens. For example, if one is a heavy smoker and distressed about it, there are a number of alternatives to help one cope. On the one hand, one can directly address the situation and quit smoking. On the other hand, one can continue smoking and reduce one's distress by denying that anything bad will happen. While successful direct action (one kicks the habit) eliminates the problem, denial may not - one may come to recognize coughing and shortness of breath as obvious consequences of smoking and these symptoms may become impossible to deny. One would guess that under such conditions, stress might reoccur.

Consequences of stress

Stress affects responses in 3 different levels or modes including physiological, behavioral, and psychological. To a certain

extent, these effects are part of stress; the sensations that accompany stress, include changes in blood pressure, heart rate, and skin conductance are related to physiological arousal involved in stress. Each of these three modes of responses will be discussed below.

Physiological effects. There are a number of physiological changes that accompany stress, and many appear to be related. One mechanism of stress responses is through the sympathetic nervous system. Results of arousal of this system during stress include increased adrenal medullary and cortical activity, increased heart and respiratory rate, increased blood pressure, and increased perspiration. These effects are part of what Cannon (1929) described as the "fight or flight" response to danger. When danger is recognized, this arousal prepares us to respond either by resisting it or fleeing it. Thus, stress involves arousal and readying of the organism.

Chronic sympathetic arousal is reflected by increases in adrenal medullary function. The adrenal medulla secretes the catecholamines epinephrine and norepinephrine into the blood. Measures of these two hormones have proven to be particularly useful in documenting a response when stress is chronic (Frankenhaeuser, 1975). Studies have found associations between occupational stress and catecholamine excretion (Frankenhaeuser, 1978) and several researchers have noted that stress increases catecholamine levels in plasma and urine (e.g., Baum, Grunberg, & Singer 1982; Levi, 1972; Mason, 1975). The adrenal cortex also is responsive to a wide variety of stressful stimuli. Research has shown that conflict, frustration, loss of control, and job pressure are all responsible for elevating levels of urinary cortisol (Collins & Frankenhaeuser, 1978; Lundberg & Frankenhaeuser, 1978; Rose,

Jenkins, & Hurst, 1978).

Stress appears to have other biological effects as well. Mason (1974) has used two standard physiological concepts to summarize these many changes. One set, catabolic processes, involves sympathetic nervous system activity mobilizing the body and is directed towards breaking down stored energy into available forms and readying the individual to respond. This class of changes is similar to Cannon's depiction of response to danger. The other set includes changes that are directed towards rebuilding tissue and energy stores. This anabolic response involving the activation of the parasympathetic nervous system usually follows the first set and ordinarily would occur following exposure to a stressor.

Behavioral effects. There are many behavioral effects of stress. Some are coping behaviors - withdrawal from crowding stress, for example, can be an active coping strategy or an effect of giving up or failing to cope successfully (e.g., Baum & Valins, 1977; Rodin, 1976). Other behavioral effects are consequences of coping. Studies have suggested, for example, that stress can cause people to narrow their attention - focus on a small part of their surroundings - and that this can reduce their sociability, and ability to detect environmental change (see Cohen, 1978). Research also suggests that stress can interfere with task performance. For example, it has been found that arousal can increase task performance to a point, but that too much arousal can interfere and result in poorer performance (Evans, 1978). To the extent that stress involves arousal, performance on tasks should also be affected.

Researchers have also found that stress can cause aftereffects -

effects that show up after the stressor has been terminated (Cohen, 1980). In one series of studies, subjects were exposed to noise and, in some conditions, showed effects after the noise had stopped (Glass & Singer, 1972). These effects included reduced tolerance for frustration (giving up quickly on frustrating tasks) and poorer performance on a proofreading task.

Psychological effects. It is difficult to separate psychological effects from the processes involved in other consequences of stress. Poor task performance may reflect reductions in one's ability to concentrate or one's motivation to succeed. The degree to which either of these causes is "psychological" as opposed to behavioral is a matter of speculation. However, stress is related to emotional states; studies have suggested that irritability, apprehensiveness, depression, psychiatric problems, and annoyance are associated with exposure to stress (Baum et al., 1983; Davis, 1975; Rose, Jenkins, & Hurst, 1978; Frankenhaeuser, 1978).

Factors that influence stress

Clearly, a number of factors are involved in appraisal of stressors and whether any of the effects noted above will occur. Responses to stressors are necessarily related to the way in which a stressor is perceived. A number of factors are responsible for the manner in which we perceive whether stimuli are stressful or not. It is often stated that such factors mediate or govern the stress response. The factors that affect stress include attitudes toward

stressors, perceptions of risk, social support, and control. It can probably be argued that perceived control is the common denominator for each of these factors.

Attitudes toward stress. Environmental annoyances as high levels of noise have been related to attitudes and stress. While high levels of noise in areas surrounding airports are highly correlated with noise annoyance reported by affected residents, the relationship between noise exposure and individual ratings of annoyance is generally not strong (Wilson, 1963; MIL Research, 1971). In fact, Tracor (1971) found that individual annoyance ratings were more highly correlated with several attitudinal measures than with various indices of physical exposure to noise. Several studies have supported this finding by demonstrating that attitudinal factors account for considerably more variance of annoyance than actual noise levels (Tracor, 1971; Leonard & Borsky, 1973; Deutsche Forschungsgemeinschaft, 1974). Further, there is some evidence (Cederlof, Honason, & Sorenson, 1967) that manipulating people's attitude changes their evaluation of aircraft noise. By simply giving one group of subjects positive findings of a questionnaire that they had completed and a nice book on the Air Force resulted in fewer reports of the inconvenience of the noise as compared to a group that received no manipulation.

Perception of risk. Assessment of risk appears to be influenced by certain biases in perception. It is often impossible or too costly to collect all available information for decision making. As a result various types of shortcuts are used to simplify the means of solving problems and tasks. Unfortunately, shortcuts may sometimes yield inaccurate evaluations due to oversimplification or

misinterpretation of the objective facts. Overconfidence in judgments or denial of reality are possible outcomes. Overconfidence in judgments is closely related to the desire for certainty, and uncertainty can produce stress, particularly if experienced for long periods. One response to stress of uncertainty is simply to deny that uncertainty exists. For example, Kates (1962) found that some of the flood victims he had interviewed flatly denied that their area would ever be flooded again. These denials were supported further by rationalizations that the flood was a freak accident and that new dams would prevent any future problems.

People believe that an event is more likely to occur if they can imagine it or easily recall examples of it. Lichtenstein, Slovic, Fischhoff, Layman, & Combs (1978) asked subjects to estimate the frequency of deaths due to a number of different causes. While the subjects were fairly accurate in assessing which causes were most and least frequent, many common causes of death (e.g., motor vehicle accidents, cancer) were underestimated and rare, but more dramatic death causes (e.g., lightning and tornadoes) were overestimated.

Social support. Another mediator of stress is social support. Social support is the feeling that a person is cared about and valued by others and that he or she belongs to a social network (see Cobb, 1976; Rabkin & Streuning, 1976). Although it has been believed that good interpersonal relationships can protect us from many ills, the effects of having or not having social support have not always been shown clearly. A number of studies suggest that having friends and confidantes helps people cope with stress (e.g., Cobb, Kasl, French, & Norstebø, 1969; Gore, 1973; Cohen & McKay, in press).

Chen and Cobb (1960) discuss the influence of social support as it reduces the degree to which stress can lead to onset of disease. Other research has indicated that social support can facilitate recovery from illness (see Wolff, 1968). Higher levels of social support have also been associated with improved adjustment during grief and bereavement (Parker, 1972; Burch, 1972).

Perceived control. Perceived control has been shown to be a powerful mediator of stress. Glass and Singer (1972) considered the effects of controllability and predictability in their studies of stress due to noise. The perception that the noise could be accurately anticipated or even eliminated resulted in fewer aftereffects of the noise stress. Sherrod (1974) found the same relationship for stress due to crowding; and Rodin, Solomon, and Metcalf (1978) reported that perceived control reduced crowding stress. Some studies have determined that the stress of surgery or of unusual medical procedures can be reduced by providing patients with accurate expectations of sensations (see Johnson, 1973; Johnson & Leventhal, 1974).

It is clear that attitudes, social support, and perceptions of risk and control affect responses to stress, but the underlying mechanisms remain a mystery. Current speculation involves the relationship between these factors and alterations of the function of the autonomic nervous system. For example, if one perceives control over a potentially stressful situation as driving on ice-slick roads, one may be insulated from involuntary activation of the autonomic nervous system. One's cognitions that he/she has demonstrated mastery on ice-slick roads and the diminished perception of threat could prevent fear and worry and accompanying tensing of muscles and stomach

activity. Similarly, an individual with a developed social support network has several possible directions to turn for help if a crisis arises. Simply knowing that we have friends who are interested in helping us with problems can relieve anxieties and buffer our autonomic responses to stress.

Now that a variety of the prominent features of stress have been discussed, it is worth asking the question: Why study stress? As with other areas of psychology we want to better understand and predict behavior and its consequences under a wide range of circumstances. It is quite clear that there is a connection between stressful events, emotional reactions, and physiological disturbances. The precise mechanisms by which stress produces disease are unknown. The following section on illness and behavior will discuss some of the most recent theory and evidence linking stress with disease.

Behavioral factors in illness

Stop it at the start, it's late for medicine to be prepared when disease has grown strong through long delays....Ovid

This section focuses on the relationship between behavior and illness. Our behavior covers a wide range of activities including working, sleeping, and leisure time. We tackle problems at work, celebrate our triumphs, and agonize over our defeats. However, at some points our normal activities and behaviors are disrupted by poor health. Such health disturbances customarily have been referred to as disease or illness.

Disease. When there is any pervasive harmful disturbance of the body's equilibrium, the label disease applies. Specifically, disease can be considered a definite morbid process having a characteristic train of symptoms. An illness may affect the whole body or any of its parts, and its origins, development, and prognosis may be known or unknown. In the past century the study of illness and disease particularly through epidemiological methods has refined our understanding of the mechanisms by which we become ill. In fairly recent times the scope of the disease process has been broadened to include not only the interaction between the host and intruding parasites or pathogens, but also significant interactions of humans with a wide variety of noxious forces in the environment (e.g., stress caused by annoying, frustrating, or distressing circumstances as in crowding, job stress, or bereavement). Concepts of disease have also been enlarged. Obesity, alcoholism, and drug abuse have been recognized as disease (e.g., Stunkard & Wolff, 1958; Himwich, 1957), although these conditions clearly involve a voluntary behavior pattern at onset prior to development of dependency. Further, some diseases unfold over the entire life cycle. For example, atherosclerosis, which usually results in stroke or heart disease, is usually seen in later decades of life and results from both genetic and environmental influences.

Krantz et al. (1981) have classified contributors to illness into 3 basic mechanisms: direct psychophysiological effects, health impairing habits, and reactions to illness. Direct psychophysiological effects refer to results of stress or bodily changes related to psychosocial events. Representative effects include changes in

cardiovascular reactivity or immune functioning. For instance, stress can cause both increased heart rate and decreased effectiveness of the immune system. These changes may, in turn, cause illnesses including heart disease, cancer, and arthritis. Recall that in the stress section we saw that stress can cause a number of physiological changes. In this section it will be shown how some of these changes can be linked to illness.

There is also extensive evidence for the ill-effects of health-impairing habits. Cigarette smoking, diet, lack of exercise, and coping styles among other aspects of one's lifestyle have been associated with physiological changes and enhanced susceptibility to disease.

Reactions to illness are comprised of behavioral factors that affect the treatment of illness. These factors include one's willingness to report symptoms or seek medical attention. Failure or delay in reporting symptoms can increase the likelihood of an illness progressing to a point where it is more difficult to treat. Further, once a patient is diagnosed, lack of compliance with treatment regimentation can also result in health complications.

These three mechanisms of behavioral influence should not be perceived to be necessarily independent or mutually exclusive. Stress and the physiological effects that accompany it may be exacerbated or moderated by one's coping style or reaction to being ill. However, the distinctions among these mechanisms are important in explaining the ways in which behavioral factors can affect health and illness.

Behavioral models of illness. While there is now a greater movement to acknowledge psychological and behavioral factors in

illness, some health professionals still adhere to a biomedical model of disease. This position is based on the belief that illness is simply a matter of biology. Sickness is caused by microorganisms or by some internal malfunction. Clearly, this perspective has been important, particularly in treating and preventing infectious diseases. We have seen a virtual end to several diseases achieved by breakthroughs in medical research. This biomedical model fails however, to acknowledge behavior patterns, or how we respond to our environment. Some diseases were already mentioned that do not fit the biomedical model. Obesity, alcoholism, hypertension, and coronary artery disease appear to develop over a life-time and are apparently caused by an interaction of a number of factors including diet, working habits, smoking, and response to stress.

In distinction to the biomedical model is a more comprehensive perspective dealing with the interaction between biological reactions and psychosocial factors. This more integrative orientation, known as the diathesis-stress model, states that biochemical vulnerability, although necessary, is not sufficient to explain the onset of many diseases (Levi, 1974). This approach is a statement of the ways in which psychological, environmental, genetic, and physiological elements should be considered in the description of disease. Each of these elements is continually interacting with the others. While one or more of these factors may be applying negative pressures toward illness, one or more other factors may be simultaneously supporting good health. An example will help illustrate a real world phenomenon.

Many health workers including physicians, come in contact with dozens of sick people in the course of every work day. Interestingly,

these overexposed health care providers have no higher illness rates than normal (e.g., Jemmott & Locke, 1984; Youmans, 1975). Further, these health professionals can actually show positive blood tests for some illnesses, yet not manifest even the slightest symptom. One of the goals of this section is to illustrate what is known about this phenomena. That is, why some people seem to be illness-prone or susceptible to disease and others are not. Selye has categorized conditions as coronary heart disease, cancer, and arthritis as diseases of adaptation. Essentially, this means that these diseases occur due to imperfections of the General Adaptation Syndrome. The remainder of this section will discuss these disorders. While these three health disturbances will be the only ones covered here, it is apparent that these are not the only diseases that have been associated with behavioral factors.

Behavior and disease

Recent studies have been conducted to explore the relationship between stress and sudden death (Eliot & Buell, 1979; Reynolds, 1974; Warheit, 1974). During the last years of the NASA program to put a man on the moon, workers who monitored and controlled the mission from the ground were studied. These workers were in exceptionally high pressured jobs and were being subjected to a rather stressful paradox. While their overall occupational goal was to put a man on the moon, these workers realized that accomplishment of this task would result in budget cut-backs and their unemployment. Initially, it appeared that

this stressful situation was responsible for increased rates of alcoholism and divorce as pressure to complete the mission increased. More alarming was a spontaneous increase in sudden death among relatively young NASA workers. These deaths, believed to be caused by heart failure, were almost fifty percent more frequent than would be expected in that age group. Further, autopsies revealed that heart damage was different than that caused by a heart attack in that the damaged hearts seemed to have been thrown into "overdrive" by heightened physiological activity of the nervous system (Eliot & Buell, 1979).

Eliot and Buell's (1979) research underscores the alarming relationship between stress and possible negative health outcomes. Unfortunately their findings are not isolated nor unique (e.g., Engle, 1971; Rahe & Lind, 1971). In addition to heart disease, research has identified a number of other diseases in which psychosocial factors enhance susceptibility to and/or exacerbate health problems. This list of health problems includes hypertension, cancer, arthritis, and peptic ulcer, among others.

Heart disease. Coronary heart disease is a general term that includes a variety of illness resulting from occlusion or narrowing of the arteries that supply the heart muscle with blood. Although heart attacks can be survived, heart disease is a prominent killer.

Risk factors for heart disease include heredity, age, diet, exercise, smoking, and cholesterol. However, according to Friedman and Rosenman (1974) a coronary behavior style (e.g., Type A) may contribute to more heart disease than all other risk factors combined. Type A

are characterized by extremes of competitiveness, aggressiveness, and time urgency. This pattern represents a coping style geared toward asserting control over potentially uncontrollable situations (Burnam, Pennebaker, & Glass, 1975).

Cancer. Cancer is the second leading cause of death in this country and more than 1 out of every 4 people will experience some form of cancer in their lives. The immune system is responsible for determining what is self and what is not self in the body. When the cells of the immune system encounter a foreign invader, they disable the intruder and remove it from the body as a waste product. When a malignant cell begins to grow, inappropriate cell surface antigens may be expressed. This could cause the malignant cell to be recognized as alien matter. For reasons that are not understood this rarely happens when malignant cells have grown to such a state as to be clinically recognized. However, studies of immunosuppressed patients (e.g. Cerilli & Hattan, 1974) indicate an increased incidence of tumors, suggesting that the immune system may reject many early cancers. Further, the experimental animal model of Vernon Riley has been devised to examine the detrimental effects of mild anxiety upon immunocompetence and resulting pathological outcomes. Riley and colleagues (see Riley, Fitzmaurice, & Spackman, 1981) claim to have demonstrated a tangible increased risk of the stressed subject with respect to malignancy.

Several studies have implicated immune deficiencies in association with behavioral factors. Some research has suggested that the loss of a close and important person is associated with reduced immune competence and could increase a person's susceptibility to

cancer (e.g., Bartrop, Luckhurst, Lazarus, Kiloh, & Penny, 1977; Tache, Selye, & Day, 1979). Such a loss has been also associated with suppression of immune system functioning. Social support also seems to be a mediating factor in the onset of cancer. Studies have suggested that a lack of close interpersonal ties has been associated with cancer (Thomas & Duszynski, 1974). In this study almost one-thousand medical students were followed for 15 years. Those who developed cancer after fifteen years reported they did not have very much family closeness.

Rheumatoid Arthritis. Rheumatoid arthritis (RA) is classified as an autoimmune disorder, yet increasing numbers of researchers are agreeing that there are psychosocial aspects of this disease. In RA the immune system produces biochemical agents that actually attack normal healthy joints. As a result joints become stiff, painful, and inflamed. If the process is not arrested, joints can be totally destroyed. As with cancer, RA is thought to critically involve immune system malfunction. Further, emotional stress has been implicated as an underlying factor in disturbing the immune system.

Some research has associated personality and coping style variables with RA. RA patients have been described by not only themselves, but also their healthy siblings as being nervous, tense, worried, depressed, high strung, moody, and inhibited in expressing anger (Moos & Solomon, 1965). Relative to normals, RA patients also have been found to resist major changes (e.g., job changes and moving residences; Mueller, Lefkovits, Bryant, & Marshall, 1961).

Although a vast portion of the population will be afflicted by heart disease, cancer, or rheumatoid arthritis in their life-time, some will be protected. Further, we know that in our natural state we are

highly colonized with potentially harmful bacteria; however, we do not always contract disease. It is interesting to speculate on the reasons why some individuals will maintain good health records and yet, other's health will be disturbed. More and more evidence links health problems with disruption of the body's natural defense mechanisms. Further, there is research to suggest that many factors including genetic predisposition, chronic stress, and coping style influence this natural system of defense.

Immune system function

Oh we trust that somehow good will be the final goal of ill....Tennyson

Before examining the evidence that stress alters immune functioning, an overview of the entire immune system will be helpful. The field of immunology is expanding at a very rapid rate. As a result, our knowledge of immune regulation and choices for measures of immune functioning are also changing.

Lymphoid cells. Because we live in a world filled with microorganisms of which some are hostile, we must have a means of identifying and resisting the ones that can potentially harm or kill us. The immune system is nature's mechanism for quickly recognizing, attacking, and destroying any foreign matter that enters the body. The main cells responsible for specific immunity are called lymphocytes. The work of Robert Good (1966) and Jonas Salk (1962) has defined two distinct lymphoid cell systems. Immature lymphocytes are produced by

stem cells in bone marrow. A population of lymphoid cells migrates through the thymus, a small gland located just under the breast bone in children (in humans it atrophies and nearly disappears by puberty) to develop into T cells. These T cells are the agents of cell mediated immunity and also help regulate B cells and antibody production (see below). They are responsible for destroying certain microorganisms, especially yeast and fungi, and for rejecting foreign tissue, including transplanted tissue and organs (Good & Gabrielsen, 1974).

A population of lymphocytes form the cells responsible for humoral immunity. These cells undergo maturation in an organ called the bursa of Fabricius in birds and in central lymphoid tissue in mammals. Lymphoid cells emerge from the bursa (or bursa equivalent) as B cells. B cells are called agents of humoral immunity because they synthesize antibodies that circulate freely in the blood. Humoral immunity is characterized by antigen reactions carried out by various classes of immunoglobulin molecules as IgA, IgG, IgM, IgE, or IgD.

Under the stimulation of a specific antigen, B lymphocytes divide, and some become memory cells, while others differentiate into plasma cells, actively producing a specific antibody. These antigen-antibody interactions are closely associated with the inflammatory process which isolates pathogen invaded tissue from undamaged tissue. The main activity of the circulating antibodies is to weaken disease causing bacteria.

When a foreign organism enters the body, circulating lymphocytes recognize the foreign particles as invaders and trigger an immunological alarm. Depending on the nature of the foreign organism, either T or B cells and sometimes both are called out to chemically

destroy the invader. It is believed that the continued presence of a foreign antigen stimulates both B and T cells to multiply, and the increased numbers of B cells to form more plasma cells which produce more antibodies, each tailor made to interact with the specific invader. T cells may also summon macrophages, large scavenger cells that literally devour and digest foreign cells. The circulating antibodies from the B cells attach to the antigens on the surface of the invading organism, rendering it more susceptible to macrophage ingestion. Alternatively, the antibody-antigen complex can interact with a blood protein substance called complement to lyse the foreign cell and kill it. Antibody can also bind toxins and deactivate them. T cells can directly attack foreign cells and kill them. T cells also function to regulate B cells by helping them recognize foreign antigens. By one or a combination of these processes, the trespasser is decomposed into chemical components that are used by the body or excreted as waste. Research suggests that immune activity is no less than a homeostatic mechanism regulating tolerance to self and intolerance to harmful invaders (Roitt, 1964).

IgG, IgM, IgE. IgG composes 70-80 percent of the serum antibodies in the human and is responsible for the antibodies to viruses, toxins and gram positive bacteria. IgM makes up between 5 and 10 percent of the total serum antibody, typically elicited by antigens of gram negative bacteria. IgE plays an important role in immediate hypersensitivity reactions as in allergic reactions.

IgA. Since the identification of IgA in normal human sera by Grabar and Williams in 1953 much has been learned about the activity of this antibody. IgA comprises about 10-20 percent of all

antibodies in serum and functions predominately in body secretions including saliva, nasal, and gastrointestinal secretions. IgA prevents colonization of the mucosal membrane. It has been clearly demonstrated (Smith, Purcell, Bellanti, & Chanock, 1966) that resistance to challenge with a major respiratory virus was more closely related to the antibody titers in nasal secretions than to serum antibody levels. These findings are of great significance in terms of the development of vaccines against respiratory disease.

Much less information is available concerning the role of secretory antibodies in local immunity and resistance to bacterial infections. Research has shown, however, that IgA plays some role in fighting both respiratory (Ehrenkrantz, 1966) and gastrointestinal infection (Smith & Little, 1922).

Stress and immune response

One important product of the stress response is its suppression of the immune system. Suppression of lymphocyte responsiveness and/or decreasing actual numbers of cells are suspected mechanisms by which stress may cause or facilitate illness (Stein, 1983). Both T cells and B cells are apparently affected.

Factors affecting immune response. There are a number of factors capable of influencing immune functioning. For example, aging reduces immune system strength (Weksler, 1983). Females appear to have twenty percent more IgM than do men; blacks have more IgG than do whites (Grunbacher, 1974). Food deprivation appears to reduce host

resistance if energy intake is substantially restricted (Kjellberg, Levi, Palmblad, Paulson, et al., 1977; Palmblad, Cantell, Strander, et al., 1976). Elements of the immune system including IgA follow a circadian rhythm (Weiner, 1972; Smolensky & Reinberg, 1977).

A systematic research program conducted by Riley and colleagues (see Riley et al., 1981) has connected a number of critical factors with immune responses in rodents. The most persuasive explanation, based upon results of Riley's work and other's (Riley & Spackman, 1977; 1978; Ader & Grotta, 1969; Mason, 1968; Monjan and Collector, 1977) for the tangible effects of stress on immunological impairment and associated tumor processes appears to be related to elevated levels of corticosteroids. There is a wealth of evidence that the basic cellular elements constituting the cellular elements of immunological apparatus, including macrophages, T cells and B cells, are all subject to modification, impairment, or destruction by adrenal cortical hormones (Monjan & Collector, 1977; Santisteban & Riley, 1973). Corticosteroids have been shown to have immunosuppressive properties and enhance tumorigenesis. The administration of synthetic corticoids has demonstrated effects upon tumor growth and host survival similar to that produced by stress (e.g., Riley et al., 1981). Research with humans also has implicated corticosteroid therapy in tumorigenesis (Cerilli & Hattan, 1974).

Some statistical evidence has been presented that suggests a positive association between stress and morbidity in various diseases including infectious illness (Rahe, 1972; Jacobs, Spiken, & Normal, 1969). More recently changes in host defense and psychological factors have been related to one another. Bartrop et al. (1977) investigated

the effect of bereavement on cell mediated and humoral immune functions as measured by mitogen challenge and E rosetting. They found that the mean T cell response to the mitogens phytohemagglutinin (PHA) and concanavalin A (Con A) was reduced approximately 8 weeks after the death of a spouse. There was a 10-fold difference in this T cell function at 8 weeks between the twenty-six bereaved spouses and controls. No difference was found in the number of T or B cells determined by rosetting. Further, radial immunodiffusion revealed no differences between bereaved and controls for serum IgG, IgA, or IgM. This demonstration has been followed by similar reports. Schleifer, Keller, McKegney, and Stein (1980) reported pre- and post-bereavement functions in six men whose wives were terminally ill. They measured total lymphocytes in blood, percentage and number of B and T lymphocytes by rosette formation, and response of blood lymphocytes in vitro to the mitogens PHA, Con A, and pokeweed (PWM). Relative to controls, bereaved subjects showed a dose response difference from PHA and PWM, yet no difference was found for number and portion of T or B lymphocytes. Further, several investigators have performed studies indicating that the risk of dying from a variety of diseases is at least twice as high for widows and widowers (Rees & Lutkins, 1967; Cox & Ford, 1970; Young, Bernard, & Wallis, 1970; Schoenberg, Carr, Peretz, & Kutacher, 1972).

Increases in interferon level, which are related to T cells, have been associated with the stress of seventy-seven hour sleepless vigil in which loud noise occurred (Palmlblad et al., 1976; Palmlblad, Petrini, Wasserman, & Akerstadt, 1979). Palmlblad also recorded perceived stress and anxiety as well as adrenomedullary,

adrenocortical, and pituitary hormones in these studies. Thyroid hormonal activity was increased as was previously shown by Levi (1972), whereas serum cortisol together with urinary catecholamine output was increased in the first study, but decreased in the second. These disparate hormonal reactions accompanying immune response modulation suggest that hormones are not the sole mediators of the effect of stress on the immune system.

Greene and associates (1978) have reported a statistically significant correlation between increased stress (defined by life change units combined with a high vigor score on profile of mood states) and a decrease in lymphocyte cytotoxicity. They hypothesized that the high vigor score reflected denial used as an unsuccessful coping mechanism in the face of increased stress. Similarly, Locke and his coworkers (1979) found a significant correlation between high stress and lowered levels of natural killer cell activity. Repeated determinations of natural killer cell activity (i.e., measured by the marker substance ^{51}Cr from target cells) were made in healthy human subjects and found to be related to a combination of life change stress and psychological symptoms during the previous year. By also considering psychological symptoms occurring during the same time, significant interactions were noted. Natural killer cell activity was highest for those subjects reporting fewest symptoms despite high levels of life change stress and was lowest for those subjects reporting most symptoms in the face of high levels of life change. This study did not find evidence of humoral immunity, but other investigators (Roessler, Cato, Lester, & Couch, 1979) studied subjects obtaining either a genuine influenza vaccination or a placebo, and

examined changes in antibody titers in relation to ego strength and life changes. Six months after the immunization, it was found that the combination of high measures of ego strength and lowered reporting of life events were related to high antibody titers.

Stress and IgA. A few recent studies have examined the relationship between salivary IgA (s-IgA) and stress. In one study (McClelland et al., 1980) males who displayed a stress-like coping style similar to Type A exhibited lower levels of s-IgA. In addition those subjects whose s-IgA concentration increased following infection with influenza virus did not become clinically ill. Conversely, subjects with low concentrations of s-IgA developed upper respiratory illness. Another study (Jemmott et al., 1983) reported on the relationship between academic stress and s-IgA. In a longitudinal design which evaluated dental students at 2 low stress and 3 high stress points in the academic calendar, a marked relationship emerged. Mean level of s-IgA was significantly lower at each of the high relative to low stress measures. Further, when a student perceived the program as more stressful, his or her s-IgA concentration was lower than when he or she perceived less stress.

It thus seems that concentration of s-IgA is not only related to susceptibility to upper respiratory infection, but also is stress sensitive. Consequently, the measure of s-IgA would be a useful measure in chronically stressed subjects who give increased report of respiratory infection. Although, it might be overly simplistic that respiratory infection results from stress induced suppression of s-IgA levels, the possibility exists and warrants more attention. Chronically stressed individuals similar to those living at TMI would

be excellent candidates in which this relationship could be studied.

To summarize, these studies have found that life changes and/or emotions evoked by life changes to be associated with depression of one or more immune reactions. A considerable amount of animal stress research also has indicated diminished lymphocyte response to mitogens (Monjan & Collector, 1977; Gialer, 1974), lymphocyte cytotoxicity (Monjan & Collector, 1977), and lymphocyte response to antigenic stimulation (Joasod & McKenzie, 1976). However, reported results are not uniform in finding immune suppression in response to stress. Some researchers have found either no relationships or even enhanced immune responding to stressful stimuli (Monjan & Collector, 1977; Mettrop & Visser, 1969; Folch et al., 1974). Since many of the experimental findings reported have used different paradigms including different stressors, different tests of immune response, and even different species, the impact on the immunologic picture has been clouded.

Neuroendocrine features of immunity

At the focus of hormonal influences of the immune system are the hypothalamus and pituitary. The hormonal and neural connections between these two structures represent a very important crossroad of the CNS and the ANS. The pituitary, often referred to as the master gland of the body, plays a significant role in carrying out the commands of the hypothalamus. Much of the investigation that is performed currently stems from Selye's early experiments on hormones governed by the hypothalamus and pituitary.

Hormonal influence. In conjunction with elevated corticosteroids, Selye (1956) described thymus involution as one of the hallmarks of the GAS. This finding lapsed largely because at the time the function of the thymus was still undetermined. Thymic hormones have since been discovered and found to influence T cell maturation as well as stimulate a number of T cell functions including suppressor effects (Bach, Bach, Carnaud, Dardenne, & Monier, 1977; Goldstein, Thurman, Low, Rossio, & Trivers, 1978). Thymectomy has been shown to increase tumor incidence in animals inoculated with tumor producing viruses suggesting T cell deficiency from thymectomy decreased host resistance to tumors (Comsa & Hook, 1973; Prehn, 1969).

Perhaps the most thoroughly studied hormones affecting the immune system are the corticosteroids. It is known that elevation of the adrenal cortical hormones results in a number of alterations throughout the immune system apparatus. It is further known that corticosteroid elevation is one of the hallmarks of stress (Selye, 1956). Effects of increased levels of corticosteroids include thymus involution, loss of tissue mass of the spleen, lymphocytopenia, reduced antibody formation, changes in lymphocyte migration patterns, and inhibition of lymphokine-macrophage communication (see Riley et al, 1981; Monjan, 1981; Ahlqvist, 1981).

Trying to unravel the tangles between the interrelated immune system and endocrine network becomes more complicated when one considers the possibilities based on the action at lymphocyte surface receptor sites. The list of hormones which have corresponding lymphocyte surface receptors includes norepinephrine, epinephrine, insulin, histamine, prostaglandin, and acetylcholine (e.g., Ahlqvist,

1976). In addition, the role of androgens, estrogens, and growth hormone have been reported to be associated with immunoenhancing effects (Rice, Abe, & Critchlow, 1978). Thus, it seems particularly important to examine the complex antagonistic and synergistic interrelationships between these hormones and attempt to determine patterns of secretory change associated with immune activity. Unfortunately, the resources required for this type of comprehensive investigation are extremely costly and beyond reach of most researchers.

Hypothalamic influence. Interesting immune effects have also been associated with lesions and electrical stimulation of the hypothalamus (e.g., Stein, Schiavi, & Camerino, 1976). Both cell mediated and humoral immunity have been influenced by these actions on the hypothalamus. For example, lower antibody titers have been observed in animals with lesions of the anterior hypothalamus relative to posterior lesions (see Spector & Korneva, 1981). Mechanisms for this action have not been revealed. There is also evidence that the hypothalamus receives feedback through some obscure afferent pathway following immunization (e.g. Spector & Korneva, 1981; Besedovsky & Sorkin, 1977; Besedovsky, Sorkin, Felix, & Haas, 1977).

Measurement problems in psychoneuroimmunology

Research involving stress and immune response measures has raised a number of methodological issues. Currently, the evidence for a link between mind and immunity in humans rests with only a few

well-controlled studies. Unfortunately, there is a tendency to over-generalize the findings from a wide range of experimental paradigms. The most insidious danger is in the comparison of immune responses of different species; however, other cautions are in order. For example, the nature and duration of stressful stimuli are quite important. Some experiments have used the laboratory and presented noise as a stressor, while other studies stressed subjects with a combination of stressors. Still other researchers have elected to collect data in response to naturalistic stressors, as with grieving reactions and the stress of examination pressure. Another potential problem embedded in the type of stress used and its duration concerns the behavior that the stress will elicit. As discussed earlier, a protracted stress allows for changes in lifestyle including diet, exercise, sleeping patterns, and drug abuse. These behaviors or reactions to stress may have more impact on the immune system than the postulated influence of hyper-activation of the autonomic nervous system.

Two other measurement problems are related to immune system dependent variables. The amount of time that elapses between stress onset and dependent variable collection is quite critical. Monjan and Collector (1977; 1980) have called attention to the fact that exposures of animals to stressors were associated with an initial depression of immune functions followed by immunostimulation. Thus, the time of data collection could determine whether or not an immune response is assessed as being compromised. Perhaps the most important issue concerns the choice of immune response. Due to cost and logistical problems, most researchers evaluate only a few indices of

immunocompetence and make interpretations of the entire immune system on the basis of limited measures. Even when the common battery of in vitro mitogen challenges is made, only a small fraction of the total immunological picture is present. The potential danger for misinterpretation of data collected and compared through any combination of these shortcomings should be emphatically stated.

TMI nuclear accident

On March 28, 1979, unit 2 of the Three Mile Island Nuclear Power Station near Middletown, Pennsylvania malfunctioned. Over the following two week period the accident continued to evolve until stabilization was reached. During this period many area residents evacuated their homes, and fears were compounded by contradictory information from authoritative sources. Through the years that have elapsed since the accident, the crippled reactor has remained a threat to those living in the immediate vicinity. Not only decontamination of the reactor, but also clean up of the facility have continued to be sources of concerns for many residents. Further, the accidental releases and the planned venting of radioactive Krypton-85 gas have added to the problems in neighboring communities. Clearly, a number of the events and ongoing problems may be viewed as stressful for area residents at TMI.

During the accident a drop in coolant water levels exposed the uppermost portion of the reactor core, and temperatures exceeded 2500 degrees Fahrenheit. According to the Nuclear Regulatory Commission's

Draft Environmental Impact Statement (1980), this led to air exposure of hot uranium oxide fuel pellets, fusing of steel assemblies in the reactor unit, cracking and crumbling of fuel, and may have caused other damage. A great deal of radioactive gas was trapped inside the containment building along with thousands of gallons of contaminated radioactive water in the cooling system. Seepage of this radioactive water into the Susquehanna River and into the water supply was a possibility and leaks of gas occurred.

Some TMI residents are still concerned about possible exposure to radiation, not to mention their ideas about being exposed during the accident and subsequent releases of radioactive gas. Although there are conflicting reports about the radiation exposure of those living near the power plant, many people firmly believe they have come in contact with doses exceeding the healthy limit.

These considerations are important in understanding the psychological impact of TMI on area residents. While fear of radiation and the extent to which individuals were exposed varies widely among those living near TMI, those who do believe they received harmful doses or may still be exposed are likely to experience stress.

Stress at TMI

Several investigators, conducting their studies at different points after the accident and examining different samples of TMI area residents, have found evidence of disturbed psychological and physiological functioning. Many have argued that although the stress

associated with the accident was intense, it was only briefly experienced dissipating after the emergency period ended (e.g., Houts, Miller, Tokuhata, & Ham, 1980). Other investigation has suggested that problems peaked within 6 months (Dohrenwend, Dohrenwend, Kasl, & Warheit, 1979). However, data are also available that suggest continuing or increasing problems beyond that expected from an acute experience (Bromet, 1980a). Bromet (1980a) reports differences in mental health between TMI and control groups a year after the accident, while Houts and Goldhaber (1981) show little or no change in symptom reporting by TMI residents over 18 months following the accident. This seems at least in part due to the acute and chronic aspects of the TMI situation. The emergency period lasted about two weeks, but accidental and planned releases of radioactive gas occurred at several points in the interim. Since the accident, there also has been little resolution with respect to decontamination and restart of the undamaged unit 1 reactor. Further, some consequences of radiation exposure (e.g., neoplastic disease and genetic defects) require years or generations to occur.

Longitudinal study of a sample of people living within 5 miles of TMI has suggested continuation of stress during the second and third years after the accident (e.g., Baum et al., 1983). Among other problems, TMI residents reported more somatic distress, anxiety, general symptom experience, exhibited elevated catecholamine levels, and performed more poorly on stress-sensitive tasks than did controls.

A number of interesting psychological, behavioral, physiological, and biochemical relationships have emerged from this data. Social support was found to mediate stress as measured through

symptom reporting, task performance and urinary catecholamines (Fleming, Baum, Gisriel, & Gatchel, 1982). Emotional management and reappraisal based coping style appeared to be the most effective means of reducing psychological and behavioral consequences of stress (Collins, Baum, & Singer, 1983). Also, subjects reporting more loss of control had more stress-associated symptoms than subjects not experiencing loss of control (Davidson, Baum, & Collins, 1982).

Inspection of the data from this longitudinal study has revealed stronger relationships among variables within a given mode as compared with variables across measurement modes (Fleming & Baum, 1982). This means that correlation coefficients were higher among self report measures than between self-report and biochemical measures. For example, a representative Pearson product-moment correlation coefficient for within modality was $r = 0.48$, and a representative coefficient for between modes was $r = 0.35$. These within/across modes correlations may foreshadow results of the strength of the associations of α -IgA levels with variables in different modes. The relationship of α -IgA with epinephrine and norepinephrine will be of particular interest as these hormones are suspected of mediating immune responsivity.

Toxic waste, the Delaware site, and stress

In December, 1982, the Environmental Protection Agency (EPA) reported a listing of toxic waste sites in the United States. At that time, a Delaware landfill (DEL) was listed among the 10 potentially

most hazardous waste sites in the country. The EPA report indicated that several hazardous chemicals had been found in the soil and water supplies serving communities threatened by the toxic waste sites. In the months that followed the December, 1982 announcement, the EPA began to conduct studies necessary to determine the extent of the toxic problem at the DEL site and to formulate a plan of clean-up and containment. While the DEL residents waited for the implementation of a remedy, the media continued to dwell upon health risks from toxic exposure. Much in the same manner that TMI residents were victims of prolonged uncertainty over radioactive exposure, the DEL neighborhood shared an experience of toxic threat.

Although there is little direct evidence of chronic stress resulting from actual or perceived exposure to toxic chemicals, a few studies suggest that it is possible. Levine (1982) reported that many of the residents of the neighborhood around Love Canal described themselves as being stressed by the situation. Edelstein (1982) made similar claims in a study of people living near a hazardous landfill in New Jersey, and Gibbs (1982) reported heightened depression when comparing people living near the same waste site with norms for these measures. Thus, it could be argued that threat of toxic exposure is analogous to cataclysmic events as defined by Lazarus and Cohen (1977). Powerful events of long duration tax adaptive abilities of exposed individuals and often have been associated with psychological disturbances (Menninger, 1952; Popkin, Stillner, Osborn, Pierce, & Shurley, 1974).

Two widely known consequences of toxic exposure can lead to worry, uncertainty, and stress. Exposure to toxic chemicals has been

linked to a number of life-threatening diseases and genetic changes. Both Levine (1982) and Edelstein (1982) reported that people living near toxic waste sites worried that they or their children might someday develop cancer or suffer genetic damage that could result in sterility or birth defects.

A recent study of DEL residents (see Fleming & Baum, in preparation) has reported that a number of negative consequences similar to those exhibited at TMI. Relative to control subjects, DEL residents exhibited disturbed responses across three dimensions of assessment including self-report, behavioral, and physiological measures. DEL subjects had more reports of somatic complaints, depression, and anxiety. Further, the DEL sample performed more poorly on a simple concentration task and had higher concentrations of urinary catecholamines. The similarity between these findings and those reported in the studies of TMI suggest that both TMI and DEL sample have been suffering from chronic stress.

Hypotheses

The TMI accident has clearly caused disturbances among area residents. These people have been bombarded by all sorts of real and imagined problems for almost five years. In fact, a part of defining their current concerns revolves around determining who or what they can believe. The information from authoritative sources has been so mixed for so long that these individuals are groping for information they can trust. Nonetheless, the fears of radiation exposure still exist, and there is the continued threat of more radiation leaks. Uncertainty over whether the plant will become operational again also looms ever-present. The prospect that resolution of the situation will come soon is doubtful. Sources of stress remain pervasive, and chronic stress effects have been recorded over two years since the accident.

The situation among DEL residents is similar to that of TMI. Delays in resolving the environmental and personal danger have enhanced feelings of fear and uncertainty. Although the Environmental Protection Agency announced the toxic waste problem eighteen months prior to data collection in the present study, no substantial clean-up action has been taken to protect residents from toxic exposure. DEL residents will probably have to wait much longer until a decision is made on how to resolve problems associated with the landfill. Thus, for similar reasons as at TMI, DEL residents are also stressed by the element of uncertainty and the threat of health risks.

There is ample evidence that stress has an influence on immune system operations. The majority of the work on the relationship between stress and immune function indicates that the body's natural defense against disease is eroded by stressful insults. Further, it has been clearly established that there are increases in catecholamines and cortisol in response to stress. And, both catecholamines and cortisol have been shown to have inhibitory effects on agents of the immune system.

The present study of TMI and DEL proposes to continue with the examination of chronic stress, but with a unique extension. By adding an index of immune function, it may be possible to make a statement of general health prognosis for the experimental subjects stifled by the atmosphere of chronic stress.

The proposed research predicts that:

1. Current levels of stress at TMI will be comparable to those found in second and third years after the TMI accident. Self-report and biochemical measures among TMI and DEL subjects will indicate symptoms of stress relative to the control group. Specifically, this means that the experimental groups will report more symptoms on the Symptom Checklist-90 (SCL-90) and exhibit higher levels of urinary catecholamines relative to the control group.

2. The increased level of chronic stress among experimental subjects will be associated with depressed levels of s-IgA relative to the control subjects. Since the experimental groups are expected to manifest a higher ambient level of stress and stress normally inhibits immunocompetence, the mean s-IgA level is expected to be suppressed for the stressed groups.

3. There will be a stronger relationship among s-IgA and the biochemical measures (e.g., epinephrine and norepinephrine) than among s-IgA and self-report measures. Further, self-report measures will correlate more highly with one another than with biochemical measures.

Thus, the proposed study is focused on determining whether the stressful circumstances existing at TMI and DEL can be associated with suppression of an aspect of immune function. This study will also show if TMI area residents are continuing to display the same symptoms and levels of chronic stress at a point nearly 5 years after the accident as they did previously at 17, 22, 28, and 34 months post-accident.

Method

The present study was designed to further investigate the consequences of environmental stressors. Specifically, the relationship between chronic stress of living near a damaged nuclear plant or living near a toxic waste site and immunocompetence was examined. This was performed by exploring the differences in responses between chronically stressed subjects and a control group.

Subjects

A total of seventy-seven subjects participated in this study. The TMI group was composed of thirty-four people living within 5 miles of the power plant. A second experimental group of twenty-four individuals living adjacent to the toxic waste site in Delaware (DEL) was also part of the design. The control group had nineteen subjects living at least twenty miles from any power generating facility in Frederick, Maryland (FRD).

Two of the communities (i.e., TMI and Frederick) studied have been matched on several demographic variables (Baum et al., 1983). The subjects in these two groups were initially recruited in June, 1980 and have participated in similar procedures 10 times. Subsequently, the Delaware group was also matched demographically to subjects at both TMI and Frederick (see Appendix A). Subjects were selected in a quasi-random fashion. Streets within neighborhoods were randomly selected, and every third house on sampled streets was approached. If

the person answering the door were an adult, he or she was recruited for an interview by the experimenter. TMI and DEL subjects were told that the study involved the psychological impact of their respective communities' environmental problem. Control subjects were given an explanation that indicated they would serve as a comparison to the TMI sample. All subjects were told that the study was a scientific one and that the results would not necessarily be applicable to the decision-making process regarding future disposition of the TMI plant or the toxic waste dump. Approximately seventy percent of those given the opportunity to participate agreed to do so, and there were no differences in response rate among the three sites.

Interviews were scheduled on the present expedition by telephone one week prior to data collection. As on past visits, interviews were performed in the subject's home and lasted about 1 hour. Subjects were paid for their participation.

Dependent Measures

Two self-report instruments of health and two physiological measures were evaluated.

Self-report measures. The following self-report measures were collected:

1. The Symptom Checklist-90 (SCL-90; see Appendix B) is a 90-item multidimensional inventory developed at Johns Hopkins University. It has been shown to be useful in examining sub-clinical levels of disturbance in a number of settings (e.g., Bromet, 1980a;

1980b; Derogatis, 1977). Symptoms are rated on a 5-point scale, and a measure of global symptom reporting as well as subscale indices are obtained. Instructions request the subject to reflect over the past two weeks, including the day of interview.

2. A Health Questionnaire, (see Appendix B) assesses one's perceptions of current health, emphasizing viral cold symptomology. This questionnaire asks 12 questions focusing on feelings within the two days preceding its completion.

Physiological measures. Physiological measures of urinary catecholamines according to radioenzymatic COMT procedures (Durrett & Ziegler, 1980; see Appendix C) were used to measure chronic sympathetic arousal. Measurement of urinary catecholamines has proven to be a useful biochemical measure of sympathetic activation (Frankenhaeuser, 1975). Moreover, stress-related increases in catecholamines have been associated with an inhibition of cellular and humoral immunity (see Rogers et al., 1979).

A salivary immunoglobulin assay by single radial immunodiffusion (Mancini, Carbonara, & Heremans, 1965; see Appendix C) was used to determine immunocompetence. This measure of salivary immunoglobulin was selected for a number of reasons. Saliva can be collected through a relatively noninvasive technique, and it is also easily and inexpensively assayed. Further, immunoglobulin A in saliva can protect against the type of upper respiratory infections that have been assessed as being disproportionately high at TMI (Baum et al, 1983; Schaeffer & Baum, 1982). Stress may predispose individuals to illness through a transient immunodeficiency (e.g., Plaut & Friedman, 1981). Thus, it was reasoned that a stress mediated depression of s-IgA could be playing

a role in the elevated infection level at TMI. In addition, at least 2 studies (McClelland et al, 1980; Jemmott et al., 1983) have been successful in demonstrating a relationship between lowered s-IgA concentrations and elevated illnesses. A protein assay (Bradford, 1976; see Appendix C) was also conducted on the saliva so that s-IgA could be expressed as a fraction of total salivary protein.

Procedure

The three groups were sampled one week apart approximately five years after the accident at TMI (this point also represented a time approximately eighteen months after the DEL subjects had been informed of the toxic waste dump). Data were collected by a trained experimenter. Each session began with a brief discussion of the procedure and a reminder that participation was voluntary. Informed consent had been obtained on an earlier visit.

The two questionnaires were briefly explained and left with the subjects to complete over night.

Subjects were asked to provide a fifteen-hour urine sample. This meant collecting all urine excreted overnight (6 p.m. - 9 a.m.) following their interview. Sodium metabisulfite was added to each sample to prevent oxidation and samples were frozen immediately after collection. Timed 1 minute samples of whole unstimulated saliva were obtained from each subject. Saliva was collected from subjects in the early evening (5 p.m. - 7 p.m.) and stored frozen. Assays were performed after all data had been collected. Laboratory assays were

Results

Analyses addressed three primary issues. First, it was important to determine whether or not TMI subjects were maintaining a pattern of stress-like responses similar to previously reported data (Baum et al., 1983). The second concern was whether any association could be made between chronic stress and an index of immune system function. Finally, the relationships between the various psychologically based and biologically based measures were explored. The primary tools used to answer these questions were oneway analysis of variance (ANOVA) and Pearson product-moment correlation. All ANOVA summary tables appear in Appendix D.

The first hypothesis addressed the comparability of levels of symptom reporting on the SCL-90 and urinary catecholamines between TMI and Frederick controls for data collected fifty-eight months after the TMI accident with data collected in the period two to three years after the accident at TMI. Figures 1-4 show that the mean levels of total complaints, somatic problems, urinary epinephrine, and norepinephrine for TMI relative to Frederick were fairly consistent over time. The urinary catecholamines, however exhibit a pronounced spike at twenty-two months post-accident. A possible explanation for the spikes on the epinephrine and norepinephrine figures is given in the Discussion section.

FIGURE 1

TOTAL SYMPTOMS REPORTED AS A FUNCTION OF TIME

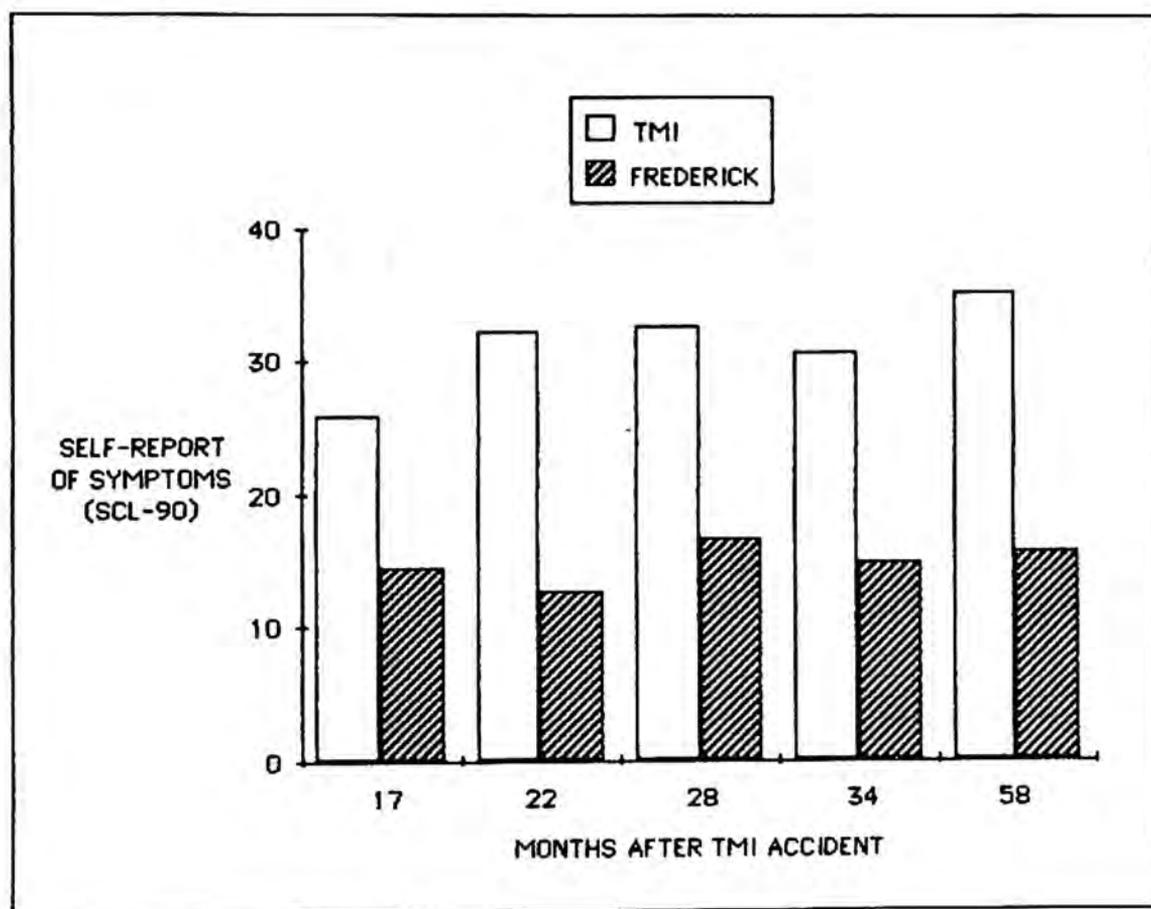


FIGURE 2

SOMATIC COMPLAINTS REPORTED AS A FUNCTION OF TIME

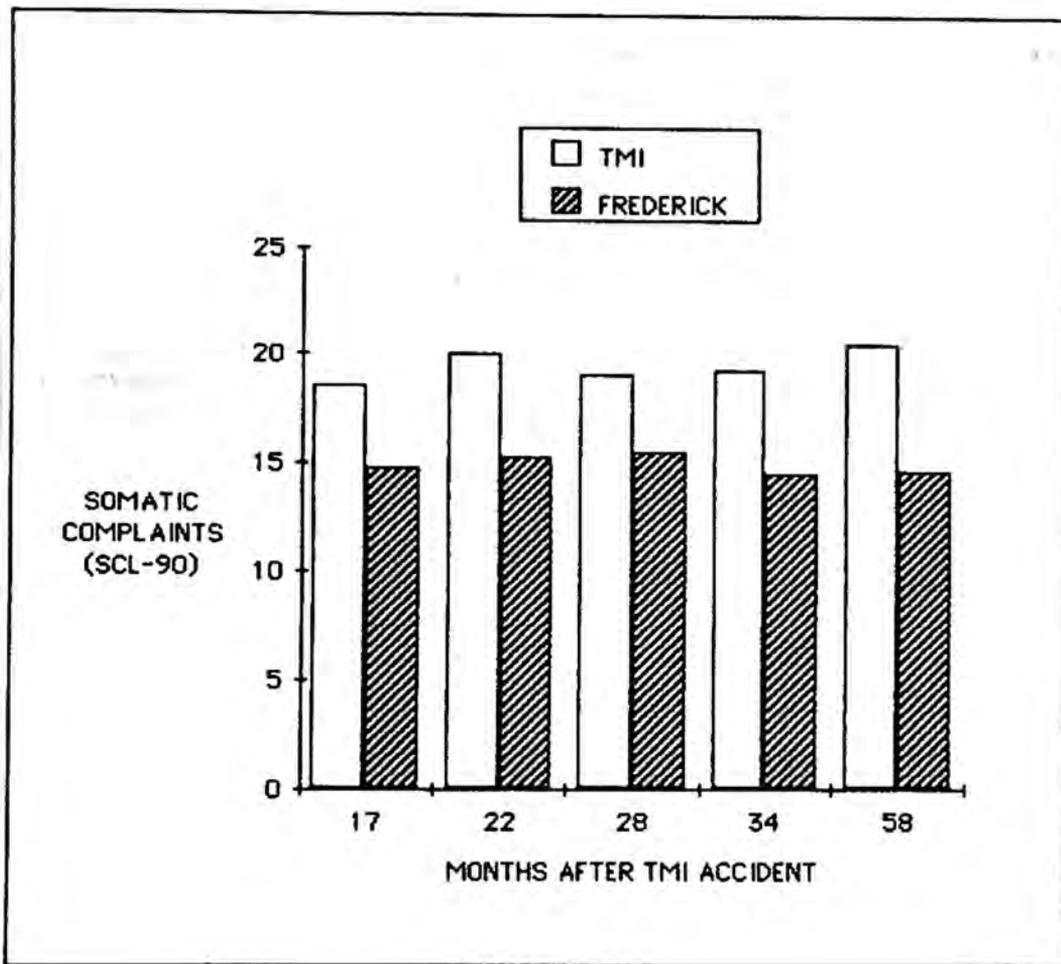


FIGURE 3
MEAN LEVEL EPINEPHRINE AS A
FUNCTION OF TIME

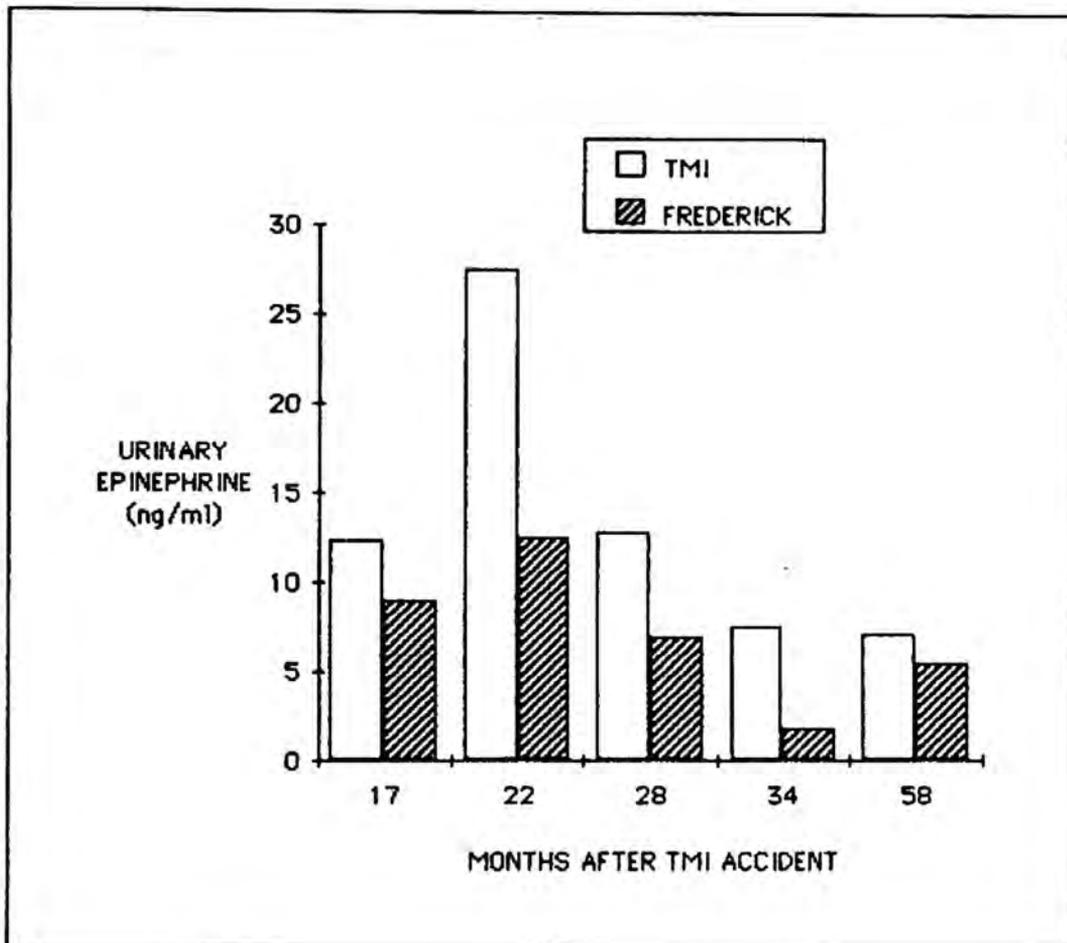
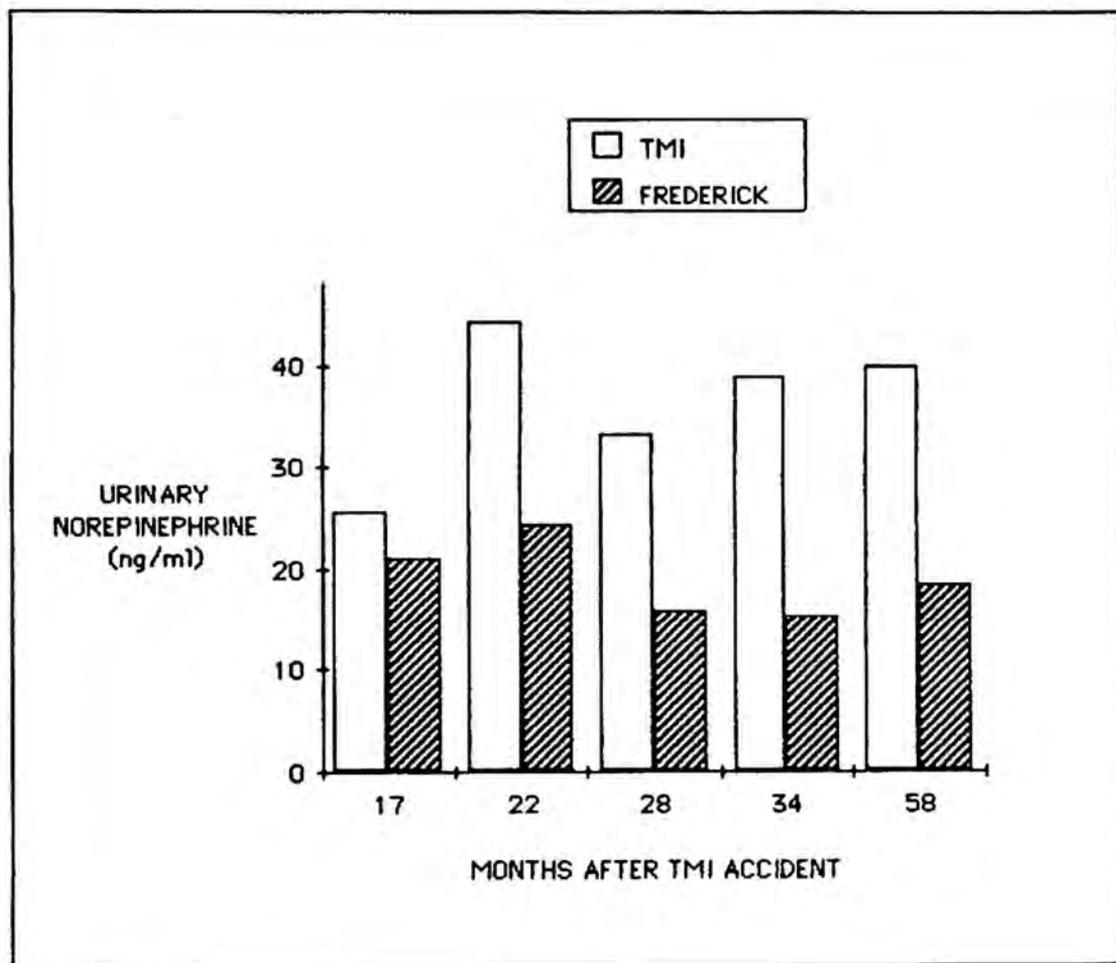


FIGURE 4

MEAN LEVEL OF NOREPINEPHRINE AS A
FUNCTION OF TIME



Self-report measures

Unless stated otherwise, all analyses include three groups (i.e., TMI, DEL, & FRD). Oneway analyses of variance (ANOVA) on SCL-90 data collected in the present study indicated that TMI subjects continued to report more total complaints than controls, $F(2,71) = 8.91$, $p < 0.001$, and also reported more somatic problems, $F(2,71) = 10.51$, $p < 0.001$ (see Table 1). In addition, planned comparisons on total complaints revealed that controls could be distinguished from TMI,

TABLE 1 Self-report Measures

MEAN LEVELS OF TOTAL SYMPTOMS (SCL-90)

	mean	standard deviation
TMI	35.3	23.8
DEL	41.6	19.2
FRD	15.6	15.6

MEAN LEVELS SOMATIC PROBLEMS (SCL-90)

	mean	standard deviation
TMI	20.5	4.7
DEL	22.7	8.4
FRD	14.7	3.1

MEAN LEVELS HEALTH COMPLAINTS (HEALTH QUESTIONNAIRE)

	mean	standard deviation
TMI	19.8	4.8
DEL	23.2	8.5
FRD	22.3	7.9

$t(71) = 3.34, p < 0.001$ and DEL, $t(71) = 4.05, p < 0.001$. Similarly, planned comparisons indicated that controls reported fewer somatic problems than TMI, $t(71) = 3.52, p < 0.001$, and less than DEL, a $t(71) = 4.44, p < 0.001$. Moreover, planned comparisons did not show significant differences between TMI and DEL on either total complaints or somatic problems. In contrast, the Health Questionnaire was concerned with somatic symptoms during data collection (the SCL-90 asked subjects to report symptoms experienced over the two weeks prior to data collection) failed to demonstrate a difference among the three groups (see Table 1).

Urinary catecholamines

Although oneway ANOVA on urinary epinephrine indicated differences in the level of this hormone among the three groups (see Table 2), $F(2,66) = 3.88, p < 0.03$, planned comparisons did not reveal a difference between TMI and control subjects. However, DEL relative to control subjects had a significantly higher level of urinary epinephrine, $t(66) = 2.72, p < 0.01$, and the comparison of both TMI and DEL with controls also was significant, $t(66) = 2.18, p < 0.04$. In addition, a marginally significant difference in the level of urinary epinephrine was found between TMI and DEL, $t(66) = 1.93, p < 0.06$. Oneway ANOVA on the level of urinary norepinephrine was highly significant, $F(2,66) = 11.40, p < 0.001$. Planned comparisons indicated that TMI had higher urinary norepinephrine levels (see Table 2) than controls, $t(66) = 3.55,$

$p < 0.001$, and that DEL also had higher levels than controls, $t(66) = 4.66$, $p < 0.001$. No difference was found between norepinephrine levels at TMI and DEL.

TABLE 2 Catecholamine Measures

MEAN LEVELS OF URINARY EPINEPHRINE (ng/ml)

	mean	standard deviation
TMI	7.0	5.0
DEL	9.7	5.4
FRD	5.4	4.8

MEAN LEVELS OF URINARY NOREPINEPHRINE (ng/ml)

	mean	standard deviation
TMI	40.1	18.8
DEL	49.2	27.7
FRD	18.3	12.1

s-IgA measures

The second hypothesis dealt with the nature of the relationship between chronic stress and s-IgA as an index of immunocompetence. Oneway ANOVA was also used to determine differences in the level of s-IgA among TMI, DEL, and controls. As can be seen in Table 3 there were no differences in mean levels of s-IgA. There were also no differences revealed when s-IgA was expressed as a fraction of total

TABLE 3 Salivary Measures

MEAN LEVELS OF s-IgA (mg/dl)

	mean	standard deviation
TMI	7.1	5.4
DEL	7.5	3.6
FRD	7.7	4.7

MEAN LEVELS OF SALIVARY PROTEIN (mg/ml)

	mean	standard deviation
TMI	1.25	0.8
DEL	1.51	0.9
FRD	1.71	1.0

MEAN LEVEL s-IgA (mg/min)

	mean	standard deviation
TMI	0.12	0.11
DEL	0.12	0.07
FRD	0.09	0.06

MEAN RATIO s-IgA TO TOTAL PROTEIN (mg/ml)

	mean	standard deviation
TMI	0.06	0.4
DEL	0.07	0.4
FRD	0.05	0.3

MEAN SALIVARY SPECIMEN VOLUME (ml)

	mean	standard deviation
TMI	1.6	0.3
DEL	1.6	0.3
FRD	1.2	0.2

protein (see Table 3). Further, an ANOVA performed on the amount of s-IgA per minute also failed to indicate any differences (see Table 3). However, analysis of saliva specimen volumes (see Table 3) revealed differences, $F(2,73) = 12.42, p < 0.001$. Although planned contrasts indicated no difference between TMI and DEL, both of the comparisons TMI vs. Frederick, $t(73) = 4.51, p < 0.001$, and DEL vs. Frederick, $t(73) = 4.38, p < 0.001$ indicated mean volume differences. In addition, oneway ANOVA failed to detect a difference in total protein of the saliva specimen among the groups (see Table 3).

Correlations between and within modes

Hypothesis three considered the strength of association among and between the self-report and biochemical measures. Pearson product-moment correlations were performed on SCL-90 subscales scores, urinary catecholamine levels, and s-IgA levels. As can be seen in Table 4, correlation coefficients were relatively high among the subscales of the SCL-90 in comparison with correlations between SCL-90 subscales and urinary catecholamines. However, the total symptoms subscale of the SCL-90 correlated highly with urinary norepinephrine, $r(69) = 0.63, p < 0.001$ as did the somatic subscale of the SCL-90, $r(69) = 0.55, p < 0.001$. In contrast, neither of the urinary catecholamines correlated as highly with the Health Questionnaire (see Table 4) as did the somatic and total symptom subscales of the SCL-90.

TABLE 4 Within and Between Mode Correlations

SCL-90 SUBSCALE CORRELATIONS

	Total	Somatic	Concen	Depression	Anxiety
Total		0.769**	0.817**	0.868**	0.821**
Somatic			0.735**	0.744**	0.767**
Concentration				0.746**	0.681**
Depression					0.775**

URINARY CATECHOLAMINES AND s-IgA CORRELATIONS

	s-IgA	Norepinephrine	Epinephrine
s-IgA		-0.140	-0.038
Norepinephrine			0.482**

MIXED MODE CORRELATIONS

	s-IgA	Norepinephrine	Epinephrine
Total	-0.148	0.630**	0.274*
Somatic	-0.036	0.554**	0.258*
Health Q	0.284*	0.224*	0.089

* $p < 0.05$ ** $p < 0.001$

The high correlation coefficients among the SCL-90 subscales in Table 4 raised an issue as to the validity of the different subscales. That is, the correlations were sufficiently high to suspect that at least a few of the subscales might have been measuring the same

problem. A multivariate analysis of variance (MANOVA) was performed using all SCL-90 subscales to represent the dependent measure. As can be seen in Table 5, the multivariate F test was significant and only the suspiciousness and alien subscales failed to achieve statistical significance (i.e., $p < 0.05$) in univariate testing.

TABLE 5 Multivariate Test on SCL-90
Multivariate Tests of Significance on 10 SCL-90 Subscales

TEST NAME	VALUE	F	DF (HYPOTH.)	DF (ERROR)	p
Pillais	0.427	1.71	20	126	0.04
Hotellings	0.606	1.85	20	122	0.02
Wilks	0.604	1.78	20	124	0.03

Univariate F -Tests with (2,71) DF for 10 SCL-90 Subscales

VARIABLE	SS HYPOTH.	SS ERROR	MS HYPOTH.	MS ERROR	F	p
Total	7531.59	30007.06	3765.80	422.63	8.91	0.000
Somatic	695.43	2349.12	347.72	33.09	10.51	0.000
Concentration	446.64	1982.71	223.32	27.93	8.00	0.001
Interpersonal	198.42	1267.37	99.21	17.85	5.56	0.006
Depression	862.93	2860.43	431.47	40.29	10.71	0.000
Anxiety	652.96	2025.25	326.48	28.52	11.45	0.000
Anger	267.32	1262.62	133.66	17.78	7.52	0.001
Fear	90.78	1063.16	45.39	14.97	3.03	0.055
Suspiciousness	45.26	4276.90	22.63	60.24	0.38	0.688
Alienation	77.97	977.99	38.98	13.77	2.83	0.066

An interesting pattern emerged, when correlations were performed on individual groups (see Table 6). For all subjects combined, higher concentrations of α -IgA were correlated with more complaints on the Health Questionnaire, $r(69) = 0.284$, $p < 0.05$. However, only at

TMI was this relationship significant, $r(31) = 0.406$, $p < 0.05$.

Although no other associations among these variables reached significance, a hypothesized negative correlation at TMI between levels of urinary norepinephrine and levels of s-IgA approached significance, $r(69) = -0.226$, $p < 0.10$.

TABLE 6

INDIVIDUAL GROUP CORRELATIONS FOR s-IgA WITH HEALTH COMPLAINTS & NOREPINEPHRINE

	ALL SUBJECTS	TMI	DEL	FREDERICK
	s-IgA	s-IgA	s-IgA	s-IgA
Health Q	0.284*	0.406*	0.299	0.232
Norepi.	-0.140	-0.226	-0.130	-0.054

* $p < 0.05$

Pearson Correlations also were calculated among the SCL-90 subscales for all subjects (see Table 4), as well as for each of the three individual groups (see Table 7). In comparing these four correlation matrices there is one outstanding feature. In the FRD control group, the anxiety and depression subscales were not significantly correlated to somatic complaints.

An attempt was made to collect information that could possibly confound the levels of s-IgA. Although age and gender of subject data

were available, other relevant measures were not. For example,

TABLE 7

SCL-90 SUBSCALE CORRELATIONS FOR TMI

	Total	Somatic	Concen.	Depression	Anxiety
Total		0.866**	0.769**	0.894**	0.815**
Somatic			0.620**	0.805**	0.734**
Concentration				0.632**	0.589**
Depression					0.758**

SCL-90 SUBSCALE CORRELATIONS FOR DEL

	Total	Somatic	Concen.	Depression	Anxiety
Total		0.699**	0.823**	0.787**	0.827**
Somatic			0.771**	0.663**	0.809**
Concentration				0.765**	0.703**
Depression					0.731**

SCL-90 SUBSCALE CORRELATIONS FOR FREDERICK

	Total	Somatic	Concen.	Depression	Anxiety
Total		0.586*	0.813**	0.840**	0.391*
Somatic			0.588**	0.246	0.231
Concentration				0.743**	0.230
Depression					0.344

* $p < 0.05$

** $p < 0.001$

prescription medication history and smoking status were requested on the bottom of a questionnaire, yet one entire experimental group of subjects neglected to respond. Thus, the results must be viewed with some degree of caution. Some variables that may have been meaningful

covariates were clearly lacking. Correlation coefficients of s-IgA, urinary catecholamines, and self-report of health complaints with age and gender can be seen in Table 8. Gender correlated with somatic complaint and depression levels as measured by the SCL-90. While men reported fewer somatic problems and less depression, women showed the opposite.

TABLE 8

AGE AND GENDER CORRELATIONS WITH SCL-90 SUBSCALES, URINARY
CATECHOLAMINES, & s-IgA

	Age	Gender
Total	-0.001	0.087
Somatic	-0.096	0.204*
Depression	-0.004	0.194*
Health Q	-0.071	0.115
s-IgA	-0.043	-0.149
Norepinephrine	-0.039	0.145
Epinephrine	-0.087	0.063

* $p < 0.05$

As a last step in the data analyses a series of multiple regressions were performed. Two important relationships were addressed: S-IgA was predicted by a group of variables including current health, urinary catecholamines, and research site; also, the Health Questionnaire data were predicted by s-IgA, urinary catecholamines, and

research site. As can be seen in Table 9, s-IgA was best predicted by health rating and urinary norepinephrine and Health Questionnaire rating was best predicted by s-IgA and urinary norepinephrine.

TABLE 9
REGRESSION SUMMARY TABLES

Dependent Variable s-IgA

VARIABLE	MULTIPLE R	R SQUARE	RSQ CHANGE	SIMPLE R	B
Health					
Complaints	0.2784	0.0775	0.0775	0.2784	0.718D-01
Norepi.	0.4296	0.1846	0.1071	-0.2565	-0.174D-01
TMI	0.4346	0.1889	0.0043	-0.1761	-0.409
DEL	0.4399	0.1935	0.0046	-0.0629	-0.314
Epi.	0.4425	0.1938	0.0003	-0.1413	-0.563D-02
(Constant)					1.979

Dependent Variable Health Complaints

VARIABLE	MULTIPLE R	R SQUARE	RSQ CHANGE	SIMPLE R	B
s-IgA	0.2564	0.0657	0.0657	0.2564	0.645
Norepi.	0.3886	0.1510	0.0853	0.2240	-0.106
TMI	0.4367	0.1907	0.0397	-0.2338	-3.538
DEL	0.4406	0.1941	0.0034	0.1570	-1.266
Epi.	0.4416	0.1950	0.0009	0.0886	-0.448D-01
(Constant)					16.630

Discussion

Where is the knowledge we have lost in information? T.S. Eliot

Before launching into a discussion on the findings in the present study, a few points of review may be helpful to underscore the impact of the results. The data from the three locations were collected almost 5 years (i.e., fifty-eight months) after the accident at TMI and eighteen months after DEL residents were officially informed of the nearness of the toxic waste site to their homes. Moreover, many of the TMI studies reported in the literature (Bromet, 1980a; 1980b; Baum et al., 1983; Gatchel et al., in press) have suggested that the psychological and physiological outcomes are linked to the experience of chronic stress. Chronic stress seems to be related to continued threat and uncertainty of the unresolved situation at TMI, particularly the matters of clean-up of the crippled reactor and the restart of the undamaged unit.

Chronic stress also seems to be associated with reactions among DEL residents. The belief that one has been exposed to toxic danger appears capable of altering self-reports, behavior, and physiological changes. The combination of the lack of direct, visible threat or visible damage, and the long duration necessary for toxic exposure to have an effect sums to a potent stressor.

With the exception of the s-IgA hypothesis, the results of the present study support the hypotheses. The failure to demonstrate s-IgA level differences may indicate that the immunoglobulin test should not

be included as an index of immunocompetence influenced by chronic stress.

The sustained, elevated levels of symptom reporting and urinary catecholamines clearly confirm the first hypothesis and are consistent with results found in earlier TMI research (e.g. Baum et al., 1983). Although it cannot be known with certainty why the catecholamine levels spiked at twenty-two months post-accident, it is possible that data collected during this visit coincided with a relatively acute stressor. The Nuclear Regulatory Commission had just released a report with threatening sounding contents concerning the clean-up operation. In addition, the media was accentuating some of the less favorable outcomes as the TMI group were being surveyed. The second hypothesis dealing with depressed s-IgA levels tracking chronic stress was not supported. Finally, results relevant to the third hypothesis demonstrated that measures within a dimension or a given mode of assessment were generally more highly related than measures across measurement modes. Each of these points will be discussed in greater detail in the following.

Consequences of chronic stress

Long-term sustained increases in symptom reporting and prolonged elevations of urinary catecholamine levels are provocative. Of particular interest are two factors: (1) The nature of the relationship between chronic stress and symptom reporting and catecholamine levels; and (2) the implications of sustained deviations from homeostasis.

Results from the present study and especially others using more

extensive controls (e.g., Baum et al., 1983; Schaeffer & Baum, 1984) suggest that these changes in symptom reporting and urinary catecholamines are largely the result of chronic stress. As reviewed earlier, both laboratory and field studies agree that stressed subjects relative to controls demonstrate a pattern similar to that reported here. Some researchers (e.g., Lazarus, Cohen, Folkman, Kanner, & Schaefer, 1980; Frankenhaeuser, 1980) have attempted to explain these results in terms of subjective appraisal and efficacy of coping style. It is not difficult to accept this form of explanation in the present research, especially as data have been reported that suggest that coping style moderated the negative outcomes at TMI (see Collins et al., 1982; Fleming et al., 1982; Davidson et al., 1982).

Data collected during the present study but not yet analyzed may reveal further interesting relationships between coping factors and stress consequences. Coping style, social support, and perceived control were all measured. Each of these factors has been shown to mediate consequences of stress. It will be interesting to determine if the same relationships already reported (Collins et al., 1982; Fleming et al., 1982; Davidson et al., 1982) still hold. Of particular interest will be possible relationships between these coping factors and concentration of s-IgA.

The prognosis for those demonstrating long-term signs of chronic stress exposure is another concern. Although the subjects exposed to chronic stress reported more health problems (i.e., SCL-90) and exhibited elevations of catecholamines, they are still considered to be in an extreme segment of the normal range. In other words, no clinical cases seem to be present in the TMI and DEL samples. However, the

sustained reporting of health complaints and prolonged elevated levels of epinephrine and norepinephrine in urine may have negative long term implications. Increases in catecholamines affect blood pressure by increasing peripheral resistance and increasing cardiac contractility (Friedman, Byers, Diamant & Rosenman, 1975). If chronic stress induces heightened catecholamine responding without commensurate adaptation to higher levels, some risk exists for uncontrolled blood pressure changes. In addition, elevated concentrations of catecholamines have immunological implications. Recent studies have identified cell surface receptors for catecholamines on activated lymphocytes (see Ahlqvist, 1981). Moreover, these lymphocyte surface receptors have been probed using beta agonists and antagonists. The findings of this research indicate that beta agonists as epinephrine suppress immune system function (Goodwin, Messner, & Williams, 1979), while beta antagonists as propranolol produce immunoenhancement (Nakazawa, Hobdy, Townley, & Chaperon, 1977; Shereff, Harwell, Lieberman, Rosenberg, & Robinson, 1973; Sherman, Smith, & Middleton, 1973).

Perhaps the first signs of a long-term problem at TMI may have already appeared. An examination of physician records has revealed that relative to controls, TMI residents have more physician noted complaints, have had more prescriptions written, and have more signs of increasing systolic and diastolic blood pressure (Schaeffer & Baum, 1982). Of greater potential impact is the fact that of the original eighty-five subjects recruited at TMI and Frederick four years ago, two subjects from TMI have voluntarily discontinued their experimental participation on account of health reasons. Both of these TMI subjects sustained strokes. No record of this severe a health outcome has been

presented from control subjects.

Chronic stress and s-IgA

It was hypothesized that s-IgA levels would be depressed among experimental subjects relative to controls, and that elevated catecholamine concentrations and increased symptom reporting would be related to s-IgA. Although the present study demonstrated a relationship between symptom reporting and catecholamine levels, s-IgA concentrations were similar among the three groups and failed to correlate significantly with catecholamine levels. S-IgA concentration also did not correlate with somatic complaints, but did correlate significantly with the Health Questionnaire scale.

Salivary mean volumes were higher for experimental relative to control subjects. This volume difference raises serious questions. Although it cannot be known with certainty why this difference in volume occurred, speculation over two alternatives is appropriate. One possible explanation is that the volume difference was biologically based and related to circumstances linked to being chronically stressed. Unfortunately, there is little justification in arguing for a biological mechanism of increased saliva volume as a function of stress. Stress is largely governed by sympathetic activation and the saliva glands are under parasympathetic control. Unless it could be demonstrated that the experimental subjects were experiencing stressful parasympathetic activation, there is little basis in justifying the volume difference. A far more plausible alternative to a biological explanation would be a

psychological or motivational one. Subjects were given the option of stepping out of view of the experimenter during the one minute allowed for providing the specimen. Most participants elected to receive start and stop signals with this option. Therefore, there was no way of being sure that subjects abided with the start and stop cues given by the experimenter. It could easily be argued that the experimental groups, having a feeling that their results may have influence on corrective environmental actions, were more compliant in following the requested procedure of salivating into the specimen tube for a full minute. A study of two samples of subjects in either an observed or unobserved condition might yield data supporting increased compliance under observation.

However, this issue has no bearing on the relationship found between s-IgA and the Health Questionnaire. Correlational analysis revealed a statistically significant association between s-IgA level and the Health Questionnaire's assessment of feeling cold-like symptoms. That is, the higher the level of s-IgA, the more symptoms of a cold or virus were endorsed on the Health Questionnaire. Further, stepwise regression analysis predicting s-IgA demonstrated that health complaints followed by norepinephrine level accounted for the most variance of all predictors in the regression equation. In addition, TMI subjects exhibited a stronger relationship than DEL, Frederick, or all subjects combined of their s-IgA levels with health complaints and with urinary norepinephrine levels. This result suggests that TMI subjects, relative to the other two groups, may have had increased antibody activity as a result of infection, and that they were actually suffering from more ill-health at the time of data collection. The self-report of health

complaints (as measured by the Health Questionnaire), however, failed to corroborate such a finding.

All of these relationships make it difficult to understand whether there is an association between chronic stress and s-IgA suppression. Although it is possible that stressful circumstances can lead to the lowering of s-IgA levels, the nature and intensity of the stress may be a critical factor. Thus, the intensity or nature of stress at TMI may have been insufficient to alter s-IgA concentrations. However, data from at least two other studies (Jemmott et al., 1983; McClelland et al., 1980) suggest an association between stress and lowered levels of s-IgA. A 5 trial longitudinal study of dental students' s-IgA during 3 examination and 2 non-examination periods showed a pattern in s-IgA concentration (Jemmott et al., 1983). The examination period measures were considered more stressful than the non-examination measures, and the mean concentration of s-IgA paralleled the relative level of stress with lower levels of s-IgA across the 3 exam points. Another study (McClelland et al., 1980) found that individuals high in need for power, high in inhibition, and high in power stress (i.e., power pattern personality) exhibited lower concentrations of s-IgA than individuals who did not display the power pattern. Although both of these studies may present an accurate depiction of results and conclusions, both are suspect for the same reason. It is not clear that examination stress or the power pattern personality affects s-IgA concentration. Perhaps life style characteristics associated with these 2 groups account for more variation in s-IgA levels than stress. For example, dental students probably exhibit changes in sleeping pattern and diet during their

examinations. It is plausible that such lifestyle factors in the absence of stressful stimulation could be sufficient to reduce s-IgA concentration. The lack of reporting of salivary volume or salivary protein in these 2 studies adds another confound.

In the TMI study, it is possible that experimental subjects failed to reveal s-IgA suppression because they were in the process of being chronically sick with the natural accompanying elevation in s-IgA levels to combat their infections.

In addition, there is no fool-proof means of knowing whether each or any of the three research sites was under viral attack. That is, an increase in colds at any given site may have been a product of chance epidemiology of the three areas. Although the relative number of physician-noted viral complaints of the three communities surveyed could have been collected to provide some epidemiological intelligence, a confound could still remain; there is no reason to assume similar health-seeking behavior among members within each of the three research locations. For example, individuals among the Frederick control group might attend to their viral-cold symptoms by seeking physician aid with higher frequency than members of the other two communities.

Despite the lack of support for the s-IgA hypothesis in the present study, recent preliminary immunological data from TMI suggest immune system suppression. Blood samples were collected from demographically matched subjects at TMI and Frederick, and were analyzed for total B, T, T-helper, T-suppressor lymphocytes using monoclonal antibodies and flow cytometry. Relative to controls, TMI subjects had fewer lymphocytes of each type (Schaeffer, Mc Kinnon, Baum, Reynolds, Rikli, Davidson, & Fleming, 1985). The planned plasma IgA assay will

address an interesting question. Although s-IgA levels may be comparable between TMI and Frederick, plasma IgA levels could show differences. Thus, it could be revealed that measures of s-IgA are inadequate for assessing immunosuppression. It will also be interesting to examine how self-report of health and concentrations of catecholamines and cortisol covary with the lymphocyte subpopulation measures.

Integration of stress responses

Another goal of this study was to examine the degree to which variables correlated with one another both within the same dimension and across measurement modes. The relatively high coefficients of correlation among the subscales of the SCL-90 indicated that there was a large component of shared variance among the different subscales. Similarly, the biological measures correlated more highly with each other than with the self-report. Also, some across modes relationships were inconsistent. For example, the correlation of s-IgA with the Health Questionnaire, but not the SCL-90 somatic subscale suggests that the complaints covered on the SCL-90 included health problems with little influence on s-IgA. However, an unexpectedly high degree of correlation was found between SCL-90 somatic complaints and urinary norepinephrine levels. Further, the relationship was strongest among TMI subjects relative to either other group or the entire sample. This relationship serves to underscore the notion that stress response across different channels is at least partially integrated (Mason, 1975). In

s-IgA or Health Questionnaire reports. However, s-IgA levels were correlated with Health Questionnaire complaints, and somatic complaints were significantly associated with catecholamine concentrations. Further, the best predictors of s-IgA were Health Questionnaire ratings and norepinephrine levels.

The present research illustrates relationships among psychological variables, health, and stress. Although experimental subjects did not exhibit the hypothesized deficit in s-IgA concentration, the study is not conclusive. However the data presented here and previous studies (Schaeffer et al., 1985; Schaeffer & Baum, 1984; Schaeffer & Baum, 1982) suggest that, relative to control subjects, TMI subjects have more negative health outcomes. Nonetheless, this finding need not be related to immune status. Thus, a physiological explanation underlying somatic problems and complaints remains unknown. The most apparent psychological difference that distinguishes TMI from Frederick subjects is one of threat perception. The backdrop of potential harm with which TMI area residents must deal is extremely powerful and difficult for many to escape. DEL subjects seem to be living in a similar scenario to TMI. Just as TMI residents must confront what they believe to be threatening, DEL residents have fears and uncertainties about the proximity of their homes to toxic danger.

Immune function and adaptation

For over one-hundred years psychosomatic theorists have been

attempting to determine how psychological variables influence health. Moreover centuries of observation and thought by maverick physiologists, scholarly thinkers, and classical philosophers have molded mind/body issues. Although it is currently hard to deny that behavior and psychological concerns are linked to health, the exact mechanisms or interface between mind/body and health outcomes remains elusive. With an unknown number of missing links between behavior and disease, we resort to more research and speculation. Speculation on the adaptive value of behavioral responses affecting health may provide some new leads.

Immune systems of vertebrates and invertebrates. Prior to theorizing on the adaptive implications resulting from behavior/health interactions, a few comments concerning evolution of the immune system might be meaningful. We know that the evolution of human immune function has paralleled evolution itself. Many primitive forms of life including invertebrates and plants are susceptible to infectious disease, just as humans are. However, these older organisms (evolutionarily speaking) have only rudiments of immune apparatus. In general, as the evolutionary ladder is ascended, increasing sophistication of the immune system is found (Weir, 1983). On the average, vertebrates, as newer evolutionary species, live longer than invertebrates. This element of lifespan has two primary implications. Longer life increases the chance of encountering pathogens and decreases the the ability to counter microorganisms by genetic variation. On the other hand, invertebrates, in general, have more numbers than vertebrates, and thus, death to a majority of any given generation of invertebrates does not threaten the species. Variants that survive will

apparently be resistant to that which eliminated most of their generation. This strategy of survival is not afforded most vertebrates.

With respect to evolution of the immune system, learning to adapt to unexpected changes in the environment is a property of populations, not individuals (Cunningham, 1977). When a new pathogen challenges an invertebrate against which their inherited defenses fail, most members may die, but a few variants will form the basis of a new resistant strain. A much more economical fashion of defense is exhibited by vertebrates. In fact, the internal population of lymphocytes in the vertebrate behaves similarly to an evolving species of invertebrates. The point here is that lymphocytes possess a learning-like quality similar to the manner that a species of invertebrates learns, and their altered characteristics are passed on to offspring. Thus, an entire evolutionary history unfolds inside one host. A very remarkable feature however, is that vertebrate offspring do not inherit acquired immunological defense, but must build their own immunological repertoire.

Is it possible that the human immune system has not evolved fast enough to counter twentieth century Western life-style? Does our fast paced, technological, dehumanizing society breed individuals susceptible to stress? Is it possible that reactions to stress govern the operation of a selection mechanism? As with our ancient ancestors, we have a wide variety of behavioral options that can be ranked in terms of their evolutionary cost. People of non-industrialized countries do not have the amenities of twentieth century lifestyle, and the average lifespan is shorter than for Western nations. In contrast, we can live comfortable suburban lives commuting to our work in the city. Although

the magnitude of apparent high risk behaviors is relatively low in modern day, it is possible that there are some hidden costs that come with our heritage of responses. For example, while the commute into the city may be relative comfortable, it may not be without consequences (Singer et al., 1978), particularly over extended intervals, and in combination with other contemporary stressors. For instance, most people can contend with job stress in combination with other routine problems. However, Eliot and Buell (1979) reported individuals in high pressure jobs that became casualties. Did these individuals who became casualties have gross changes of their interior milieu that resulted from stress? Could it be possible that residents of TMI and DEL are experiencing changes in their bodily system responses similar to those discussed by Eliot and Buell (1979). Moreover, were the casualties reported by Eliot and Buell (1979) the victims of natural selection?

Comparison of immune and nervous systems. On one hand, stress consequences may have deleterious effects on health and even be an insidious mechanism of natural selection, yet stress responses could be quite the contrary. Earlier a statement was made about learning and adaptation of the immune system. Specifically, it was stated that learning was characteristic of populations, not individuals (Cunningham, 1977). Normally, learning is a construct referring to central nervous system function. It is interesting that both the central nervous system and immune system are similar in that they both undergo adaptive change. The similarities do not end there. Both the central nervous system and immune systems receive information from outside and inside the body. Specific methods of processing this information differs in each system, yet at a general level, processing

is similar. Just as most neurons of the brain do not make sensory or motor connections, but govern one another, the immune system hardware also is dedicated primarily to self-regulation. Thus, both of these complex systems have a huge investment in information processing. The nervous and immune systems, as already mentioned, are involved in making adaptive response to unexpected and unpredictable environmental stimuli. Each of these systems must be versatile enough to recognize and deal with entirely new information never encountered by either the host or any member of the host's species. However, recognition of a new stimulus is associated with previous experiences. Moreover, the nervous and immune systems both show memory and tolerance. Although these systems share these properties, their functions apparently are not redundant, but parallel (Cunningham, 1981). Until recently these similarities have not had implications.

Immune system as a sensory organ

It has been suggested by recent experimentation that the immune system has a sensory organ function (e.g. Blalock, 1984a). Further, this immune system sensory function seems to be interfaced with neuroendocrine signals. The most sensational observations of immune system - neuroendocrine interactions have been in witnessing what appears to be intriguing features common to the two systems; features more remarkable than the gross similarities already mentioned. Blalock (1984a) reviewed evidence along three lines demonstrating provocative immune system neuroendocrine interactions. This included immune system

system components and neuroendocrine peptide hormones with common functions; common receptors in immune and neuroendocrine systems for peptide signals; and common peptide hormones for immune and neuroendocrine systems.

The following examples of communication between nervous and immune systems will probably be shown to have novel implications. Research has demonstrated that interferon, a lymphokine, has the ability to produce norepinephrine-like increases in beat frequency of mouse myocardial cells (Blalock & Stanton, 1980). Moreover, interferon also exhibited an ACTH-like activation of the adrenal cortex to trigger steroid production (Blalock, 1984b). On the other hand, neuroendocrine peptide hormones have also been shown to function as lymphokines in terms of regulation of the production of other lymphokines. The abilities of neuroendocrine peptide hormones to function as lymphokines and lymphokines to cause hormonal responses has led to the possibility that the neuroendocrine and immune systems might share peptide signals that have common structures and thus, an economy of function. The finding that lymphocytes produce not only ACTH but also endorphin-like peptides supports this notion.

Results showing this apparent redundancy between the immune and nervous systems has fueled speculation for the existence of a lymphoid-adrenal axis (Blalock, 1984a). This axis has lymphocytes serving a sensory function by detecting noncognitive stimuli including bacteria, viruses, and antigens that are not recognized by the central nervous system. This information is then relayed to the neuroendocrine system which in turn mandates physiological responses. In a sense, this makes the immune system analogous to a messenger for the nervous

system. Thus, the information processing capacity of the body is rendered more efficient.

In contrast to viewing the physiological consequences of stress and health outcomes as a natural selection barrier, the work reviewed by Blalock (1984a) suggests an economy of responses. The crosstalk between immune and neuroendocrine systems could allow more versatility and adaptability. It could be that we are just beginning to uncover mechanisms for the body's efficiency in combatting infection.

Unfortunately, neither of these views of the adaptive value of behavioral neuroendocrine immune system interaction can explain all the facts. One must not forget to step back from theorizing and remember that the answers are embedded in complex interactions and not simple main effects. The number of variables involved in addressing the relationship between behavior and health is nearly unfathomable. Many possible mechanisms have been offered ranging from pituitary to adrenal hormonal mediation of immune system function. Thus, the basic problem is one of distinguishing important actual mechanisms from possible ones.

Conclusion

....in the medicine of the future the interdependence of of mind and body will be more fully recognized, and the influence of the one over the other may be exerted in a manner which is not now thought possible....Sir William Osler

Study of TMI residents has suggested that they have remained chronically stressed almost 5 years after the nuclear accident.

Self-report of somatic problems and urinary catecholamines have been elevated for TMI, relative to control subjects, during this interval. It was postulated that chronic reports of somatic problems and elevated urinary norepinephrine were linked to immunosuppression, as a function of exposure to chronic stress. A possible measure was offered that s-IgA levels would be suppressed in a chronically stressed population, but only ambiguous evidence was found to support of this index of immunocompetence. Even if further TMI study reveals that suppression of s-IgA is not a possible mechanism for explaining health outcomes, it will not necessarily mean the actual phenomenon has been established. The actual mechanisms will remain a problem to solve with new methodologies, advances in technology, and creative thought.

APPENDICES

APPENDIX A

TABLE OF DEMOGRAPHICS

BACKGROUND CHARACTERISTICS FOR TMI, FREDERICK, AND DELAWARE SAMPLES

Characteristic	TMI	DELAWARE	FREDERICK
Age	37	45	34
Sex (% female)	65	63	58
Per Cent Married	88	84	85
Children Under 18 (%)	78	40	77
Own Home (%)	91	96	100
Education			
(% high school degree or less)	78	40	65
(% college degree or more)	22	36	35
Family Income			
(% < \$20,000)	33	27	6
(% \$20,000-\$30,000)	33	23	37
(% > \$30,000)	15	33	5
Years in Current Home	7	12	5

APPENDIX B**SELF-REPORT INSTRUMENTS**

INSTRUCTIONS
Symptom Checklist-90

Below is a list of problems and complaints that people sometimes have. Please read each one carefully. After you have done so please circle one of the numbers to the right that best describes HOW MUCH THAT PROBLEM HAS BOTHERED OR DISTRESSED YOU DURING THE PAST 2 WEEKS INCLUDING TODAY. Mark only one circle for each item.

For example, if you have experienced a backache recently and it bothered you constantly in all postures you might circle the 5 below.

not at	a little	moderately	quite	extremely
all	bit		a bit	
1	2	3	4	5

not at all	a little bit	moderately	quite a bit	extremely
1	2	3	4	5

HOW MUCH WERE YOU BOTHERED BY:

1. Headaches	1	2	3	4	5
2. Nervousness or shakiness inside	1	2	3	4	5
3. Unwanted thoughts, words, or ideas that won't leave your mind	1	2	3	4	5
4. Faintness or dizziness	1	2	3	4	5
5. Loss of sexual interest or pleasure	1	2	3	4	5
6. Feeling critical of others	1	2	3	4	5
7. The idea that someone else can control your thoughts	1	2	3	4	5
8. Feeling that others are to blame for most of your troubles	1	2	3	4	5
9. Trouble remembering things	1	2	3	4	5
10. Worried about sloppiness or carelessness	1	2	3	4	5
11. Feeling easily annoyed or irritated	1	2	3	4	5
12. Pains in heart or chest	1	2	3	4	5
13. Feeling afraid in open spaces or on the streets	1	2	3	4	5
14. Feeling low in energy or slowed down	1	2	3	4	5
15. Thoughts of ending your life	1	2	3	4	5
16. Hearing voices that other people do not hear	1	2	3	4	5
17. Trembling	1	2	3	4	5
18. Feeling that most people cannot be trusted	1	2	3	4	5
19. Poor appetite	1	2	3	4	5
20. Crying easily	1	2	3	4	5
21. Feeling shy or uneasy with the the opposite sex	1	2	3	4	5
22. Feelings of being trapped or caught	1	2	3	4	5
23. Suddenly scared for no reason	1	2	3	4	5
24. Temper outbursts that you could not control	1	2	3	4	5
25. Feeling afraid to go out of your house alone	1	2	3	4	5
26. Blaming yourself for things	1	2	3	4	5
27. Pains in lower back	1	2	3	4	5
28. Feeling blocked in getting things done	1	2	3	4	5
29. Feeling lonely	1	2	3	4	5
30. Feeling blue	1	2	3	4	5
31. Worrying too much about things	1	2	3	4	5
32. Feeling no interest in things	1	2	3	4	5
33. Feeling fearful	1	2	3	4	5
34. Your feelings being easily hurt	1	2	3	4	5
35. Other people being aware of your private thoughts	1	2	3	4	5

	not at all 1	a little bit 2	moderately 3	quite a bit 4	extremely 5
36. Feeling others do not understand you or are unsympathetic	1	2	3	4	5
37. Feeling that people are unfriendly or dislike you	1	2	3	4	5
38. Having to do things very slowly to insure correctness	1	2	3	4	5
39. Heart pounding or racing	1	2	3	4	5
40. Nausea or upset stomach	1	2	3	4	5
41. Feeling inferior to others	1	2	3	4	5
42. Soreness of your muscles	1	2	3	4	5
43. Feeling that you are watched or talked about by others	1	2	3	4	5
44. Trouble falling asleep	1	2	3	4	5
45. Having to check and double check what you do	1	2	3	4	5
46. Difficulty making decisions	1	2	3	4	5
47. Feeling afraid to travel on buses, subways, trains	1	2	3	4	5
48. Trouble getting your breath	1	2	3	4	5
49. Hot or cold spells	1	2	3	4	5
50. Having to avoid certain things, places, or activities	1	2	3	4	5
51. Your mind going blank	1	2	3	4	5
52. Numbness or tingling in parts of your body	1	2	3	4	5
53. A lump in your throat	1	2	3	4	5
54. Feeling hopeless about the future	1	2	3	4	5
55. Trouble concentrating	1	2	3	4	5
56. Feeling weak in parts of your body	1	2	3	4	5
57. Feeling tense or keyed up	1	2	3	4	5
58. Heavy feelings in your arms or legs	1	2	3	4	5
59. Thoughts of death or dying	1	2	3	4	5
60. Overeating	1	2	3	4	5
61. Feeling uneasy when people are watching or talking about you	1	2	3	4	5
62. Having thoughts that are not your own	1	2	3	4	5
63. Having urges to beat, injure, or harm someone	1	2	3	4	5
64. Awakening in the early morning	1	2	3	4	5
65. Having to repeat the same actions as touching, counting, washing	1	2	3	4	5
66. Sleep that is restless or disturbed	1	2	3	4	5
67. Having urges to break or smash things	1	2	3	4	5
68. Having ideas or beliefs that others do not share	1	2	3	4	5

	not at all 1	a little bit 2	moderately 3	quite a bit 4	extremely 5
69. Feeling very self-conscious with others	1	2	3	4	5
70. Feeling uneasy in crowds, such as shopping or at a movie	1	2	3	4	5
71. Feeling everything is an effort	1	2	3	4	5
72. Spells of terror or panic	1	2	3	4	5
73. Feeling uncomfortable about eating or drinking in public	1	2	3	4	5
74. Getting into frequent arguments	1	2	3	4	5
75. Feeling nervous when you are left alone	1	2	3	4	5
76. Others not giving you proper credit for your achievements	1	2	3	4	5
77. Feeling lonely even when you are with people	1	2	3	4	5
78. Feeling so restless you could not sit still	1	2	3	4	5
79. Feelings of worthlessness	1	2	3	4	5
80. Feeling that familiar things are strange or unreal	1	2	3	4	5
81. Shouting or throwing things	1	2	3	4	5
82. Feeling afraid that you will faint in public	1	2	3	4	5
83. Feeling that people will take advantage of you if you let them	1	2	3	4	5
84. Having thoughts about sex that bother you a lot	1	2	3	4	5
85. The idea that you should be punished for your sins	1	2	3	4	5
86. Feeling pushed to get things done	1	2	3	4	5
87. The idea that something is seriously wrong with your body	1	2	3	4	5
88. Never feeling close to another person	1	2	3	4	5
89. Feelings of guilt	1	2	3	4	5
90. The idea that something is wrong with your name	1	2	3	4	5

INSTRUCTIONS
HEALTH QUESTIONNAIRE

Each of the following statements involves some aspect of how you rate your health. Please answer each item by circling the appropriate number on the 5-point scales. Consider the way you have felt only in the last 2 or 3 days. The numbers on the scale are illustrated below:

Not at all	A little bit	Moderately	Quite a bit	Extremely
1	2	3	4	5

HEALTH QUESTIONNAIRE

Not at all	A little bit	Moderately	Quite a bit	Extremely
1	2	3	4	5

IN THE LAST 2 OR 3 DAYS:

I have had symptoms of a cold or flu:
 1 2 3 4 5

I have felt very tired and run down:
 1 2 3 4 5

I have had a congested nose:
 1 2 3 4 5

I have had headaches:
 1 2 3 4 5

I have had a fever, chills or sensations of running a temperature:
 1 2 3 4 5

I have had an upset stomach:
 1 2 3 4 5

I have had a cough:
 1 2 3 4 5

I have had body aches not associated with exercise:
 1 2 3 4 5

In all I would rate my health in the last 2 or 3 days as:

1	2	3	4	5
much worse than usual	a bit worse than usual	same as usual	a bit better than usual	much better than usual

In the last 2 or 3 days I have felt as if I have just caught a cold or flu:

YES NO

In the last 2 or three days I feel as if I have just recovered from a cold or flu:

YES NO

In the last 2 or 3 days I have called a doctor to make an appointment or ask about my health:

YES NO

APPENDIX C

ASSAY PROCEDURES

Catecholamine Assay

Durrett and Ziegler (1980) have described a sensitive radioenzymatic technique of quantifying the catecholamines epinephrine and norepinephrine in body tissues and fluids. This assay converts catechols to their radioisotope-labeled amine metabolites. After a reaction mix has been added and this conversion initiated, samples are incubated for about 90 minutes, and the reaction is stopped. Next, the samples undergo organic solvent extraction in order to separate catecholamine metabolites from excess radioisotope that may be present. The metabolites produced by the reaction are then separated by chromatographic procedures and remaining radioactivity is measured. This radioactivity is used to determine the concentration of each catecholamine present in the original sample. A reference curve based on known concentrations of standards is used to obtain concentrations of unknowns.

The procedure used in the current study is performed as follows:

Reagents

1. Stock Standards

Norepinephrine (N) D,L-Norepinephrine HCl, MW=205.7
(MW=169.2)

(-)-Norepinephrine Bitartrate (hydrate),
MW=337.3

L-Arterenol Bitartrate (hydrate - 1.5
H₂O/mole) MW=319.3

Epinephrine (E) L-Epinephrine Bitartrate, MW=333.3
(MW=183.2)

Dopamine (D) 3-Hydroxytyramine HCl, MW=189.7
(MW=153.2)

A. 1 mg/ml in 0.2 N HAc

Prepare 10 ml of each (N, E, & D) separately and store in refrigerator.

B. 100 ug/ml NED combination for "NED-A" Aliquots

Combine 0.5 ml of each standard (N+E+D, 1 mg/ml in 0.2 N HAc).
Add 3.5 ml 0.2 N HAc.

Aliquot 100 ul into a series of 14 ml polypropylene tubes labeled "NED-A" and store in freezer. (10 ug of NED/100 ul)

C. Prepare further dilutions for standard curve from dilution A.

Standard Dilutions

100 pg=100 ul NED-A + 9.9 ml 0.01 N HCl. Add 10 ul to appropriate tube.
500 pg=100 ul NED-A + 1.9 ml 0.01 N HCl. Add 10 ul to appropriate tube.
1000 pg=100 ul NED-A + 0.9 ml 0.01 N HCl. Add 10 ul to appropriate tube.
2000 pg=100 ul NED-A + 0.4 ml 0.01 N HCl. Add 10 ul to appropriate tube.
4000 pg=100 ul NED-A + 0.15ml 0.01 N HCl. Add 10 ul to appropriate tube.

2. O-BHA 31.9 mg O-Benzylhydroxylamine Hydrochloride/10 ml
3. TEM pH 8.3
 -0.09 M MgCl₂ (MgCl₂-6H₂O, 4.57 g/250 ml) MW=203.3
 -20 mM EGTA (ethylene glycol-bis-(B-amino-ethyl ether)
 N,N'-tetraacetic acid, 1.9 g/250 ml) MW=380.4
 -0.2 M TRIS (6.1 g/250 ml) MW=121.1
 -adjust pH with HCl
 -will go into solution once TRIS is added
4. 0.75 M Borate buffer with 25 mg/ml EDTA, pH 10
 -11.59 g Boric Acid crystal + 6.25 g EDTA
 -add NaOH until pH 10
 -adjust total volume to 250 ml
5. 1% Tetraphenylboron (TPB)
 -1.0 g/100 ml in GDW
6. Cold Carriers
 1 mg/ml of each in 0.01 N HCl:
 Normetanephrine NME·HCL 120 mg/100 ml
 Metanephrine ME·HCl 118.6 mg/100 ml
 3-Methoxytyramine 3MT·HCl 120 mg/100 ml
7. 3:2 Toluene : Isoamyl alcohol (2400 ml toluene: 1600 ml
 isoamyl alcohol)
8. 0.1 N HAc (Acetic Acid 99.5%, 5.7 ml/L)
9. Cold Carrier + Ethanol/HCl 5 ml H₂O + 100 ml ethanol
 + 10 ul 1 N HCl + 32 mg NME·HCl + 31 Mg ME·HCl
 + 32 mg 3MT·HCl.
 Add H₂O + HCl to cold carriers to dissolve. Then add ETOH.
10. Ethylamine Solvent (prepare fresh for each chromatography jar)
 -80 ml Chloroform
 -15 ml Ethanol
 -10 ml Ethylamine
11. 2 N NH₄OH 135 ml/L of 28% solution
12. 4% NaIO₄ freshly prepared (0.4 g/10 ml)
13. 10% Glycerol keep refrigerated
14. 10 N Acetic Acid 288 ml/500 ml of 99.5% (glacial)
15. "Phosphor-Only" 240 ml PPO-POPDP in 4 liters toluene
16. 0.05 N NH₄OH
17. "TIAL"
 -2100 ml toluene
 - 900 ml isoamyl alcohol

- 150 ml fluor (PPO-POPOP)

PROCEDURE

1. Pipette 100 ul aliquot for two replicates of each sample into 14 ml round bottom polypropylene tubes. Make 1:100 dilution of 100 ul urine aliquots with GDW.
2. Blanks - 100 ul fluid in one tube (i.e., blank tube)
200 ul COMT mix in second tube
Controls - 100 ul fluid
Standards - various concentrations of N, E, D added to 100 ml
3. Keep samples on ice.
4. Add 10 ul 0.01 N HCl to each sample.
5. Add 100 ul of COMT incubation mix to each tube:
Mix = 1 ul O-BHA
84 ul TEM
0.6 mg/ml glutathione (reduced)
5 ul ³H-SAM
10 ul COMT
Incubate for 90 minutes at 37 degrees Celsius.
6. Return tubes to ice. Add 200 ul 0.75 Borate buffer with 25 mg/ml EDTA (pH 10) to each tube.
7. Add 50 ul cold carrier to each tube and vortex.
8. Add 50 ul 1% TPB and vortex.
9. Add 7 ml 3:2 toluene : isoamyl alcohol to each tube, cap, and shake for 5 minutes. Centrifuge at 3000 RPM for 5 minutes and uncap.
10. Place tubes in a dry ice/ethanol bath to freeze aqueous layer. Decant organic phase into 14 ml polypropylene tubes containing 250 ul of 0.1 N acetic acid.
11. Cap and shake for 5 minutes. Centrifuge at 3000 RPM for 5 minutes and uncap.
12. Aspirate organic phase. Wash remaining aqueous layer with 3 ml 3:2 toluene : isoamyl alcohol. Recap tubes, shake 5 minutes and centrifuge at 3000 RPM for 5 minutes and uncap.
13. Aspirate organic phase. Freeze samples in -70 degree Celsius freezer. Turn on refrigerator in lyophilizer to 0 degree Celsius or lower.
14. Put samples in shelf chamber and lyophilize aqueous layer of tubes.

THIN LAYER CHROMATOGRAPHY OF METHYLATED PRODUCTS

1. Remove samples from lyophilizer.
2. Add 50 ul cold carrier + HCl/ethanol solution and centrifuge for 30 seconds at 3000 RPM.
3. Spot solution onto prescored silica gel TLC plates with fluorescent indicator.
4. Add 50 ul cold carrier + HCl/ethanol solution again as in 2 above, but refrain from centrifugation.
5. Develop plates in hood in TLC jars containing thylamine solvent system. Line jars with chromatography paper to equalize solvent vapor.
6. Visualize spots on plate using U.V. light and mark with a soft pencil.
7. Scrape the 3 methoxytyramine, normetanephrine, and metanephrine spots into separate 7 ml liquid scintillation vials.

COUNTING OF DOPAMINE (non-beta-hydroxylated product)

1. Add 1 ml 0.05 N NH_4OH to each vial, cap, and shake slowly for 15 minutes.
2. Add 5 ml "TIAL," cap, shake vigorously and count 5 minutes per vial. (Be sure to let samples sit in the counter, in the dark for about 4 hours before beginning to count in order to minimize chemiluminescence.

COUNTING OF EPINEPHRINE AND NOREPINEPHRINE (beta-hydroxylated products)

1. Add 1 ml 2 N NH_4OH to each counting vial and shake for 15 minutes.
2. Add 50 ul freshly prepared 4% NaIO_4 to each vial.
3. After 5 minutes stop the reaction by adding 50 ul 10% glycerol to each vial.
4. Add 200 ul 10 N acetic acid to each vial.
5. Add 5 ml "Phospho-Only," cap, shake vigorously and count 5 minutes per vial. (Be sure to let samples sit in the

counter, in the dark for about 4 hours before beginning to count in order to minimize chemiluminescence.

6. Plot standard curve and evaluate unknowns.

Salivary IgA Assay

Mancini and coworkers (1965) described the relationship between antigen concentration and the diameter of an immunoprecipitin ring formed in an antibody-gel system. The precipitin ring stops increasing at the point where diffusible antigen is reduced and antigen-antibody complexing attains equivalence. At equivalence a linear relationship exists between the antigen concentrations for equal volumes of test samples and their corresponding ring diameters squared. Although this measure is independent of variation in time and diffusion rate, temperature exerts an influence.

The IgA assay in the present study was performed using the Kallestad Laboratories Low Level Immunoglobulin Test Kit. Equal volumes of reference sera are added to wells in an agarose gel containing a monospecific horse antiserum. As the reference sera (i.e., antigen) diffuses through the gel, a disc shaped precipitin ring is formed with the antisera in the gel. A reference curve is constructed by plotting reference concentrations as a function of the precipitin ring diameter squared. Concentrations of unknown samples are obtained by locating the projection onto the reference curve of the square of each test sample's diameter.

The specific procedure is performed as follows:

1. Allow the agarose plate and reference sera to equilibrate to room temperature after removing from refrigerator. Be sure that no moisture or condensation is present on the plates.
2. Mix the reference sera and unknowns several times by inverting.
3. Using a volumetric pipette, dispense 5 ul of each of the three reference sera and control serum provided into separate wells of the test plate. Step three should be followed for each plate necessary to accommodate the group of unknown samples.
4. Using a volumetric pipette, dispense 5 ul of each unknown into a separate well. Unknowns should be dispensed in at least duplicate wells for reliability. After waiting about 15 minutes for the 5 ul of unknowns to diffuse, dispense an additional 5 ul of unknown to each respective unknown's well. This extra 5 ul of unknown is to bring the concentration into a more sensitive range as the kit is designed for IgA in sera.
5. Let the covered plates sit on a level surface at constant room temperature for 48 hours, making sure that the plates are not disturbed.

6. At 48 hours read the precipitin ring diameters to the nearest 0.1 mm.
7. Construct a reference curve on linear graph paper by plotting the diameter squared on the abscissa and the concentration of the reference on the ordinate. The control sample should lie on the line defined by the three reference samples.
8. Concentration for each of the unknown samples is determined by reading concentration on the reference curve for each of the respective squared diameters.
9. Multiply each sample value obtained from the reference curve by 0.7. This adjustment is made to correct for saliva as the kit is specified for IgA in sera. Salivary IgA diffuses to 70 percent of that of IgA found in serum. As twice the amount of unknown is dispensed with saliva samples (i.e., 5 ul times 2 = 10 ul) the correction factor equals $1.4/2$ or 0.7.

Protein Assay

Bradford (1976) demonstrated a differential color change of a dye in response to various concentrations of protein. Bradford's technique has replaced other assays for a variety of reasons. In general, it is easier to use and requires only a single reagent. Further, the time required is about five minutes and protein-dye complex is relatively stable.

The present study used a protein assay kit by Bio Rad. This assay kit is based on the observation that the absorbance maximum for an acidic solution of Coomassie Blue G-250 shifts from 465 nm to 595 nm when binding to protein occurs. Several dilutions of a protein standard are used to create a standard curve from which unknown samples can be quantified. Each dilution of protein standard combines with dye reagent to produce a color gradient. The relative degree of color manifest by protein-dye complex is assessed by a spectrophotometer.

The procedure used in the current study is performed as follows:

1. Prepare dilutions of protein standard for 20, 15, 10, 5, and 2.5 ug/ml. Filter dye reagent through Whatman no. 1 paper.
2. Place 0.8 ml of each standard in clean, dry 7 ml test tubes. Place 0.8 ml of sample buffer in "blank" test tube.
3. Add 0.2 ml dye reagent to each of the 5 dilutions of standard, as well as reagent blank, and vortex, but avoid excess foaming.
4. After 15 minutes but less than 1 hour measure optical density on the spectrophotometer (OD 595) versus reagent blank.
5. On linear graph paper, plot the optical density (ordinate) as a function of the concentration of each dilution of standard.
6. If plot reveals a straight line, prepare dilutions of unknown of 1:500 and 1:100.
7. Place 0.8 ml of each unknown dilution in clean, dry 7 ml test tubes.
8. Add 0.2 ml of dye reagent to each tube and vortex.
9. After 15 minutes but less than 1 hour, use the spectrophotometer to measure optical density (OD 595).

10. Assess unknowns by projecting a line from standard curve to x-axis of graph to determine protein concentration.

ANALYSIS OF VARIANCE SUMMARY TABLES

Analysis of Variance Summary Table for Total Symptoms

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	7531.59	2	3765.80	8.91	0.000	0.20
RESIDUAL	30006.93	73	422.63			
TOTAL	37538.52	75				

Analysis of Variance Summary Table for Somatic Complaints

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	695.43	2	347.72	10.51	0.000	0.23
RESIDUAL	2349.11	71	33.09			
TOTAL	3044.55	73				

Analysis of Variance Summary Table for Health Questionnaire

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	149.53	2	74.77	1.62	0.21	0.05
RESIDUAL	2963.57	64	46.31			
TOTAL	3113.01	66				

Analysis of Variance Summary Table for Epinephrine

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	192.53	2	96.26	3.88	0.03	0.11
RESIDUAL	1639.30	66	24.84			
TOTAL	1831.82	68				

Analysis of Variance Summary Table for Norepinephrine

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	9689.19	2	4844.59	11.40	0.000	0.26
RESIDUAL	28058.00	66	425.12			
TOTAL	37747.19	68				

Analysis of Variance Summary Table for s-IgA

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	5.34	2	2.67	0.12	0.89	0.003
RESIDUAL	1631.75	73	22.35			
TOTAL	1637.09	75				

Analysis of Variance Summary Table for Salivary Protein

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	2.60	2	1.30	1.72	0.19	0.05
RESIDUAL	55.10	73	0.76			
TOTAL	57.69	75				

Analysis of Variance Summary Table for Ratio s-IgA/Protein

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	0.014	2	0.007	0.49	0.62	0.01
RESIDUAL	1.103	73	0.015			
TOTAL	1.112	75				

Analysis of Variance Summary Table for s-IgA/minute

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	0.010	2	0.005	0.645	0.528	0.02
RESIDUAL	0.571	73	0.008			
TOTAL	0.581	75				

Analysis of Variance Summary Table for s-IgA Volume

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	2.03	2	1.01	12.81	0.000	0.26
RESIDUAL	5.78	73	0.08			
TOTAL	7.811	75				

Analysis of Variance Summary Table for Anxiety Symptoms

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	652.96	2	326.48	11.45	0.000	0.24
RESIDUAL	2025.25	71	28.53			
TOTAL	2678.21	73				

Analysis of Variance Summary Table for Depression Symptoms

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	862.93	2	431.47	10.71	0.000	0.23
RESIDUAL	2860.43	71	40.29			
TOTAL	3723.36	73				

Analysis of Variance Summary Table for Concentration Symptoms

SOURCE OF VARIATION	SUM OF SQUARES	DF	MEAN SQUARE	F	p	ETA ²
GROUP	446.64	2	223.32	8.00	0.001	0.18
RESIDUAL	1982.70	71	27.93			
TOTAL	2429.34	73				

TABLE OF ABBREVIATIONS

ABBREVIATIONS

ACTH	Adrenocorticotropic hormone
ANOVA	Analysis of variance
ANS	Autonomic nervous system
CNS	Central nervous system
COMT	Catechol-O-Methyl transferase
DEL	Delaware (the sample of subjects living near the toxic waste sample)
FRD	Frederick, Maryland (control sample of subjects living at least 20 miles from any power plant)
IgA	Immunoglobulin A
IgD	Immunoglobulin D
IgG	Immunoglobulin G
IgE	Immunoglobulin E
IgM	Immunoglobulin M
RA	Rheumatoid arthritis
SCL-90	Symptom Checklist-90
s-IgA	Salivary Immunoglobulin A
TMI	Three Mile Island (experimental sample living within five miles of the damaged nuclear reactor)

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