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Stress

Definitions and Pathways to Disease

Stress is essentially reflected by the rate of all wear and tear caused by life.

—Hans Selye, 1956

Scientific and Popular Definitions

It makes little sense to write about stress *management* (SM) unless there is clarity about the phenomenon that is to be managed. For this reason, a broad but by no means exhaustive review of the term *stress* and its importance for health is provided first. In this chapter, the meaning of the terms *stress* and *management* is explored, and research is described that reveals how they can be connected.

"Stress" has become so ubiquitous and so much a part of everyday language that, at first glance, there appears to be no need for a definition. Selye (1976), a pioneer of stress research, points out that "stress is a scientific concept which has suffered from the mixed blessing of being too well known and too little understood." Consistent with Selye's view, it is argued here that when concepts from basic science become popularized, there is potential for oversimplification or alteration of the term that may ultimately belie its origins and add to confusion.

When seeking definitions, the general populace does not read scientific journals. People are much more likely to refer to other "gold standards" of definition like *Webster's Dictionary*. Ideally, definitions contained therein are in full accord with scientists' definitions but just

appear in a simpler or broader language. What, then, can one learn from consulting a dictionary?

Webster's dictionary (*Webster's Illustrated Encyclopedic Dictionary,* 1990) gives six definitions, ranging from a generic definition to more specific ones depending on areas of application. The first, most generic, one is: "Importance, significance, or emphasis placed on something." The second, third, and fourth deal with stress as a feature of spoken language and sound: "The degree of force with which a sound or syllable is spoken"; "The relative emphasis given a syllable or word in verse in accordance with a metric pattern"; and finally, "an accent" in music. The next definition relates stress to physics: "An applied force or system of forces that tend to strain or deform a body, measured by the force acting per unit area." Finally, a definition is given that is more psychological in nature: "A mentally or emotionally disruptive or disquieting influence, or alternatively, a state of tension or distress caused by such an influence." One can easily see differences in these many definitions such that only the definitions used for physics and psychology contain elements of an action and a result, a challenge and a response. The novelty of the term *stress* also provided a considerable challenge for translation into other languages; for example, there are no equivalent terms in French or German, and in the end it was largely decided to use the word *stress* in the same way across many different languages. Given that Selye (1976, p. 51) saw stress as the result of a process, he further felt a need to label the beginning of the process in a manner distinct from the outcome and coined the term *stressor* to refer to a causative agent, a trigger for this process.

A two-step sequence of "stress" is also reflected in definitions found in psychological textbooks. Girdano, Everly, and Dusek (1993, p. 7) state, "Stress is the body reacting. It is psychophysiological (mind-body) arousal that can fatigue body systems to the point of malfunction and disease." Hence, popular and scientific definitions see "stress" as a process in which external and internal stimuli, forces, or systems interact, where triggers activate a response system that may lead to exhaustion and vulnerability (Wheaton, 1996).

My definition of stress, as applied to stress management, is this:

> Stress is a mediational process in which stressors (or demands) trigger an attempt at adaptation or resolution that results in individual distress if the organism is unsuccessful in satisfying the demand. Stress responding occurs at physiological, behavioral, and cognitive levels. Stress is more than just acute subjective or physiological activation and has its potentially most deleterious health effects when it becomes chronic.

Before delving further into the history and basic research on the stress concept, it should be clarified that, consistent with my definition of stress, the emphasis is going to be on chronic stress and its health consequences rather than on a singular, traumatic kind of stress exposure. Exposure to a traumatic event, like witnessing or being subjected to violence, is a profound event with potentially grave and long-lasting psychological sequelae; in their most severe form, these sequelae qualify for posttraumatic stress disorder, which can be quite debilitating. Little is known about the long-term physical health consequences of traumatic stress (with the exception of early life exposure to trauma, discussed below) and the treatment techniques embraced by stress management (Ong, Linden, & Young, 2004) are not treatments of choice for posttraumatic stress disorder (Taylor, Lerner, Sherman, Sage, & McDowell, 2003).

Also of importance is the recent introduction of the term "acute stress disorder" (American Psychiatric Association [APA], 1994), which was meant to describe initial reaction to trauma that in turn predicts posttraumatic stress disorder. There is considerable debate whether science and clinical practice are well served by having two disorders that are so closely interlinked, and that are really distinct only in the time period required for their manifestation (2 days to 4 weeks relative to at least 1 month post trauma; Harvey & Bryant, 2002). Notwithstanding this debate, neither acute stress disorder nor posttraumatic stress disorder will receive much attention here.

How Can Stress Be Measured?

Having a clear definition of a construct is a useful and necessary precursor for its measurement. In the case of stress, which was defined as a multistep process, the answer to the question posed in the title of this section is anything but simple. The great majority of what has been written about the measurement of stress is really the measurement of the *stress response,* that is, the *result* of the stress process. Because stress responding can occur at behavioral, cognitive, and physiological levels, measures of stress responses at each level would ideally correlate highly with each other, meaning that they would be synchronous. Unfortunately they are often desynchronous, and some observations made in my laboratory and a brief anecdote may serve as illustrations of the relative desynchrony among various stress measures.

When exposing individuals to controlled laboratory stressors, we routinely request participants to provide a rating of the stressfulness of the

experience, primarily to serve as a validation check. This method has been very effective in showing that a mild stressor like exposure to white noise receives a mean rating of 3 on a 10-point scale whereas an arithmetic challenge with interjected harassing feedback is likely to rate on average of 7 out of 10, thus validating the anticipated differences of the severity of the stressors. However, irrespective of the type of stressor used, and provided that a large sample was tested, some participants rated the exact same stressor 1 out of 10 whereas somebody else rated it 10 out of 10. What accounts for such whopping differences in perception? It is posited that these often greatly varying ratings of the same stimulus reflect a blend of (a) stable, natural response tendencies toward repressing or sensitizing to individually relevant affective information; (b) the subjective, idiosyncratic meaning of the stressor; (c) possible differences in the ability to perceive simultaneous physiological activation; and (d) possible mood priming via pleasant or unpleasant daily events that preceded participation in the research study.

A researcher who sees such great variability in the judgment of the exact same stressor develops great doubt about the comparability of subjective stress ratings across individuals, and develops a cautiousness that outsiders may not readily share. Along these lines, I had been approached by a TV reporter who was aggregating information from "experts" and the lay public about the presumably growing level of stress in the Canadian populace. The TV production team wanted to measure the absolute level of "stress" by conducting a representative telephone survey and using self-reported stress levels as the index of "real population stress." When I told the reporter that in my opinion this method of assessment was not an adequate way of measuring "population stress," he was quite surprised and asked for an explanation. The analogy I used was that measuring "stress" was a lot like measuring "winter." We all (especially we Canadians) know what winter is, but it is also clear that there is no single defining characteristic of "winter." That notwithstanding, people know and even agree on a number of features that jointly characterize winter, including below-freezing temperatures, reduced daylight, snowfall (or increased rain in some climate zones), a time epoch in the calendar ranging from December to March, and so forth. My position with this reporter was that the more of these features we measure, the more we capture the global phenomenon "winter," and that measuring "stress" is very much the same.

An attempt at applying this reporter's crude definition to a real-world problem may further serve to strengthen the point. If one accepted that self-reported stress by one individual was a fully satisfactory definition of stress,

then workers' compensation boards and various insurance companies would likely go bankrupt as a consequence of the resulting number of "stress disability" claims they would have to pay out on. In a variety of jurisdictions, workers' compensation boards already have to deal with these issues and have categorically decided that subjective self-report is clearly not sufficient for a stress-related disability.

In principle, reliance on self-report of stress would make sense if there were a close correlation (with high sensitivity and specificity) of self-reported stress with the biological markers that are known to play a critical role in the process of activation, failure of recovery, and exhaustion. Unfortunately, the literature indicates that biological changes and self-reported stress, even under relatively transparent circumstances, are at best moderately correlated, as research on acute physiological reactivity in the laboratory shows. Even in well-controlled laboratory environments with reduced stimulus complexity, physiological and parallel mood changes rarely show correlations exceeding $r = .3$. Self-reported distress rarely explains more than 10% of the variance in physiological change (Linden, 1987). While disappointing, this is not really surprising because (a) there are few direct pathways between central nervous system activity and conscious awareness, (b) researchers have observed marked individual differences in ability and willingness to sense and report physiological changes (Pennebaker, 1982), and (c) people rely heavily on contextual clues for inferring physiological changes from mental representation of environmental events ("This is an important test and I know that I am ill-prepared, so whatever I feel must be 'stress' and my fast-beating heart confirms this"). At the level of sensation, there is inherently limited awareness of biological markers, ranging from complete inability to sense, for example, lipid changes or platelet aggregation in the blood, to a rather modest awareness of blood pressure or heart rate changes, to reasonably accurate knowledge of breathing rates or rising blood alcohol levels (although even in the latter cases false feedback studies show that only large changes are accurately perceived). Understanding the relationships between context use and accurate physiological sensing requires delving into basic psychological research that differentiates sensation from perception.

The problems that are endemic to people's relative inability to accurately sense stress-related biological changes, and to the unavoidable influence of context variables on self-reports of stress, are particularly worrisome when important decisions with long-term impact have to be made and objective indices are hard to come by (see the discussion above on the workers' compensation systems that process claims for stress-related disability).

Is there an answer to the question, "Can stress be measured?" In an absolute sense, the answer has to be emphatically "no." Given that stress is not a fixed state but a process with multiple phases and with interacting cognitive, behavioral, and physiological processes, we cannot readily index stress and should not even attempt to draw inferences from it from any single index, whether subjective or physiological. We can, however, aggregate information from self-reported distress, observe behavior, and determine physiological activation that is known to be relevant to the stress arousal and exhaustion process. Grossi and his collaborators (Grossi, Perski, Evengard, Blomkvist, & Orth-Gomer, 2003), for example, have compared people with self-reported high and low burnout and found a reasonably high level of parallel self-reported stress and physiological marker activity in neuroendocrine and immune systems. Self-reported stress levels were also sufficient to predict significantly greater mortality risk over 5 years in a cohort of 6,920; this effect held true even after controlling for sociodemographic and known cardiovascular risk factors (Rasul, Stansfield, Hart, Gillis, & Smith, 2004). No class of measurable phenomena that are correlates of stress (and certainly not any single index within each class) can be accepted as absolutely reflecting "stress"; any inference needs to involve understanding of the context and needs to establish the concordance of various stress markers. One can take, for example, cortisol and its precursor ACTH, which are widely considered to be good markers of the stress response. In addition to reflecting varying stress levels, they are also influenced by naturally occurring diurnal patterns, individual differences, and random fluctuations that prevent absolute inferencing of cortisol activity to mean "stress."

Nevertheless, I do believe that it is meaningful to study subjective reports of stress in the same individual over time (as is done in diary studies) and then relate them to parallel occurring objective events, given that the individual difference variables in stress reporting are presumably stable over time. This claim needs to be tempered, however, with the fact that reactive situations (like stress and pain reports in claimants for a disability) threaten the trustworthiness of subjective stress reporting.

A History of Models for Stress and Health

The decision to start with a chapter on the history of stress should not be taken to mean that an exhaustive review and discussion will follow; the intent here is to focus on those features of previous theorizing that have most

prominently contributed to shaping this book and its objectives. Readers who want more in-depth reviews of theories and proposed biological pathways from stress to disease can seek out a large number of books and review articles. As such, there are many excellent undergraduate textbooks in health psychology that provide broad overviews, and for greater depth of facts and discussion, I recommend Lovallo's (1997) excellent discourse, *Stress and Health,* as well as McEwen's (1998), Ray's (2004), and Kelly, Hertzman, and Daniels's (1997) review articles.

These caveats notwithstanding, some background on major theories and empirical findings needs to be presented early in this text so that sound, empirically based psychophysiological rationales for stress management interventions can be offered, and so that my criticisms of extant thinking and writing on stress management can be solidly grounded.

What may appear to be modern approaches to understanding stress have roots in ancient views of health and disease that can be traced to beliefs and practices of Oriental (around 2600 B.C.) and Greek physicians (around 500 B.C.) who advocated moderation, avoidance of excess, and concepts of balance and harmony. The current practices of acupuncture, meditation, yoga, biofeedback, self-hypnosis, and Autogenic Training can be traced back to these ancient views of health as a state of good balance.

Cannon (1928) can be credited with describing a view of physiological balance that at once reconnects medicine with historical views of a healthy balance and also represents a sound approach to physiology that is actually measurable and quantifiable. His work underscored that the autonomous nervous system response to challenges needs to be understood as a dynamic interplay of sympathetic and parasympathetic activation in the autonomous nervous system. These two regulatory forces of the nervous system have opposing actions and both need to be strong and responsive to achieve or maintain health.

Selye's (1956) general adaptation syndrome can be seen as an elaboration of Cannon's work in that he showed conditions and pathways for nervous system activity to become unbalanced. The general adaptation syndrome describes stress as a potential 3-step sequence of events in which a challenge (like the appearance of an aggressor—step 1) precedes the body's activation of its innate coping abilities to deal with the challenge: fight, flee, or otherwise adapt (step 2). Frequently, the whole process of challenge and response ends right there because the challenge has been effectively met, and the constructive arousal that accompanied the stress resistance and that allowed active responding is no longer needed and can return to a physiological resting state. Consistent with Cannon's work, it

can be seen that after initial sympathetic activation, the body's natural inhibitory systems "kick in" in the form of counterregulatory, de-arousing, parasympathetic activation. However, not all challenges are of time-limited nature and/or allow quick, decisive responding, and the body continues to resist, becoming by necessity exhausted at some point (step 3). This physiological exhaustion is considered to carry disease potential because the body is now weak and unable to resist. Interestingly, the term *exhaustion* found in Selye's work has been carried forward into other researchers' work and, for example, a Dutch research group has coined the term *vital exhaustion,* which they have shown as critically preceding myocardial infarction (Van Diest & Appels, 2002). Vital exhaustion describes a psychophysiological state of mental numbing that is related to perceived low self-efficacy (i.e., an awareness of one's own low level of effectiveness), inability to cope, and a subjective sense of low energy and fatigue, thus vividly describing a blend of biological and emotional features that aptly represents Selye's notion of exhaustion.

Selye's original work posited a whole-body response such that external challenges were held to lead to the same cascade of physiological responses. The typically occurring physiological changes in response to a challenge are well established and described in numerous textbooks. Figure 1.1 describes the paths and the sequence of activities in Selye's activation-exhaustion model (1976).

This coarse model of Selye's activation/exhaustion model leads to a series of questions that need answering if the full process is to be understood: (a) Which stimuli (or stimulus properties) activate the process? (b) What is the physiological chain of actions that mark an activation process? (c) Who, under what circumstances, adapts and who, under what circumstances, becomes exhausted? Satisfactory answers to these core questions ought to provide the stress management researcher with the critical knowledge needed to develop a sound rationale for interventions.

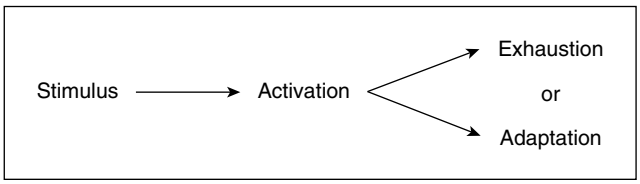

Figure 1.1 The Selye Model of Stress

Stress-triggering qualities of stimuli will not be discussed first (a detailed review is found at the beginning of Chapter 2). Instead, the physiological activation process is described first because it is central to the originality of Selye's work. Selye believed in response universality; that is, all stimuli above perception threshold are held to trigger similar physiological stress responses across different species and across situations. This presumably universal cascade of events (adapted from Sarafino, 2002) is as follows:

1. Environmental stimuli that are judged to be of subjective importance trigger cortical activation that sends chemical messengers to the hypothalamus, where
2. they stimulate the production of corticotrophic releasing factor (CRF) and other chemical messengers that, in turn, activate two distinct tracks of bodily reactions.
3. In the first track (also commonly referred to as the sympathetic adrenal medullary axis), these messengers feed information forward to the pituitary gland, which
4. changes the chemical structure of the messengers and releases adrenocorticotropic hormone (ACTH) into the bloodstream.
5. When ACTH reaches the adrenal glands, it initiates the production of cortisol, which, in turn, increases metabolic rate. Cortisol inhibits the function of phagocytes and lymphocytes in the immune system (i.e., it serves as a messenger for needed adaptations of the immune system).
6. On the second track (commonly referred to as the hypothalamic-pituitary axis), chemical messengers leave the hypothalamus and trigger electrochemical changes that advance as signals down the brain stem and the spinal cord toward the adrenal glands.
7. At the level of the adrenal gland, this activation leads to release of epinephrine, which supplies extra glucose to musculature and brain. Epinephrine also increases suppressor T-cells and decreases helper T-cells, thus revealing a second connective pathway of stress reactivity to immune function.
8. The adrenal glands also release norepinephrine, which then speeds up heart rate and increases cardiac output and blood pressure.
9. Ultimately these activities and their results are fed back to the hypothalamus, which serves as the "master controller" of this whole process.

This cascade of physiological responses to challenge involves intricate interplays and feedback loops of biochemical and electrophysiological processes that regulate autonomic nervous, endocrine, and immune system activity. Within the autonomic nervous system, activation of the sympathetic branch (via release of ACTH) prepares organs for the fight-or-flight response by dilating pupils and bronchi, increasing the rate and force of the heart's pumping action, constriction of blood vessels, secretion of epinephrine, and decreasing peristalsis. An important physiological control function is assigned to the parasympathetic branch of the autonomous nervous system that opposes these actions and is functionally designed to facilitate recovery. One can readily see that the teaching and learning of techniques to maximize parasympathetic system flexibility is of critical importance to physiological stress management.

This activation process, that is, the fight-or-flight response, does not carry within its definition any connotation of inherent maladaptiveness; if anything, the opposite is true as long as fight or flight is really necessary for survival. In the evolution of species, fight-or-flight responses are highly useful tools for survival because they maximize the availability of muscular energy, sensory acuity, and protection of tissues from injury. However, a critical and widely accepted feature of Selye's view of the activation response is that our biological systems cannot sustain this activation for a long period of time; all living creatures become exhausted if the fight-or-flight response does not lead to resolution of the challenge. The changed flow of blood during activation relative to rest can be used to show how initial adaptiveness of the activation process can turn into a long-term health threat. During rest, most of the body's blood volume circulates between the heart and the viscera so that needed nutrients and oxygen are available for organ function; that is, about 60% of blood flow during rest goes to the kidneys, skin, digestive system, and bones. During fight-or-flight responses, however, the bulk of the total blood volume is made available to the muscles and the brain, with only a fraction still being available to support visceral functions (in that case, only about 20% of the blood volume goes to skin, digestive system, kidneys, and bones; Astrand & Rodahl, 1970). Just as whole living beings cannot stay alive without nutrients or oxygen for an extended period of time, neither can individual organs. Recovery from the stress-induced blood redistribution to muscles and brain needs to occur relatively quickly if the organ tissues are not to suffer damage from lack of nutrients and

oxygen. This relatively simplistic description of how activation can turn to exhaustion is quite suitable for explaining the stress-exhaustion process to patients who present with stress-related psychophysiological disorders.

Selye's idea of response universality has been challenged by subsequent models and research findings discussed in more detail below. What was initially a simple stimulus-response model was expanded to include genetic and early learning differences in responsivity as well as acute response modulation through behavioral and cognitive activity.

In order to understand how macro-level effects at the community level can affect cellular activity and vice versa, Brody has described a 17-layer system in which levels of influence for stress and health are organized on a continuum from mini to macro activity, from atom to molecule, to cell and tissue, to organs, systems, whole person, and finally community and society (Brody, 1973). He presumes that each level of activity influences the ones directly above and below so that ultimately a connection can be shown between molecular change and societal change. The direction of influence can be ascending and descending on this continuum.

A particularly influential model of stress and health is Levi's (1972) interactional model (Figure 1.2), which extends Selye's work by arguing that the magnitude of a stress response can be better predicted by understanding the stressor in the context of a person's predisposition, thus opening the door for a better understanding of individual differences in the stress response magnitude.

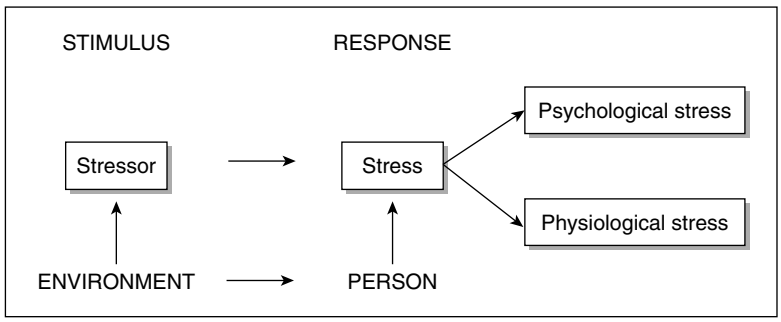

Figure 1.2 The Stress Diathesis Model

While useful for driving and organizing further research, Selye's and Levi's models are now considered simplistic by more cognitively oriented researchers. Before continuing to discuss more expansive models, it may be of use to organize existing models into categories. For the purpose of this book, the categorization structure proposed by Feuerstein, Labbe, and Kuczmierczyk (1986, p. 122) was adopted here; it differentiates the following four types of models: (1) response-based models, (2) stimulus-based models, (3) interactional models, and (4) information processing models.

Selye's model is considered a response-based model because it presumes that all stimuli trigger the same cascade of physiological responses and that the nature of the response (activation and resolution vs. activation and exhaustion) ultimately dictates the health outcome. Levi's model is more of an interaction model because it opens up the possibility that the response to a stimulus is not universal but affected by the type of stressor and the context, which, if understood, allows a prediction of the magnitude and likelihood of a subsequent stress response. The problem with simple response- and stimulus-based models is that they do not account for the great variation that people actually show under equally demanding conditions. Interactional and information processing models allow for the existence of feedback systems and presume a more cyclical nature of stress processes. In one such model (Cox & McKay, 1978), a critical element in determining the magnitude of a potential stress response is the cognitive appraisal of a demand situation in that stress is presumed to result when the perceived capability to cope does not meet the perceived demand. This "imbalance" is by definition "stress." Perceived ability to cope is in part determined by actual capability, and perceived demand is in part determined by actual demand. Discrepancies between actual and perceived demand and actual and perceived coping capability are further moderated by prior learning and personality differences. Cox and McKay further posit that individuals judge the adaptivity of their coping attempts and that information is fed back to the individual, who may then reevaluate the stressfulness of the situation, or the levels of (perceived and actual) demand and capability.

Information-processing models are fairly similar in that they focus on attention, appraisal, and memory processes. Hamilton (1980) sees perceived stress levels as the aggregated result of a stressor recognition and evaluation process that integrates the importance and meaning of the stressor, the amount of attention that the system allocates to it, and memories about past effective and noneffective coping experiences. According to Hamilton, stressors themselves can have three challenging qualities:

(1) anticipation of physical pain or danger, (2) threat of social isolation or rejection, and (3) stimulus complexity involving either concurrent response demands or novelty and complexity. More than one of these qualities may be present at the same time, and it is reasonable to predict that stressors are ultimately leading to greater stress responses if two or even three of these qualities are present simultaneously.

When trying to use models of stress to build an empirically grounded rationale for stress management, one needs to realize how application of various stress theories to different species also creates unique challenges and opportunities for studying stress-related disease etiology. Applying basic research findings from the animal model to human applications is particularly challenging for understanding attempts at prevention and intervention. This can be illustrated by relating stress models to plants, animals, and humans and by highlighting similarities and differences. Bernard (1961) makes the case for a reductionist approach to understanding survival of simple organisms like plants. These organisms are dependent on their environment to supply nutrients, water, light, and so forth, and if these "supplies" become exhausted, the organism dies. Yet even this reductionist perspective allows adaptation in that plants may evolve to thrive in more or less light, or varying degrees of water supply; ultimately, however, they are still supply-dependant. Animals, on the other hand, have mobility and can actively seek out supplies, and this search can lead to extreme efforts such as the annual migration of geese over thousands of miles, even from one hemisphere to the other, in order to obtain stable food supplies. This greater mobility translates into much greater activation potential of the organism, but that, in and of itself, also carries the potential for quicker physical exhaustion as can be seen, again, in the example of migratory birds who may not survive a lengthy migratory flight to their winter (or summer) location. In humans, there is the same principal dependence on environmental features as applies to all organisms (e.g., oxygen and nutrients), there also is mobility (fight or flight) as is seen in animals, and, in addition, humans possess cognition and mental representation that can serve as stress triggers (which will be discussed later in this book). Cognition is also a potential source of stress resolution. Without denying the possibility of thought processes and a degree of consciousness in animals, findings from tests of animal models offer little generalizability to human cognitions. Stress triggers for humans can range from very physical (like lack of air supply during an asthma attack, which is of course a factual challenge to survival of the organism), to very psychological and human-specific triggers, like a sudden fear response to the teacher's announcement

of a pending test for which a student did not study, or a husband's sudden realization that he forgot to get a birthday gift for his wife. Hence, the gamut of potential stress triggers for humans is almost infinite, covering physical, objective challenges inherent in the environment at one end of the spectrum, as well as symbolic and learned challenges at the other end.

The most recent models of stress and health have challenged Cannon's (1935) relatively rigid notion that a homeostatic state is needed and desirable for survival, and have attempted to classify the types of challenges that do not merely trigger acute responses but also possess potential to become chronic stress triggers. Theorizing about ideally functioning physiological systems had initially focused on the idea that there are ideal values (reflecting homeostasis in the sense of Cannon) and elevated, that is, maladaptive, values (as is the case with blood pressure). However, this model implied a rather static definition of homeostasis and has been replaced by the recognition that living systems must adapt, change, and accommodate to changing circumstances to guarantee survival of a species. A system's ability to achieve long-term stability and health through ongoing adjustment change has been labeled allostasis (Sterling & Eyer, 1988). Allostasis presumes that physiological systems strive to remain within a healthy range of function that allows optimal responsivity to external challenges while maintaining their own control functions. The allostasis concept is not meant to be in contradiction to the homeostasis concept; rather it modifies the definition of homeostasis as a desired variability within a healthy range instead of a fixed static level. A good example of the danger of "excessive stability" in the physiological domain is the observed lack of variability in the intervals between heartbeats that precede sudden cardiac death (Kamarck & Jennings, 1991). Similarly, the immune system works at its best when responding to immune challenges, and it is argued that repeated challenges can strengthen the system's ability for future adaptive responding; this principle is, of course, the well-known rationale for vaccinations. The same can be stated for the value of physical exercise, which, when applied in moderation, serves as a stress buffer because it enhances the body's ability to adjust, to respond quickly to challenges. At a psychological level, parents, for example, must adjust their expectations about reasonable rights and responsibilities for their growing children; as the children mature, curfews and allowances may need to be adjusted upward, and increasing levels of responsibility can be expected in return. Failing to make such adjustments is almost guaranteed to create family strain and prevent desired maturation.

The extent of challenges or demands on a system is, then, referred to as the allostatic load, which at some point may exceed a given system's ability to cope. McEwen (1998) describes four types of situations in which the nature of the challenge and the resulting allostatic load may exceed the body's capacity to respond and therefore lead to damage. The first such scenario is the frequent repetition of exposure to a stimulus with no time for recovery before the next stressor is represented. Figure 1.3 displays this "repeated hits" scenario.

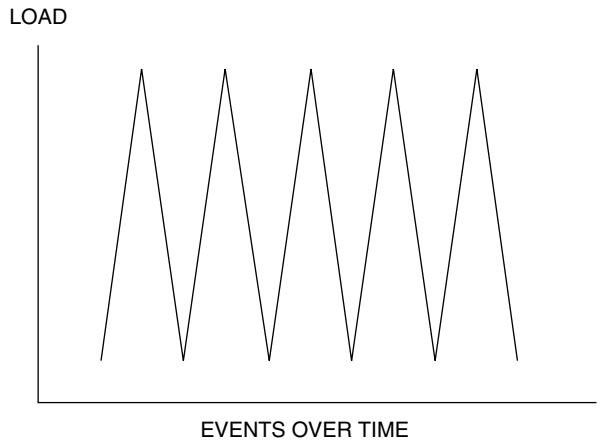

Figure 1.3 Repeated Hits Model

A real-world scenario that represents this type of situation would be emergency room staff in a busy city hospital where recent personnel cuts have led to serious understaffing that requires frequent overtime work. Anybody watching an episode of *E.R.* on television will see this scenario come to life! The potential for quick burnout and exhaustion in this environment is readily apparent.

A second type of allostatic overload is also characterized by repeated stressor appearance but differs in that some individuals fail to show adaptation that others are capable of. An example would be adjustment (or the lack thereof) to living close to a fire station; some people may develop the capacity of sleeping through repeated siren noise in the night whereas others simply fall farther and farther into sleep deprivation. This scenario is displayed in Figure 1.4.

A third type of stressor situation with high "overload potential" is one where badly needed recovery is delayed or fails to happen. This type of situation (displayed in Figure 1.5) arises, for example, through chronic work stress or in response to interpersonal conflict, as diary studies of marital interactions (DeLongis, Folkman, & Lazarus, 1988) and interpersonal

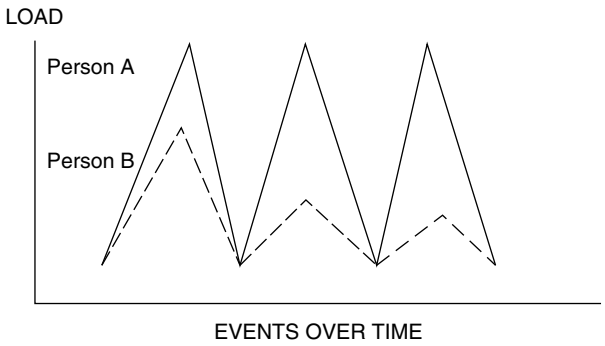

Figure 1.4 Lack of Adaptation Model

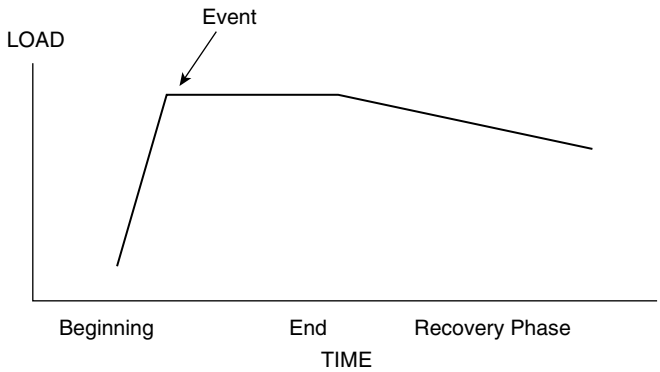

Figure 1.5 Lack of Recovery Model

laboratory stressor studies (Earle, Linden, & Weinberg, 1999; Linden, Rutledge, & Con, 1998) have shown. Such scenarios are not particularly rare, as Frankenhaeuser (1991) has shown in her psychophysiological evaluations of working mothers. These women showed understandable stress

responses to heavy demands at the workplace, and the return home provided no reprieve either (as was shown by tracking stress hormone release) because there still were housework and other family responsibilities waiting for them.

A fourth situation is not displayed graphically because it involves multiple, complex, interacting systems; here the inadequate response of one allostatic system triggers a compensatory response in other systems. An example of this nature provided by McEwen (1998) describes stress hormone activity. If cortisol secretion in response to a challenge does not occur, then inflammatory cytokines are released that make animals (and presumably humans alike) susceptible to autoimmune disturbances.

The addition of the allostatic load concept to stress research represents an expansion, refinement, and evolution of Selye's concept of the adaptation syndrome but does not contradict its basic premises. With the addition of research on allostasis, there now is a richer, better-documented picture of how to differentiate normal from pathological stress responding, and extensive descriptions exist of various critical situations as well as a rich body of studies on the physiological pathways and their interactions for understanding the linkage of stress to disease outcomes. Interestingly, neither Selye's original work nor the expansion model arising from the allostasis concept deals with how the stimuli themselves come into existence, whether or not they deserve attention, and whether they can be eliminated or manipulated. These stress models do not address the question of potential modifiability of the stimuli themselves. The inherent message is that stressors exist and that physiological systems (and the people who are governed by these systems) must respond; that is, people are not seen as creators or shapers of their own environment, they are simply considered to be reactors.

Understanding Stress Responsivity

Individual Differences in Stress Responding and Their Origins

As any astute reader of scientific articles on stress reactivity will quickly find out (especially when reviewing tables of results in stress reactivity studies), people's responses to the exact same stimulus vary greatly. In my laboratory, we have obtained such evidence in numerous controlled studies where participants were exposed to contrived stressors (like physical exertion, mental arithmetic, simulated public speeches, or affect

provocation). It is normal and typical that under the exact same stimulus condition one can see an average increase of 10 beats in heart rate and maybe an *average* of 10-mmHg (millimeters of mercury) increase of systolic and diastolic blood pressure (SBP and DBP, respectively) in a healthy sample. Yet one not-infrequently observed extreme in response variability can be an actual *drop* in heart rate and blood pressure (of –5 points) under acute stress (relative to resting baseline). At the other extreme, heart rate increases of +50 beats/minute, SBP increases of +40 mmHg and DBP increases of +30 mmHg are also often observed in the most responsive research participants, who, incidentally, may not show any signs of cardiovascular disease at the time. Understanding the reasons for this remarkable variability in subjective and in cardiovascular stress responsivity may hold important clues for changing reactivity, and it may provide information for what to build into the rationales for stress management.

For this reason, the current section is devoted to a description of the wide range of variables that are known to mediate and moderate stress reactivity. The reader should note that (similar to the above section on stress-disease pathways) this section can serve only as an illustration and not an exhaustive review of all prior research on stress reactivity. For more detail, the reader can consult Lovallo's (1997) book, or a special issue of *Psychosomatic Medicine* where the status quo of the cardiovascular reactivity concept was placed under a magnifying glass (Kamarck & Lovallo, 2003; Linden, Gerin, & Davidson, 2003; Schwarz et al., 2003; Treiber et al., 2003). In the following pages, known classes (or types) of moderating and mediating factors are described, and many examples are given of how they interact to buffer against stress consequences or how they may act to worsen stress responses.

Genetic Predispositions

On the surface, it makes sense that SM researchers and practitioners are knowledgeable about but not overly interested in genetic predispositions for exaggerated stress responses because genetics are not open to modification; however, the same argument also underlines the importance of modifying those risk factors that are actually open to change. When one is known to be at risk, the subjective importance of modifying what is open to change ought to increase. Especially individuals with a genetic predisposition for stress-related diseases ought to have a keen interest in changing modifiable risk factors. Ewart (1991), for example, has presented a persuasive pathway model of how genetics and environment interact in the etiology of hypertension. He presents evidence that hostility aggravates the frequency and intensity of

stress activation and that hostility is at least in part transmitted within families. This observation is supported by data on intra-class coefficients for siblings' personalities; among monozygotic twins the heritability coefficient for personality is estimated as .50; this decreases to .25 for dizygotic twins, and drops to .05 for adopted siblings. In sum, it is well established that family history of hypertension increases risk of the disease, and it is paired with typically heightened reactivity to stress. Personality, which is also partly genetic, has been shown to predict physical disease (Booth-Kewley & Friedman, 1987), and some personality features like hostility are predictive of greater stress responses.

Early Learning

In addition to genetic predispositions for differential stress reactivity, there is growing evidence that exposure to traumatic events early in life can serve a similar predispositional role that leaves some individuals more susceptible to long-term stress effects. Kendler and his colleagues (2000), for example, have investigated life event stress exposure and its predictive power for development of major depression and generalized anxiety disorder. They assessed life events that included dimensions of loss, humiliation, entrapment, and danger in a sample of 7,322 male and female twins and determined depression and anxiety prevalence. Not only did life events indeed predict prevalence of affective disturbance, but distinguishable event dimensions had specific consequences in that loss alone was not very predictive of long-term affect, but loss paired with humiliation was particularly predisposing for depression whereas loss and danger experiences jointly were more likely to lead to elevated anxiety.

The Kendler et al. study is one of many that provide compelling epidemiological evidence that adverse experience during childhood increases the likelihood of alcohol and drug dependence, eating disorders, affective disorders, posttraumatic stress disorder, and suicidal behavior (for a review see Surtees et al., 2003). Although epidemiological work can provide only "surface" descriptions of relationships, other researchers have extended this work by studying biological pathways, using animal models that center around maternal separation and abandonment stress (Caldji et al., 2001; Meaney et al., 1996). These researchers have shown consistent magnifying effects of early stress exposure on the nature of the hypothalamic-pituitary-adrenal axis response to stress. Similar impact of early stress exposure on cell-mediated immunity and subsequent survival has also been shown in rhesus monkeys (Lewis, Gluck, Petitto, Hensley, & Ozer, 2000), MRI

technology has permitted showing how early trauma affects brain morphology in humans (DeBellis, 2001), and an autopsy study of Japanese children has confirmed adverse early trauma sequelae in terms of compromised immune function (Fukunaga et al., 1992). Using health care use as an index of the cost of stress, Biggs, Aziz, Tomenson, and Creed (2003) have also demonstrated that childhood adversity was an independent predictor of health care use in functional gastrointestinal disorders.

Personality

A connection of personality (i.e., enduring patterns of behavior) and disease may come about via different, typically indirect pathways. One such influence pathway sees certain personality types as translating into response predispositions that ultimately affect physiological regulatory systems (Schwartz et al., 2003). Another potential pathway is via stable individual differences in magnitude and frequency of stress responses (details follow in a later section), and a third one is via the influence that personality has on influencing other risk factors for disease.

Small but significant, simple linear relationships of personality predictors of blood pressure exist and have been found for trait anger/hostility, anxiety, depression, and defensiveness (Rutledge & Hogan, 2002). Rutledge and Hogan conducted a meta-analysis of studies that measured personality features and that also studied blood pressure change with follow-ups of 1 year or longer (averaging 8.4 years). Significant r values between .07 and .09 were observed for anger, depression, anxiety, and defensiveness, with defensiveness being the least often studied but overall strongest predictor.

Finally, there is evidence for linkages of personality factors to tonic physiological indices, which themselves are disease predictors. Using ambulatory blood pressure monitoring, Linden and his collaborators (Linden, Chambers, Maurice, & Lenz, 1993) showed that low social support in women, and high hostility and defensiveness in men, were associated with elevated levels of blood pressure even after the statistical effects of traditional risk factor effects had been partialled out. They also observed that high social support was negatively correlated with hostility, thus indicating a link between a personality factor and a stress-buffering feature. Further, in a randomized, controlled clinical trial of psychotherapy for hypertension, those patients with the greatest hostility reductions and those with improvements in use of constructive anger expression behavior showed the greatest blood pressure reductions during treatment (Linden, Lenz, & Con, 2001).

Miller and his collaborators (Miller, Cohen, Rabin, Skoner, & Doyle, 1999) assessed major dimensions of personality and tonic cardiovascular, neuroendocrine, and immunological parameters in 276 healthy adults. While neuroticism was generally unrelated to any physiological function, low extraversion was associated with higher blood pressure, epinephrine and norepinephrine, and natural killer cell activity. Low agreeableness (which is conceptually similar to hostility) was positively related to higher systolic and diastolic blood pressure and epinephrine. The magnitude of personality and physiology intercorrelation was small, accounting for no more than 7% of the variance. Interestingly, health practices that are presumed to represent one possible path for stress leading to disease did not mediate the association between physiology and personality.

Miller et al.'s findings map well onto results of Denollet and his collaborators (Denollet, Sys, & Brutsaert, 1995; Denollet et al., 1996), who have shown that a novel personality construct (coined "Type D," and consisting of social introversion and emotional inhibition) is highly predictive of cardiac death in cardiac patient populations. When the Type D construct was used to predict acute reactivity in the laboratory, the overall Type D construct did not predict cardiovascular reactivity per se (Habra, Linden, Andersen, & Weinberg, 2003). However, the two subfactors of Type D were independently predictive of differential cardiac and endocrine reactivity in a harassing laboratory paradigm; this was particularly true in men (Habra et al., 2003).

While most of the attention in the personality-disease literature has been given to indices of affective distress (i.e., anxiety, depression, anger/hostility), there is also a growing literature referred to as the "positive psychology" movement that attempts to identify psychological traits that buffer and protect from stress consequences (Lutgendorf, Vitaliano, Tripp-Reimer, Harvey, & Lubaroff, 1999). Some of that attention has been directed at the construct of sense of coherence (Antonovsky, 1979) and cannot be written off as simply being the opposite of negative affect.

Sense of coherence (SOC) is akin to possessing a meaning, a sense of purpose, a positive spiritual strength. In a sample of older adults who were about to relocate, SOC played a significant mediational role in buffering against the stress of relocation that was indexed by natural killer (NK) cell activity (Lutgendorf et al., 1999). This study compared healthy older adults about to move with a matched control group that was not moving, and found that poorest NK activity was seen in "movers" with a low sense of coherence. Fournier, de Ridder, and Bensing (1999) have studied the role of optimism in coping with multiple sclerosis; these researchers found

optimism incorporated three distinct subfactors, namely outcome expectancies, efficacy expectancies, and unrealistic thinking. Unrealistic thinking was clearly related to mobility restrictions and was considered maladaptive; outcome and efficacy expectancies explained depression but were unrelated to mobility. The presence of optimism and social support were independent predictors of good physical outcomes in cardiac patients during their rehabilitation phase (Shen, McCreary, & Myers, 2004).

In sum, there is a growing literature that supports personality factors explaining small amounts of variance in predictor models of acute stress reactivity and in the etiology of stress-related diseases. Both stress-increasing and stress-buffering personality features have been identified. Although such linear independent contributions of personality to stress-related health indices have been established, current theoretical models place more emphasis on interactive models such that personality may exacerbate responses to acute stress and maintain chronic stress. Personality plays a more potent role in disease development when it is seen as a response predisposition that has its full effect when it is paired with the presence of environmental triggers that activate its hyperarousal propensities.

Stressor Exposure and Stress Reactivity as Predictors for Disease

The relationships between various stress response system markers, types of stressors, and response mediators and moderators have been extensively studied (for a review see Lovallo, 1997), and only summaries can be provided here. The trend in this literature is to move away from simple, direct cause-and-effect models and study multiple interacting systems and their short- and long-term adaptations. There is little doubt that complex models map much better onto the observed data on biological pathways and that, as a by-product, it becomes ever more challenging for researchers to advance the field because the best studies are the ones that broadly capture multiple response systems, predispositional factors, and consider both short- and long-term psychological and physiological adaptation.

The cascade of physiological events in response to a stressor described above includes activation of a multifaceted cardiac and hemodynamic response cluster that, however, would not likely be of any health consequence if recovery following activation was swift and complete (Linden, Earle, Gerin, & Christenfeld, 1997; McEwan & Stellar, 1993). Hence it was necessary for stress researchers to show how short-term activation can lead to long-term changes that are deleterious in nature.

A full understanding of pathways for stress leading to disease requires that researchers show how existing, adaptive self-regulatory systems change (or get "corrupted") by stress. A good example of a regulatory system that is critically affected by chronic stress, and that shows compensatory and ultimately harmful "adaptation," is the baroreceptor control system for blood pressure regulation. Baroreceptors are pressure sensors found in the walls of blood vessels that serve a critical role in the feedback system of brain-heart interactions. When pressure rises in response to a demand, the increased blood pressure is detected by the baroreceptors, which inform higher cortical centers that a fight-flight response has taken place. If the brain interprets a stress response as no longer needed, it reduces cardiac activation and the baroreceptors contribute by feeding information back to the brain that the down-regulation process is, at some point, complete. In essence, this system functions like a thermostat in a home, telling the "controller" that the heat activation can be stopped because a heat comfort level (or threshold) has been reached. Such systems have a set point that the regulatory systems are trying to maintain. However, if the demand becomes chronic and no brain signal for recovery is activated, then the baroreceptors react by actually changing the set point or threshold so that now a higher baseline or tonic level is considered the desired target. It is critically important to note that such set points are relatively stable but not absolutely resistant to change and resetting. Both animal (Dworkin, Filewich, Miller, & Craigmyle, 1979) and human studies (Elbert, Pietrowsky, Kessler, Lutzenberger, & Birbaumer, 1985) have provided supportive evidence for a resetting phenomenon that raises target levels and ultimately maintains higher blood pressure levels; that is, an upshift in tonic blood pressure occurs when no signals of stress resolution are fed back to cortical control centers.

Critical individual difference factors that mark higher risk for stress reactivity are familial history of hypertension, greater exposure to acute stressors, a propensity to show exaggerated acute responses to acute stressors, and a lessened ability to recover quickly (Linden et al., 1997; Roy, Kirschbaum, & Steptoe, 2001; Schwartz et al., 2003; Stewart & France, 2001; Treiber et al., 2003). Folkow (1982) has shown that individuals with a positive family history of hypertension have higher vascular resistance that, when activated, enhances cardiac responsivity to a stressor (Light, 1987). It is important to note that both initial reactivity to a stressor and recovery speed are individual difference factors that are relatively stable dispositions over time (Burleson et al., 2003; Frankish & Linden, 1996; Rutledge, Linden, & Paul, 2000), thus granting the candidate potential to play a significant role in pathogenesis.

Frequency and magnitude of acute stress responding is exaggerated and recovery from acute stress is slower in hostile individuals (Earle et al., 1999; Suls & Wan, 1993) and in defensive individuals (Rutledge & Linden, 2003); this finding is particularly true for men. A defensive personality style predicted blood pressure change over 3 years in a sample of 125 research participants, as did initial blood pressure hyperreactivity; when both variables were entered into a mediational model, it could be shown that individuals with high defensiveness *and* high initial reactivity also showed the relatively greatest blood pressure change over time (Rutledge & Linden, 2003). Similarly, the additive effects of three risk predictors (i.e., family history of hypertension, initial hyperreactivity to stress, and acutely high stress levels) represented a much greater odds ratio for hypertension development than either predictor alone, or than a combination of two predictors (Light et al., 1999).

The importance of personality style as a mediating factor in stress effects can be seen in a prospective study of 166 young adults who were studied over a 2-year period (Twisk, Snel, Kemper, & van Mechelen, 1999). The researchers tracked changes in daily hassles, life events, and behavioral and biological risk factors and assessed how changes were interlinked. The results showed that increases in daily hassles were predictive of a worsening lipid profile, decreased physical activity, and increased smoking behavior. All of these connections were particularly strong in participants with a "rigid" personality style.

A particularly useful model of the synergistic results of acute stress effects when superimposed on chronic strain is the study of caregivers to elderly Alzheimer's patients (Vitaliano, Zhang, & Scanlan, 2003). Caregiving itself is considered a chronic stressor, and the additional effects of vulnerabilities and resources on preclinical and clinical disease states can be studied in this model. A graphical display of the factors involved in this path model may facilitate the explanation of critical interrelationships. While most concepts in this model are self-explanatory, the term *metabolic syndrome* should be more clearly specified here. It refers to an intercorrelated cluster of risk factors that include elevated glucose levels, lipid levels, insulin activity, and obesity risk inherent in genetics and sedentary lifestyle. Although the sheer number of arrows in this pathway model (see Figure 1.6) gives the appearance of "conceptual clutter," the complex interactions suggested in Vitaliano et al.'s model are well justified in light of the evidence on risk factor interactions.

A review of the intricate relationships and relative contributing weights of these predictors for disease has been undertaken in a major

review (Vitaliano et al., 2003) where it is shown that the presumed chronic stress of caregiving alone is not a sufficient predictor for disease. Chronic stress, however, accentuates and sets the stage for many risk aggregations. Caregivers of chronically ill patients, for example, are more likely to have poor health habits that contribute to metabolic syndrome. One can also expand or redraw this model by thinking of disease itself can as a "chronic stress platform" that accentuates more disease (Vitaliano et al., 2003). Given the typically advanced age of many caregivers, they themselves may be ill, and caregiver samples can be subdivided into those with and without history of heart disease or cancer. Caregivers who themselves were ill had worse health habits than had those without heart disease, for example, and they also reported fewer uplifting life events (Vitaliano et al., 2003). Suggestive evidence for one discrete pathway linking acute and chronic stress effects in caregivers comes from von Kaenel, Dimsdale, Patterson, and Grant's work (2003) on blood coagulation. Caregivers with high additional life stressors (assessed via structured interviews) showed poorer hemostatic function than did caregivers with the same level of caregiving demand and other medical risk factors but without the acute stressor exposure.

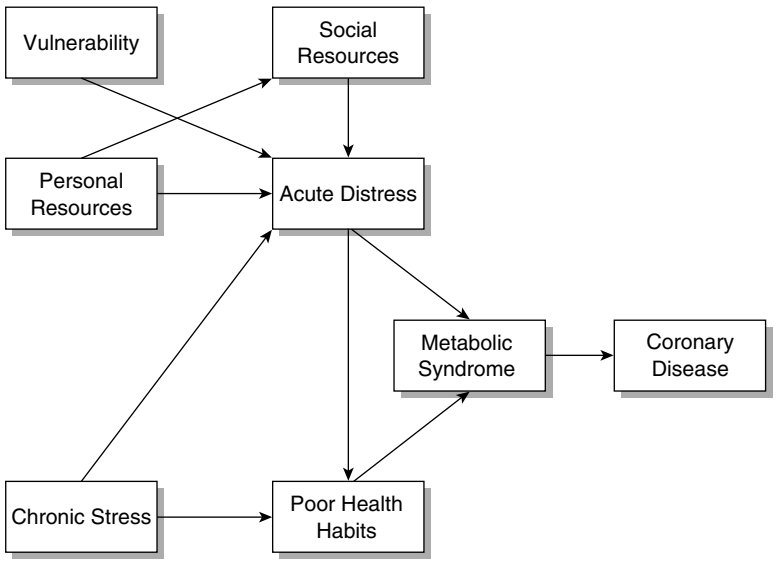

Figure 1.6 A Mediational Model for the Role of the Metabolic Syndrome

Another interesting model of study for synergistic effects of high stress exposure and other risk factors is that of job strain. Job strain (defined as being in a high-demand and low-control job) was found to cluster with negative affect, reduced levels of social support, and a preponderance of negative sentiments towards coworkers (Williams et al., 1997). Similarly, high job stress seen in firefighters has been shown to negatively affect their overall stress responsivity and lead to greater alcohol consumption (Murphy, Beaton, Pike, & Johnson, 1999), thus showing an indirect pathway for stressor exposure to lead to negative health outcomes.

The study of stress reactivity has been of great interest because controlled stress provocations are considered to provide a window into real-life stress and its consequences (Linden et al., 2003). Although stress reactivity research has flourished (especially in the cardiovascular arena), there is growing but still imperfect evidence for its predictive power in cardiovascular disease etiology (Schwartz et al., 2003). The predominant models of reactivity research have been challenged as representing too small a window because they pay little attention to recovery (Linden et al., 1997) despite many promising studies that elucidate the critical role that recovery plays in understanding how stress can lead to disease.

Epidemiological as well as acute provocation studies provide intriguing insights. In one of the largest studies on lifestyle changes to date, researchers have also studied the health effects of vacation as a type of planned recovery (Gump & Matthews, 2000). A sample of 12,338 patients who had completed a lifestyle program was followed for 9 years and the effects of holidays on mortality and morbidity were studied. The researchers reported a roughly 30% reduction in cardiac mortality and morbidity for those who took regular annual vacations.

Sleep is also worth studying in the recovery context given that is considered a primordial element in the body's "program" to seek low activation states and to facilitate recuperation from fatigue. Research on sleep is hampered by the difficulty of measuring sleep quality because reliance on self-reported data is problematic and acquisition of hard data by studying large numbers of individuals in sleep laboratories is often prohibitively expensive. The result is a general lack of trustworthy data. Fortunately, more reliable findings have become available in the form of a prospective study with 185 healthy older adults who provided sleep-lab data and whose mortality rates were then studied during a mean follow-up length of 12.8 years (Dew et al., 2003). Defining sleep quality via use of EEG data, these researchers showed a 2.13:1 mortality risk ratio for those with long sleep latencies (i.e., an index of poor sleep quality) after controlling for coexisting medical burden.

Elevated risk (1.94:1) was similarly apparent for lower sleep efficiency. In the same vein, Akerstedt et al. (2004), in a sample of 5,720 healthy employed men and women, have shown that disturbed sleep was a stronger predictor of fatigue than workload or lack of exercise.

Evidence Linking Stress and Stress-Related Risk Factors to Specific Disease Pathways

The previous sections were partially designed to describe linkages of single stress-related factors, in direct influence models, to disease etiology and to health maintenance at large. This effort revealed limited evidence for direct influence models; in its stead, most of the previous sections ended with demonstrations of how individual difference factors in stress responding relate to one another and how their aggregation and interactions augment health risks. Although previous sections focused on descriptions of generic pathways from stress to disease, the following section is designed to provide more specific evidence for the usefulness of the complex pathway models to describe *specific* disease outcomes and its unique predictor sets.

A 3-year prospective cohort study of 10,432 Australian women revealed that perceived stress was an independent predictor of new diagnosis of symptomatic coronary heart disease even if traditional risk factors had been accounted for. The associated risk (odds ratio [OR]) was 2.4:1, which exceeded the risk ratios observed for other risk factors. Note that an odds ratio (OR) of 2.4:1 means that an individual who carries a certain risk is 2.4 times more likely to develop the disease than one without the risk factor present. Perceived time pressure was not a significant predictor, whereas lack of social support (OR 1.4:1), body mass index (OR 1.9:1), poor nutrition (OR 2.1:1), diabetes (OR 1.9:1), and hypertension (OR 1.7:1) were. Alcohol intake and a physically active lifestyle, on the other hand, served as protective factors (ORs 0.4:1 and 0.6:1, respectively).

Also, Eaker, Pinsky, and Castelli (1992) reported outcomes from a 20-year follow-up of 749 healthy women from the Framingham study. Low education, high perceived tension, and no vacations predicted MI or cardiac death after controlling for age, smoking, blood pressure (BP), diabetes, gender, cholesterol, and obesity. Although a study like Eaker et al.'s cannot tell us what the pathway to disease was, there was strong experimental support that at least part of the influence of stress on health is via the influence that subjective stress has on unhealthy behaviors. Based on a survey of 12,000 individuals in 26 different worksites, Ng and Jeffrey (2003) reported that self-reported high stress was consistently linked (for men and women alike)

with higher-fat diets, less frequent exercise, increased smoking, and greater number of relapses from being an ex-smoker.

Support for the needed demonstration of pathways can also be derived from controlled investigations of cardiac dysfunction under mental stress showing reduced supply of blood to the heart (Jiang et al., 1996; Krantz et al., 1999; Rozanski et al., 1988), reduced ability of blood to clot (Grignani et al., 1992), dysfunction in blood vessel walls (Ghiadoni et al., 2000), and reduced blood flow at sites with atherosclerotic plaque deposits (Yeung et al., 1991). Recent evidence on the linkage between inflammatory processes, stress, and cardiovascular disease has been diligently reviewed by Black and Garbutt (2002) and suggests a complex but empirically well-documented pathway from stress to cardiovascular disease via causation and/or aggravation of inflammatory processes. These authors argue that the inflammatory process is contained within the acute stress response, and—up to a point—stress responding is described as adaptive within the definitions of the fight-or-flight response. Hence, any psychological intervention that may reduce inflammation brought on by chronic stress also has considerable potential for preventing cardiovascular disease.

An additional pathway for linking cardiovascular health outcomes to psychological factors has been described in a series of programmatic studies that link specific cardiovascular changes to loneliness (Cacioppo et al., 2002). Cacioppo and his collaborators showed greater age-related blood pressure changes and poorer sleep in lonely than nonlonely older adults.

Evidence also links stress to immune dysfunction. Cohen et al. (1998) inoculated 300 volunteers with the common cold virus and monitored them for symptoms of illness. Participants who reported exposure to stressors lasting more than 1 month developed colds at a two to three times greater rate than those with low stress. Similarly, it has been demonstrated that stress negatively affects duration and intensity of illnesses such as herpes, hepatitis B, meningitis C, and human immunodeficiency virus (Cohen, Miller, & Rabin, 2001; Herbert & Cohen, 1993; Kemeny, Cohen, Zegans, & Conant, 1989). Social stress appears to play a distinctive vulnerability role in outbreaks of latent herpes viruses (Padgett, Sheridan, Berntson, Candelora, & Glaser, 1998). Owen and Steptoe (2003) tested the relationship of acute mental stress, immune and cardiovascular function in 211 middle-aged adults. Independent of other risk factors, high heart rate reactivity was associated with plasma interleukin 6 and tumor necrosis alpha whereas heart rate variability (an index of the heart's ability to adjust to varying needs) was not associated with immune function. Given

that differences on absolute levels of heart rate had different effects than variations in heart rate variability, Owen and Steptoe concluded that individual differences in sympathetically driven cardiac stress responses are associated with compromised immune function, hence giving support to the rationale that stress management should target sympathetic arousal reduction.

While research on cardiovascular adjustments to acute, contrived stressors suggests that initial hyperreactivity is a useful predictor of long-term hypertension development (Treiber et al., 2003), the lab reactivity paradigm is not as useful for the study of acute stress and immune function. Segerstrom and Miller (2004) culled data from 300 studies and concluded that exposure to brief, contrived stressors was typically associated with adaptive up-regulation of immune function, in particular for natural killer cell activity. Only chronic stressors were associated with suppression of both cellular and humoral measures of the immune system. These findings suggest that time-limited stressor exposure may actually serve to strengthen immune function and entail a vaccination-type effect.

Interestingly, it is not necessary to document quantifiable, salient environmental stress triggers to show a link with disease vulnerability; mere perception of high stress was associated with lowered antibody production after vaccination (Burns, Drayson, Ring, & Carroll, 2002).

Despite limited evidence for the reliability of stress self-report due to contextual factors and individual differences (for more detail see section titled "'Take-Home Messages' That Are Pertinent to Stress Management," below), self-reported, perceived stress is consistently related to certain stimulus environments and has been shown to associate with other risk factors. Perceived stress (a) is higher in some occupations than others (low decision control, high demand), which themselves carry differential risks for disease (Williams et al., 1997); (b) is higher in low socioeconomic strata; (c) is associated with greater consumption of tobacco, higher relapse in previous smokers, worse diets, reduced physical activity, and poorer sleep (Cartwright et al., 2003; Ng & Jeffrey, 2003); and (d) contributes to physical inactivity and poorer diet thus worsening lipid profiles and contributing to the metabolic syndrome.

Research on cancer progression has shown mixed evidence for the role of stress but does elucidate a role for indirect linkages: Stressed cancer patients showed decreases in healthy behaviors and increases in unhealthy behaviors (like smoking), which in turn may affect cancer progression (Lacks & Morin, 1992). Another interesting development in immune

research has been the discovery that not only does the brain regulate immune function, but the immune system itself triggers brain activity by alerting the brain to infection or injury by releasing a protein called pro-inflammatory cytokine (Maier & Watkins, 1998). This protein triggers a cascade of responses, including fever and listlessness, that in turn are held to serve an adaptive function by reducing energy output.

Earlier in this book there was mention of Selye's belief in the universality of a fight-or-flight response to challenge. This belief had to give way to the recognition that there are other possible types of responses. A particularly intriguing suggestion of a different response type is that of energy-preserving response (Maier & Watkins, 1998) that appeared to explain Kemeny and Gruenewald's (2000) results; these researchers have shown a cognitive equivalent to a proinflammatory cytokine activation in that HIV-positive men with rather optimistic outlooks developed AIDS symptoms less quickly than did those with negative though realistic aspirations.

While by no means exhaustive or comprehensive, the above discussion makes a strong case for the shared pathways of stress, genetics, and behavioral risk factors for physiological dysregulation and diseases of the cardiovascular, immune, and endocrine systems. One can readily see how stress reduction would affect other behavioral and biological risk factors and disease outcomes; these relationships can be made apparent by a more visual display. In Table 1.1, evidence is summarized about which risk factors predict which disease. Note that this table was selected for its illustrative value, not because it reflects the latest evidence. At the time of writing this book, the evidence has actually grown stronger.

Each x in the table signifies that, according to the Center for Disease Control (USDHHS, 1986), scientific evidence for a consistent link of risk to a specific disease outcome exists; it is striking how few cells in this table remain empty. What this table cannot show is how risk factors themselves are linked to one another and then cause synergistic effects on health. A great deal of information regarding clustering of risk factors was described above, and a particularly good demonstration of such clustering was provided above in Figure 1.6, which in turn is backed by statistical, meta-analytic review data (Vitaliano et al., 2003).

To summarize, a great deal of evidence links quantifiable stress (both self-report and physiological indices) to disease markers (Bunker et al., 2003). Although the term *disease marker* was consciously chosen to reflect imperfect evidence of causality, the available knowledge makes a strong case for a likely causal role of physiological exhaustion and lack of recovery in disease development.

Table 1.1 Diseases Potentially Brought On by Risk Factors

Risk Factor	*Disease*			
	Heart Disease	Stroke	Cancer	Diabetes
Tobacco	x	x	x	x
Alcohol			x	
Cholesterol	x	x	x	x
Hypertension	x	x		x
Diet	x	x	x	x
Obesity	x	x	x	x
Inactivity	x	x		x
Stress	x		x	x
Drug Use			x	x
Occupation	x		x	x

SOURCE: Adapted from the U.S. Department of Health and Human Services, 1986.

"Take-Home Messages" That Are Pertinent to Stress Management

Stress is well understood at the subjective, experiential level; it is simply part of modern life (if one is allowed to use such a platitude). Yet it is difficult to define operationally and then to measure because it is a process and not a state. This review of the literature revealed that the field has steadily evolved by expanding and elaborating early models, and has revealed much consistency in the observation of powerful and complex, interconnected pathways for stress-disease linkages, showing mutual influences of the nervous, endocrine, and immune systems. Studies of short-term as well as long-term exposure to stress, in animals and humans, confirm the critical role of chronic stress in disease development even though many of these pathways remain insufficiently understood (Kelly et al., 1997; Lovallo, 1997). Both self-reported stress levels and physiological

markers possess usefulness in showing stress disease linkages, especially in repeated measures designs.

Early models like Selye's have in good part held up to scrutiny, and more recent models have typically expanded on earlier thinking rather than invalidating it. One notable exception to the claimed veracity of early models is the criticism leveled against Selye's belief that stress responses are ubiquitous, "whole system" responses in which all physiological response components operate in synchrony. One could wish that he had been right, because that would make the measurement of stress a lot easier! However, as knowledge of nervous system function has expanded, Selye's belief in a whole system response has required modification.

At least partly consistent with the general adaptation syndrome is the later subdivision of the nervous system responses into activities along a sympathetic-adrenal axis versus activation of a hypothalamic-pituitary-adrenocortical axis (HPA), but the presumption that both are always operating in parallel and are of equal importance to disease development is no longer held to be true (Dienstbier, 1989). The work of Frankenhaeuser (1991), Haynes, Gannon, Oromoto, O'Brien, and Brandt (1991), and Linden et al. (1997) make a strong case that physiological arousal of the sympathetic axis is not likely disease-contributing unless it is paired with substantial activation of the HPA axis and/or unless physiological recovery is delayed. This also implies that researchers interested in studying stress-disease linkages need to include measures of sympathetic activation (e.g., electrodermal activity) as well as HPA activation (e.g., cortisol) and use study protocols that are of sufficient length to permit adequate study of poststressor recovery. Cortisol changes relative to resting baseline, for example, may be demonstrable for as long as 1 hour poststressor even in what are clearly contrived, relative minor stressor exposure paradigms (Linden et al., 1998). Stress management should therefore target arousal reduction skills to facilitate *and* accelerate recovery, as well as teach skills to minimize initial reactivity that exceeds the biological/survival needs inherent in a given challenge.

In sum, at this time we have a much clearer sense of how diverse stress-related events and processes affect short- and long-term adjustments of the cardiovascular system (Kop, 1999), the immune system (Cohen et al., 1998; Sklar & Anisman, 1981), and the endocrine system (Dienstbier, 1989; Frankenhaueser, 1991). On the whole, there is weak, at best mixed, evidence that mere exposure to stressors is a sufficient trigger for disease, but there is overwhelming evidence in support of interaction models, such that predispositions to hyperreactivity (e.g., via genetics, personality, prior exposure)

paired with acute challenges lead to exaggerated responses, slow recovery, and sometimes exhaustion. The coexistence of these features in the same person contributes strongly to disease development. In support of this now dominant line of thinking, there is rapidly growing knowledge of how physiological systems interact, and there is a solid understanding of how stress can affect disease, possibly in a causal manner.

Knowing the effects of stress on multiple, pivotal regulatory physiological functions, it can no longer surprise that stress can affect many different disease processes. Even if not clearly demonstrated to be causal, it can at least be shown how maintenance and exacerbation of health problems can occur under high chronic stress (Lovallo, 1997; Segerstrom & Miller, 2004). This knowledge can and has been applied to diseases of the immune system (e.g., cancer, AIDS, lupus, multiple sclerosis, common colds), endocrine dysfunctions (e.g., diabetes), and cardiovascular health (e.g., high blood pressure, myocardial infarction, sudden cardiac death). As such, stress has been shown to be important to almost all causes of mortality and chronic disease processes.

Stress plays a critical role in understanding the impact of early trauma responses on disease susceptibility. The magnitude of acute stress responses and speed of recovery are also likely predictive of disease development, although the research base in this area is still weak. Outcomes are positively affected by the presence of buffers (physical fitness, presence of support, an optimistic outlook, a sense of meaning, enjoyable activities) and negatively influenced by the presence of chronic strain in everyday life, negative mood, defensiveness, anger/hostility, anxiety, and depression. There is evidence of gender differences in that men and women may not benefit equally from buffers like social support (i.e., women tend to benefit more) or be equally detrimentally affected by the presence of hostility and rumination (in this case, men are more likely affected). Similarly, reactivity to particular stressors may be gender- and population-specific.

In aggregation, this overview makes a convincing case that stress reduction (however brought about) has far-reaching beneficial consequences for physiological adaptation and health maintenance, and prevention of exhaustion. Stress reduction benefits achieved in one critical physiological system (e.g., the cardiovascular system) are likely to show generalized benefits for other systems (e.g., strengthening of immune function). Creation of stress buffers (i.e., forces or personality characteristics that protect against stress consequences) can also contribute to benefits across many physiological functions. This observation implies that research on stress reduction outcome can reveal benefits in physiological functions that

were not even the primary target of intervention and measurement, and that broad, multisystem measurement is needed to uncover the full benefit of stress reduction efforts.

If stress management is taught to initially healthy individuals, then it is logically necessary to follow them for many, many years if researchers do not want to miss out on seeing initially nonexistent, then slowly accruing but potentially powerful benefits. Failing to see large immediate physiological benefits of stress management training applied to healthy individuals does not imply failure because healthy individuals will begin training at healthy levels of physiological function; detecting change is therefore difficult due to floor effects.

Not only do researchers need to consider long-term, parallel, interacting, and counterproductive effects in multiple regulatory systems, they should also differentiate potential health benefits in physiological *resting* functions from those reflected in differential *acute reactivity* to a challenge. This is a standard approach in studying immune system functionality and stress-health linkage (Glaser, Rabin, Chesney, Cohen, & Natelson, 1999) and provides unique opportunities to study outcomes. Lastly, documented immediate stress reduction does not necessarily lead to long-term benefits, and the researcher has a mandate to demonstrate lasting effects.

Given that the experience of stress has objective and subjective components, and that pertinent physiological systems are interconnected and interdependent, researchers can and should consider a wide range of potential measurement targets. For example, Miller and Cohen (2001) conducted a meta-analysis of the effects of psychological treatments on immune function (for results, see Chapter 3) and reported that the various studies had evaluated no fewer than 15 different markers of immune health! Similarly, adaptive cardiac functions can be subdivided into resting measures as well as reactivity indices and may be represented in more than a dozen endpoints, including systolic and diastolic blood pressure, pulse pressure, pulse-transit time, blood volume pulse, peripheral resistance, baroreceptor activity, time- and frequency-modulated aspects of heart rate variability, and so forth. In addition, subjective distress reports can be obtained from research participants, and dozens of standardized scales are available to achieve this; they may include simple one-item rating scales, a variety of standardized stress coping tools, self-report of negative affect, and peer or clinician ratings. Although the section on stress measurement was critical of self-report, this was not meant to discourage all self-report, given existing evidence of its predictive validity when studied within the same person. Finally, there are many behavioral expressions and consequences

of high stress loads that can be tapped, ranging from acute changes in facial expressions of affect to return-to-work statistics or hospital emergency visits. Researchers in stress management are urged to broadly assess as many pertinent outcomes as possible. While this expectation greatly complicates the life of the researcher and drives up the cost of research, it also enhances the opportunity to show extensive, generalized benefits of "hard" outcomes that can convince consumers and policymakers of the value of psychological intervention (Linden & Wen, 1990).