STRESS
CONFUSION & CONTROVERSY

An established theory of stress is challenged by experimental evidence suggesting the importance of psychological factors

BY ROBERT J. TROTTER

"It was in 1925 that I first discovered the existence of what I later called stress. . . . When studying internal medicine at the University of Prague, during one of the initial lectures in internal medicine, we were shown several patients in the earliest stages of various infectious diseases. The professor carefully pointed out all the specific signs and symptoms characteristic of each disease, but what struck me most was that each of these patients felt and looked ill, had a coated tongue and complained of more or less diffuse aches and pains in the joints and of intestinal disturbances with loss of appetite and loss of weight. The patients . . . had a common syndrome, but the professor attached very little significance to the signs that were common to all these diseases because they were 'nonspecific' and hence 'of no use' to the physician in making a correct diagnosis or prescribing the appropriate treatment."

And this, explains Hans Selye of the University of Montreal, was his first insight into the phenomenon known as stress. Selye saw what appeared to be "a general syndrome of sickness" superimposed on all individual diseases, and he could not understand why his professor did not pay serious attention to it.

It was 10 years later that Selye's insight began to pay off. Attempting to isolate a new sex hormone, he was injecting extracts of cow ovaries into mice. The extracts produced a three-part response: enlargement of the adrenal cortex, bleeding ulcers of the stomach and duodenal lining and atrophy of the thymus and lymph nodes. At first Selye believed that the reactions were due to a new hormone in his ovarian extract. It soon became apparent, however, that extracts of all other organs—in fact, toxic substances of all kinds—produced the same changes.

Disappointed that he had not discovered a new sex hormone, Selye "suddenly remembered my classroom impression of the 'syndrome of just being sick.' In a flash, I realized that what I had produced with my impure extracts and toxic drugs was an experimental replica of this condition. This simple hunch . . . was the basis for the development of the entire stress concept."

Now Selye's entire stress concept, as well as years of research, is itself undergoing a form of stress as it reacts to a theoretical challenge backed up by a growing body of experimental data.

Chief among Selye's challengers is John W. Mason of the division of neuropsychiatry at the Walter Reed Army Institute of Research. Both he and Selye presented their positions at a recent symposium sponsored by the Kittay Scientific Foundation.

Stress, according to Selye, is "the nonspecific response of the body to any demand made upon it." The patients he saw as a student and the animals in his early experiments (according to this definition) were suffering from stress or responding to demands made by infectious or toxic substances. All living beings, Selye explains, are constantly under stress, and anything (pleasant or unpleasant, physical or emotional) that speeds up the intensity of life causes a temporary increase in stress. A painful blow and a passionate kiss, for instance, can be equally stressful. Indeed, he says, complete freedom from stress is death.

But stress, itself, can lead to disease and death. And Selye, through what he calls the "general adaptation syndrome" (GAS), has explained how stress might be related to disease.

The syndrome has three stages: an alarm reaction, resistance and exhaustion. During the first stage, the body recognizes the "stressor" and the pituitary-adrenal cortical system responds by producing the arousal hormones necessary for either flight or fight. Speeded-up heart and lung operation, elevated blood sugar levels, increased perspiration, dilated pupils and slowed digestion are among the physiological responses to this initial stage of the GAS.

During the resistance (or adaptive) stage, the body begins to repair the damage caused by arousal, and most of the initial stress symptoms diminish or vanish. But if stress continues, the acquired adaptation is lost as the body attempts to maintain its defenses. Eventually the body runs out of energy with which to respond and exhaustion sets in. During this final stage, bodily functions are slowed down abnormally or stopped altogether.

Continued exposure to stress during the exhaustion stage can lead to what Selye calls the "diseases of adaptation." Various emotional disturbances, schizophrenia, migraine headaches, certain types of asthma as well as cardiovascular and renal disease are among the conditions that have been linked to stress. Apparently, says Selye, conditioning (particularly hereditary predisposition, diet and environmental factors) determines which organ or system is weakest and breaks down most readily under the influence of stress.

That stress and a variety of diseases are related is not in question. Selye's research and concepts have had an enormously stimulating effect on research in many areas of medicine and biology, says Mason. At the World Congress of Medical Psychology in 1956, for instance, Frank Engel called Selye's work "breathtaking in its scope," and said, "It has permeated medical thinking and influenced medical research in every land, probably more rapidly and more intensely than any other theory of disease ever proposed."

Despite the importance of Selye's work, Mason feels that a reexamination of the concept of stress is necessary if research is to progress in what many believe to be a confused field. Part of the confusion, suggests Mason, stems from Selye's definition of stress as a "nonspecific reaction." According to such a definition, almost any stimulus, including exercise, disease, fasting, heat, cold and emotional or psychological stimuli might be responsible for the reactions described in the GAS.

Mason and his colleagues at Walter Reed have been compiling evidence which suggests that the stress response is much more specific than Selye claims. In particular, they say, what has been called nonspecific may be (in many cases) specific. And the specific stimulus seems to be a psychological one.

For 15 years, Mason has been involved in an experimental approach to the study of the body's neuroendocrine machinery. The work includes a measurement of the hormones produced by various glands, including the pituitary-adrenal cortical system (involved in the GAS). Hormone assay data are collected in response to psychological as well as physiological stimuli.

In a typical experiment, for instance, hormone levels were measured in a male rhesus monkey before and while it was confined in a restraining chair. The physiological factors in such an experiment are minimal (as compared to, say, starving an animal or administering painful electric shocks). Even so, the hormone changes registered while the animal was confined were significant. This, says Mason, suggests the extraordinary sensitivity of neuroendocrine systems to psychological stimuli (in this case, the fear or psychological arousal associated with being confined). The results of this and of a number of similar experiments raised questions concerning the validity of the "nonspecificity" concept, explains Mason. Could it be, for instance, that the hormonal responses related to stress are the result of specifically psychological factors rather than just "any demand"?

In subsequent experiments, Mason and his co-workers introduced precautions designed to minimize possible psychological reactions. In a test of hormonal responses to fasting, the following safeguards were taken with the experimental animals:

1. Minimize novelty and uncertainty. Allow lengthy period for adaptation to experimental set-up. No location changes. Adapt animal to urine and plasma collection. Animal handled only by familiar persons.
2. Minimize extraneous psychosocial stimuli. Animal kept in private, sound-resistant booth. Cubicle entered only for feeding, cleaning, sample collection or other experimental procedures.
3. Minimize discomfort. "Placebo food" (nonnutritive, fruit-flavored cellulose pellets) given to animals to reduce discomfort of empty gastrointestional tract.

According to Selye's theory, fasting is a "stressor" that should cause the pituitary-adrenal cortical system to go into action. And in previous experiments, this has seemed to be the case. When two of a group of eight monkeys were not fed for three days, says Mason, the fasting

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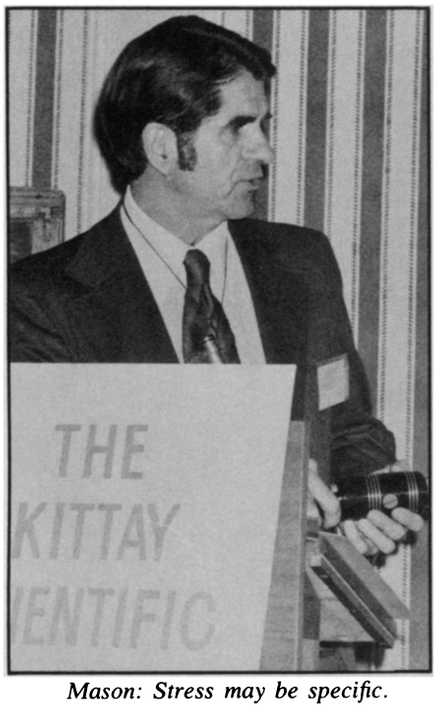

Mason: Stress may be specific.

Kittay Scientific Foundation

Selye: Stress is nonspecific.

animals showed obvious signs of stress—especially when the other animals were being fed. The hormones of the pituitary-adrenal cortical system were significantly elevated.

But when four fasting monkeys were simply placed in a quiet, private cubicle without the presence of nonfasting monkeys, the predicted stress response did not occur. "The pituitary-adrenal cortical system," says Mason, "does *not* appear to be stimulated in 'nonspecific' fashion by fasting under these conditions."

Similar results were obtained during muscular exertion experiments with monkeys and with young men. And the most compelling data, says Mason, have emerged from our work in relation to heat exposure. Young men exposed to an uncomfortable level of heat (105 degrees F. for three hours), but protected from psychological stimuli, showed no elevation of the hormones thought to be involved in stress.

While Mason cautions that this work is "preliminary," he contends that "it now appears likely that the 'nonspecific' element in early 'stress' experiments may have been to a considerable extent a reflection of ubiquitous psychological reactions to various experimental conditions.

"This is not to conclude," Mason continues, "that the pituitary-adrenal cortical system responds *only* to psychological stimuli, nor that all 'stressors' act through psychological mechanisms. . . . Rather, the point is simply to emphasize that psychological influences upon the pituitary-adrenal cortical system are potent, often subtle, easily overlooked and more ubiquitously present as interfering variables in laboratory experiments than has been generally realized."

What does all of this mean to the stressed and overstressed individuals of our society? It might mean that physically dangerous or damaging stress reactions are more often the result of psychological rather than of physical conditions. For example, "I hate my job!" vs. "The work is hard, but I don't mind it." But is a psychologically unsatisfying job more likely than a physically exhausting job to lead to stress-related diseases? The question probably can't be fully answered at this point because, according to Mason, for 20 years stress researchers had no good reason to suspect the importance of psychological variables and, therefore, did not attempt to discriminate between psychological and physiological factors.

Twenty years ago, psychological variables were regarded as negligible experimental factors. Nobody believed that psychological stimuli could affect something as concrete as hormone secretion. Now, says Mason, the shoe is on the other foot. The burden of proof is on investigators to show that psychological influences are not responsible for hormonal changes seen in stress experiments—and this throws the whole field of stress research into confusion and doubt. If Mason is right, most previous research will have to be reexamined with an eye out for psychological influences.

How does Hans Selye, the father of modern stress research, react to such charges? At the Kittay symposium, Selye applauded and praised Mason's work. He did not, however, show any inclination to change his position or his basic theory of stress. Instead, he attempted to explain away Mason's findings with a metaphor: Stress is like electricity. Both are nonspecific but can be "conditioned" or channeled in specific ways. Depending on conditions, electricity can turn on a light bulb or a refrigerator. Stress can turn on the pituitary-adrenal cortical system or various other hormone systems.

There is some question, however, as to whether Selye's analogy adequately explains the experimental findings reported by Mason. Mason's work indicates that specific stresses (not conditions imposed on one general type of stress) produce specific responses. One type of stress (psychological) turns on the pituitary-adrenal cortical system. Another specific type of stress (physiological) activates other hormone systems.

Even though their positions differ substantially, Mason does not see his work as an attack on Selye. Rather, he sees it as an extension and a refinement of Selye's years of research. "The most I would hope for at this point," says Mason, "is that Dr. Selye might join me in kind of an appeal that stress investigators reexamine this question of the stimuli more carefully—whether there is nonspecificity."

But even without Selye's complete endorsement, a reevaluation of stress research is underway. A new quarterly, THE JOURNAL OF HUMAN STRESS, opened its pages in March with a paper by Mason titled "Confusion and Controversy in the Stress Field." The second issue of the journal will contain part two of Mason's paper, discussing the theoretical implications of his work as well as a response by Selye.

"The main reason that I bring this all up now," Mason told SCIENCE NEWS, is that investigators are being misled. "The nonspecificity notion implies that it doesn't matter what the nature of the stimulus or the stress is that produces this stereotyped response. So it has led to a tendency to neglect paying close attention to and discriminating between the stimuli or independent variables. . . . Such a tendency seems certain to delay progress in the field, and it is important that we resolve this question [of nonspecificity] as soon as possible in the interest of a greater return on our experiments in the stress field." □

Robert J. Trotter has returned to the SCIENCE NEWS *staff after completing the manuscript for a college textbook on psychology.*