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HOW VALID ARE SELYE'S DISEASES OF ADAPTATION

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Hans Selye's concept of stress evolved as the result of a laboratory accident, which later led him to conclude that very severe but different threats always produced three identical pathological changes in rats; an increase in the size of the adrenals, shrinkage of the thymus and lymph nodes and ulcerations of the stomach. He viewed these seemingly unrelated responses to "noxious" stimuli as an attempt to mobilize the body's defense mechanisms during "biologic stress". He called this an "**Alarm Reaction**" in his initial 1936 letter to *Nature* entitled "A Syndrome Produced by Diverse Nocuous Agents". The word stress did not appear since the editor decided to delete it. He felt it would be misleading because most people associated stress with nervous strain, especially in emotional females. The editor also substituted "nocuous" for noxious since noxious had the connotation of a subjective reaction to someone or something, rather than a significant degree of pathological damage that would be obvious to everyone. Continued confusion over the meaning of stress was to haunt Selye the rest of his life, and he eventually had to create a new word, stressor, to distinguish cause from effect.

Also Included In This Issue

The Alarm Reaction And The General Adaptation Syndrome

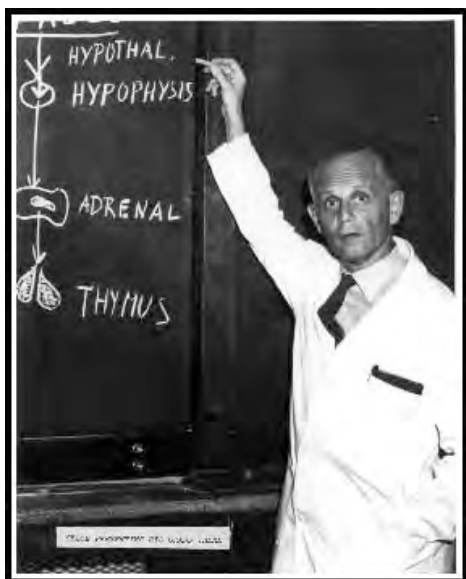
The Diseases Of Adaptation — From Pathology To Philosophy And Publicity?

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Further studies revealed that these Alarm Reaction changes occurred within 4 to 6 hours and were characterized by an initial shock phase in which the adrenal medulla secreted large amounts of adrenaline into the blood stream. As Walter Cannon had previously shown, this resulted in an increase in heart rate, blood pressure and respiration, as well as other adrenal and sympathetic nervous system activities designed to facilitate life saving "fight or flight".

The Alarm Reaction And The General Adaptation Syndrome



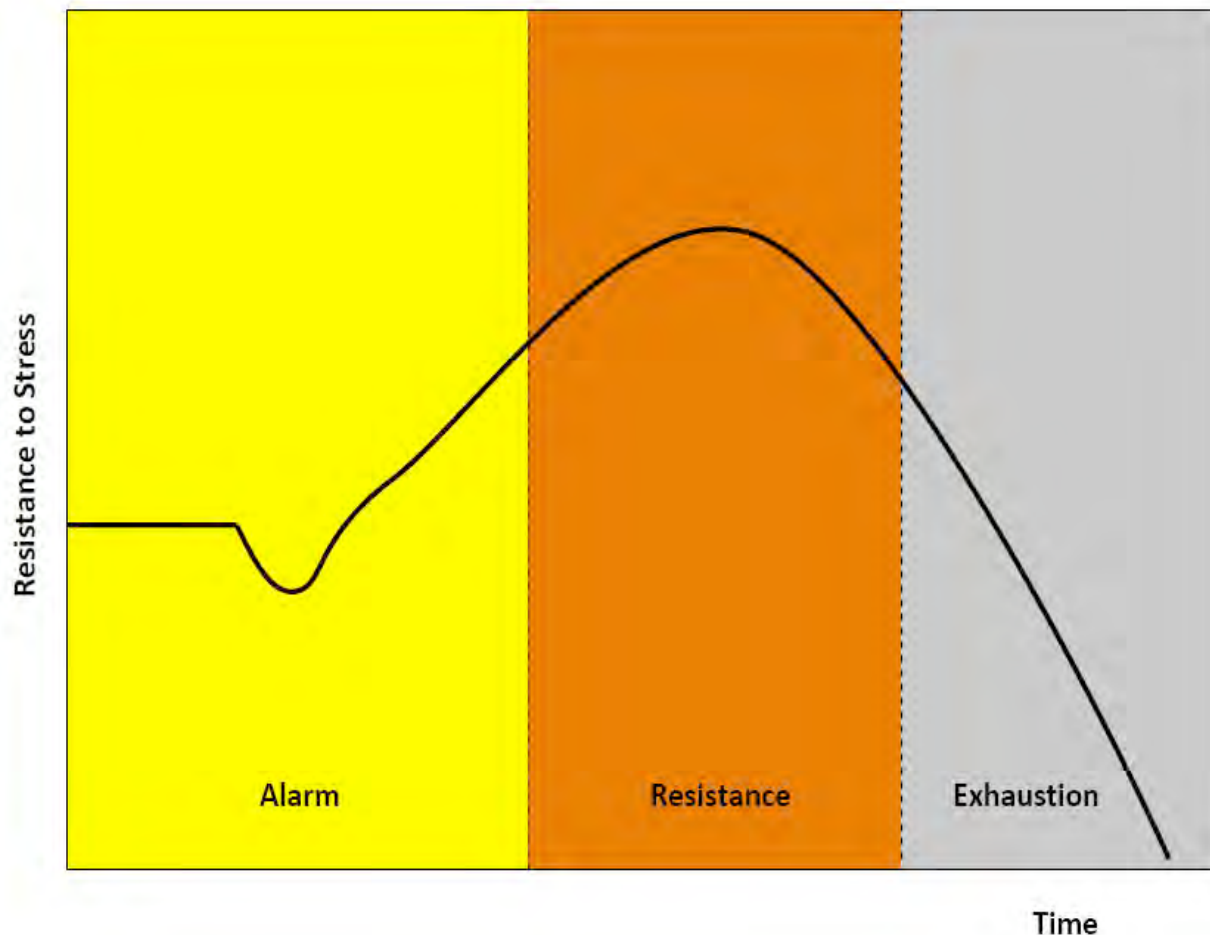
But Selye discovered there was also another rapid response initiated by hypothalamic stimulation of the pituitary gland. This signaled the adrenal cortex to secrete certain steroid hormones that had strong anti-inflammatory effects in its initial shock phase. Microscopic studies revealed that adrenal cortical cells discharged their hormone laden lipid granules into the blood stream until their reserves were almost completely depleted. This was followed by a countershock phase, which stimulated parasympathetic actions that increased resistance and reversed this depletion.

The connection between the changes in the adrenal, lymphoid structures and stomach ulcerations seen in the Alarm Reaction were not clear until Selye showed that the enlargement of the adrenals was due to an increase in the size of the adrenal cortex, and that the outpouring of anti-inflammatory cortisone-like hormones it produced damaged the inner lining of the stomach, resulting in ulcerations. The size of the lymph glands and thymus was also significantly reduced, and in extreme instances, death could occur.

If the stressor continued for over 48 hours and the animal survived, a second **Stage of Resistance** followed that was the opposite of the Alarm Reaction. Secretory granules in the adrenal cortex were now abundant, the abnormal blood findings and signs of stress previously seen disappeared, and the ability to resist damage was now greater than normal. However, this could not be sustained, and more prolonged exposure resulted in a third **Stage of Exhaustion** with findings similar to the Alarm Reaction that were irreversible and were eventually followed by death. As he later explained when he tried to extrapolate his animal studies to humans, "At the end of a life under stress, this was **a kind of premature aging due to wear and tear**, a sort of second childhood which, in some ways, resembled the first."

Selye termed this three-tiered response to persistent stress **The General Adaptation Syndrome** (GAS). His reasoning was that it was general because only those stressors that had a general effect on large portions of the body produced it. It was adaptive since it required successfully adapting or becoming acclimated to the stressor by stimulating defense mechanisms that increased resistance to injury. While a syndrome usually refers to a group of symptoms that are characteristic of a disease or pattern of social

behavior, Selye was conversant in numerous languages and the origin of their words. He believed that syndrome was appropriate because it was derived from Greek roots meaning, "Run together". Although his adaptation syndrome would not be considered a disease, he explained that he felt justified because the individual manifestations of each of these three stages were coordinated, and to some extent interdependent, as illustrated below.



The Three Staged General Adaptation Syndrome And Changes In Resistance

Resistance initially falls in the shock phase of the Alarm Reaction, but the subsequent countershock phase is associated with increased resistance. This continues into and reaches a peak in the second stage of the General Adaptation Syndrome, only to plummet and disappear in the third. Selye was able to reproduce the pathologic changes seen in the Alarm Reaction not only in rodents, but also cats, dogs, apes and other animals. The same was true for the other stages of the General Adaptation Syndrome. But the question was whether any of these observations in laboratory animals subjected to extreme and/or prolonged stress had any relevance for people.

Selye thought they might, because autopsy studies conducted during various phases of this syndrome revealed pathological changes similar to those seen in patients with hypertension, ulcers, kidney disease, rheumatoid arthritis and other collagen diseases. He labeled these **"Diseases of Adaptation"**.

The Diseases Of Adaptation — From Pathology To Philosophy And Publicity?

Selye first reported this in a 1946 article entitled "The General Adaptation Syndrome And Diseases Of Adaptation". This 113-page paper with 700 references was considered to be so revolutionary that *The Journal of Clinical Endocrinology* decided to devote a special edition to it. As the editor wrote,

The importance of this work is well established. When Dr. Selye first became interested in this, over ten years ago, it was difficult to see how a series of studies of severe traumata in rats could lead to anything. Yet, the care with which he made his observations, and his fertile imagination, and abetted by his colleagues in Montreal, gave us concepts that are of importance in our understanding of the problems of wound and burns and other disorders.

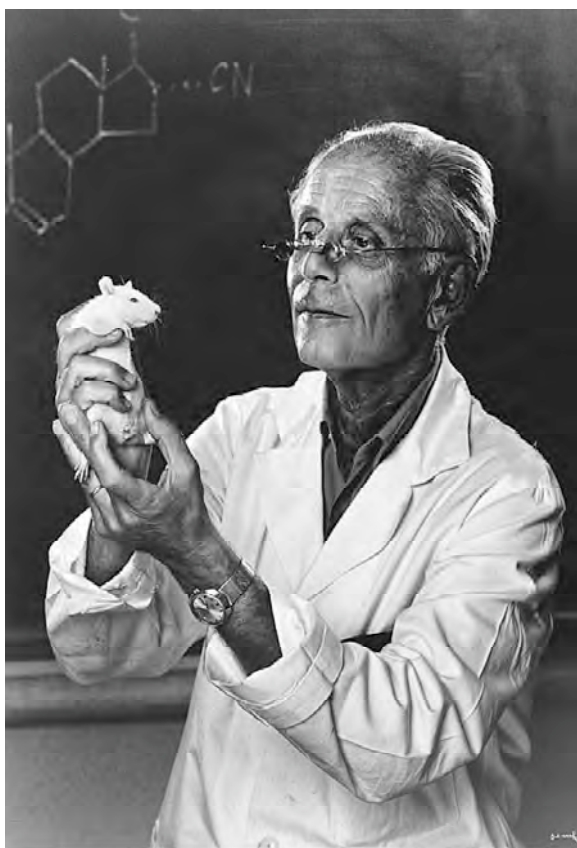
This was just after the conclusion of World War II and he felt that Selye's discussion of traumatic shock and severe burns had important treatment implications. This was particularly true, since intravenous adrenal extracts like Eschatin had been used effectively by the Allies for the treatment of both, and it was rumored that the Germans utilized similar products obtained from beef adrenals to prevent hypoxia in Luftwaffe pilots.

This paper was also the first time many researchers and most physicians had any knowledge of Hans Selye and his concept of stress, much less diseases that could be caused by stress. Their reaction was divided. Many enthusiasts saw this as the vindication of psychosomatic medicine, which was wildly popular at the time, and was also gaining respect because of its success in treating some cases of wartime neuroses and "shell shock" in veterans. Some believed that Selye's theory was also an exciting and novel way to study the etiology of physical diseases, and might lead to their prevention and treatment. Others, who acknowledged that his findings in animals could not be disputed, doubted that they applied to people for various reasons. A few clinicians and basic research scientists, who were particularly vehement about this, pointed out that the acronyms for General Adaptation Syndrome (GAS) as well as Diseases of Adaptation (DOA) were very appropriate, since they respectively really stood for "hot air" and "dead on arrival".

However, the journal did not have a very large number of subscribers at the time, and things did not heat up until the publication of Selye's 1950 magnum opus *Stress*. This huge tome, with its more than 1,000 pages and over 5,000 references, attracted international attention and quickly made

him famous, not only in scientific and medical circles, but law, sociology, politics, education, ecology and other professions and disciplines that found his concepts appealing. His opponents were even more infuriated when he subsequently wrote books for the public, which attempted to explain how his research findings in rats could explain not only how ordinary people could develop hypertension, ulcers and rheumatoid arthritis, but also headaches, neurodermatitis, depression and other complaints that were not included in his *Diseases of Adaptation*. His 1956 *The Stress of Life* quickly soared to the top of the *New York Times* "Best Seller" list, remained on it for over a year, and was translated into 16 languages. It was reprinted several times over the next two decades until it was replaced by an updated and expanded 1976 edition. Some of his other very popular books included *The Story of the Adaptation Syndrome* (1952), *From Dream to Discovery* (1964), *In Vivo*, (1967), *Stress Without Distress* (1974) and *The Stress of My Life* (1977).

During the course of his career, Selye published 40 books and over 1,700 articles, the vast majority of which were targeted to scientists and physicians. However, he had become such a charismatic celebrity, that anything he wrote or did was frequently commented on in newspaper health columns, magazine articles and other lay publications. Celebrities and/or wealthy individuals from all over the world sought his advice for medical problems they believed were stress related. He always politely declined, possibly because he may not have been licensed to practice medicine in Canada. To the best of my knowledge he never saw a patient, but referred many to me. I particularly recall the portrait photographer Jousuf Karsh, whom I saw shortly after Karsh had captured Selye in the 1973 photo below.



Karsh was already world renowned for his depiction of Winston Churchill on the cover of *Life* magazine in 1941, said to have been the most reproduced portrait photograph in history. Of the 100 most notable people of the century listed by the 2000 *International Who's Who*, Karsh had been commissioned to photograph more than half, including Popes Pius XII and John Paul II, Presidents Roosevelt, Kennedy and their wives, Prince Rainier and Grace Kelly, Albert Einstein, Albert Schweitzer, Gandhi, Princess Elizabeth, Humphrey Bogart, Elizabeth Taylor, Clark Gable and other stars of stage and screen. There were also famous authors (Hemingway), musicians (Horowitz, Casals), architects (Frank Lloyd Wright), artists (Picasso), playwrights (George Bernard Shaw, Tennessee Williams) composers (Sibelius, Rogers and Hammerstein) and numerous other luminaries. Karsh photographs were featured in the Metropolitan and other major museums and could cost up to \$45,000.

Karsh usually stayed at The Waldorf-Astoria when he was in Manhattan, and I shared an office at the Waldorf Towers at the time. Since I was not sure how much time would be required, I scheduled him for the last appointment of the day. As it turned out, we talked about so many other things, including Selye and other dignitaries he had photographed, that two hours quickly slipped by. I had asked him how he was able to achieve such dramatic effects in his photographic portraits, and he explained that his first goal was to learn more about his subjects so that he could capture certain telltale characteristics. This was often achieved by concentrating on facial expressions, especially the mouth and chin (Churchill and Eisenhower) or, as in Selye's portrait, the hands. He took numerous photos using different angles, positions and lighting effects, until he was satisfied that most viewers would be subtly attracted to what he wanted to focus on, without any semblance of it being a caricature. I was so fascinated that I forgot I had a dinner date with Norman Cousins, who would later become a Founding Trustee of The American Institute of Stress, and apologetically explained this. Norman, who was editor of *The Saturday Review of Literature* had recently published *Improbable Triumvirate: John F. Kennedy, Pope John, Nikita Khrushchev*, which described his role in bringing the Soviet-American test ban treaty to fruition at Kennedy's request. Karsh, who was aware of this, immediately insisted that I invite Cousins to have dinner with us at the Waldorf, since they had mutual friends and he was anxious to meet him. Norman was delighted, and although Karsh was a member of the Waldorf's exclusive Marco Polo Club, he could not obtain a suitable reservation on such short notice. I was lucky to get one at their Bull & Bear Steakhouse, since the *maitre d'* had been a patient. He seated us in a secluded area and the next few hours of animated conversation also quickly slipped by. It was an unforgettable experience. Since Cousins and Karsh admired and almost seemed in awe of Selye, much of the discussion centered about Selye's concepts as well as his personality. In particular, they could not understand the resistance from some physicians and scientists about his stress and disease theories, and were anxious to know if I could explain this.

How Some Of Selye's Critics Responded To His Concept Of Stress

A major source of contention was Selye's inability to define what he meant by stress. As noted in a previous Newsletter, in helping him to prepare his *First Annual Report on Stress* in 1951, I included the complaint of one critic that had recently been published in the *British Medical Journal*. Using verbatim citations from Selye's own writings, he had come to the conclusion that **"Stress, in addition to being itself, was also the cause of itself, and the result of itself."** In addition, this confusion about the meaning of stress caused numerous problems when his articles and books had to be translated into foreign languages because there was no suitable word or phrase that conveyed what he meant. Selye had originally defined stress as

"the nonspecific response of the body to any demand for change." In trying to explain his views to a lay audience, he later redefined stress as "The rate of wear and tear on the body". Since this was also not very helpful, the only solution was to substitute *le stress, il stress, lo stress, el stress, der stress*, for European languages, or simply "stress" in Russian, Japanese, Chinese, or Arabic, that used characters rather than the Latin alphabet.

In addition, critics resented what they felt were his unfounded views about stress as the cause of so many very different diseases, especially since he was not a practicing physician. Some may have been concerned or jealous about how famous he had become in such a short period of time, which they attributed to superb salesmanship rather than any scientific achievements that would benefit patients. Selye received numerous international Awards and honors, and had been invited to visit heads of state ranging from Joseph Stalin to Juan Peron. In 1968, he received Canada's highest honor, Companion of The Order of Canada, which had been established the year before by Queen Elizabeth. In "Selling the Code", a chapter of his *The Stress of My Life*, he boasted that he was so well known in Canada because of numerous radio, television, and public speaking engagements, that he resorted to traveling about in a wig and dark reflecting sunglasses. "Even I could not recognize myself", he wrote, but after he was instantly identified by a fellow passenger, who said "Oh Dr. Selye, how you have changed!" He gave up the disguise and resorted to eating garlic and/or taking garlic pills. Garlic not only curtailed unwanted conversations with strangers, but he was convinced that it also had important health benefits.

Selye was aware of only two-dozen or so adrenal cortical steroids and found that the vast majority had no hormonal activity. He classified those that did into three categories depending on their primary actions: **glucocorticoids** that elevated blood sugar, **mineralocorticoids** that retained sodium, and **testoids**, which had mild androgenic activity. Glucocorticoids, which also had powerful anti-inflammatory effects, appeared to be the only corticoids that were significantly involved in the response to stress or pituitary stimulation. It is now known that the adrenal cortex manufactures over 60 steroids and in addition to its own corticoids, is capable of synthesizing all the steroid hormones made in the body, including, estrogens, progestogens and androgens. Nevertheless, to Selye's credit, everyone still uses his original classification system, since it has stood the test of time for 70 years. As indicated previously, Walter Cannon had already shown that the "fight or flight" and sympathetic nervous system responses to severe stress were associated with an outpouring of adrenaline-like hormones from the inner adrenal medulla. Selye later demonstrated there was also an Alarm Reaction initiated by pituitary stimulation of the adrenal cortex (outer shell) to secrete increased amounts of glucocorticoids. These caused pathologic changes in

certain tissues and organs and influenced the subsequent stages of the General Adaptation Syndrome. Glucocorticoids were assumed to be a major contributor to Diseases of Adaptation because of their effects on resistance.

Although Selye had dedicated his groundbreaking 1946 article to Walter Cannon, many felt that he did not adequately pay homage to him and others who previously expressed some of his views, often using the same phrases and words. Sir William Osler had written in 1892 that it was "wear and tear" that resulted in arteriosclerosis, as well as some types of kidney disease. In Cannon's 1925 report, he had demonstrated that even the limited disturbances in homeostasis during fever caused an increased secretion of adrenaline. Decades later, it was shown that adrenaline could also stimulate the hypothalamic-pituitary-adrenal axis to increase glucocorticoid secretion. And a year before Selye's 1936 brief letter that first described the Alarm Reaction (but did not mention stress), Cannon had published a summary article entitled **"The stresses and strains of homeostasis"**. It anticipated some of the problems Selye would have with his definition of biologic "stress", which he should have referred to as "strain". In an effort to extricate himself from the confusion he had created, Selye later explained

I should have called my phenomenon the "strain reaction", which causes "stress", in parallel with the use of these terms in physics. Hence, I was forced to create a neologism and to introduce the word "stressor" for the causative agent, retaining stress for the resulting condition. Stress and strain in physics correspond to stressor and stress in biology and medicine."

However, that was in 1956 and the damage had been done. Cannon had been dead for over a decade and there was no acknowledgement of his clear recognition of this important distinction.

Cannon was skeptical that glucocorticoid effects on resistance were major causes of disease and disagreed with the definition of stress as a nonspecific response to disturbances in homeostasis. He showed that the specific stabilizing or homeostatic reaction to lack of oxygen was quite different from the body's response to cold, which was virtually the reverse of that required to resist heat, but never used "stress" to describe this. From an evolutionary perspective he doubted that Selye's stereotyped nonspecific response pattern would have provided any advantages in the process of natural selection and therefore would not have survived in all vertebrates. Unlike Selye, he recognized the importance of psychological as opposed to physical responses during stress. He differed with the prevailing James-Lange theory that physiologic responses to stress occurred first, and then caused varied emotions. Cannon proposed that we feel emotions when, in response to a stimulus, the thalamus sends signals to the cerebral cortex as well as the sympathetic nervous system. These evoked two simultaneous but separate

reactions; awareness of emotions and physiological excitement. Neither caused the other, and emotional responses could surface first.

Subsequent studies showed that such reactions to stress differed in humans due to genetics, conditioning and gender, so they were hardly nonspecific. Men were apt to exhibit aggressive responses whereas women were more likely to "tend and befriend" and seek social support. Jim Henry's superb studies of the effects of psychosocial stress in "microsocieties" of mice emphasized the important role of emotions in eliciting either an aggressive defense or passive defeat response in animals. Challenges that represented a mere threat to control tended to produce a Defense Reaction by activating Cannon's sympathetic-adrenal medullary responses. An irreversible and complete loss of control evoked Selye's pituitary-adrenal cortical axis, along with signs of depression. These identical responses have been confirmed in rodents, dogs, cats, monkeys and man, and as explained in previous Newsletters, may contribute to either hypertension or metabolic syndrome. In humans, depending on how the severity of the threat is interpreted, there may be elements of both of these disorders. Based on genetic and other influences there could also be increased or decreased predisposition to cardiovascular and/or gastrointestinal damage.

As the famous 19th century physicist Lord Kelvin noted, **"To measure is to know. If you can not measure it, you can not improve it."** But there were no objective methods of quantifying stress or glucocorticoid excretion until cortisol was identified and normal blood levels could be established. The only test available in the early days of Selye's research was measurement of 24-hour urinary 17-ketosteroid excretion, which was very crude and often inaccurate. Selye reported in 1937 that there were consistent white blood cell changes during the Alarm Reaction, including an increase in neutrophils but especially a pronounced decrease in lymphocytes that paralleled the degree of atrophy of the thymus and lymph glands. Two year later, he noted that this was preceded by a decrease in eosinophils that was followed by an increase in these cells during its countershock phase. Dougherty and White, Pincus, and several others subsequently showed that the reduction in lymphocytes resulted from pituitary stimulation of the adrenal cortex since it could be reproduced by giving ACTH or glucocorticoids. Similarly, it had also been observed that patients with Cushing's syndrome, who have high levels of cortisol due to a pituitary tumor or over activity of the adrenal cortex, had a decrease in lymphocytes and eosinophils. Conversely, these cells were increased in patients with adrenal insufficiency (Addison's disease) due to low cortisol levels. In 1948, Harvard's Forsham and Thorn showed that while administering ACTH caused a 74% fall in circulating eosinophils in normal individuals, in contrast to only 4% in Addison's disease. Around the same time, Laragh and Almy reported that adrenaline, insulin, and the stress of

surgery also caused a fall in eosinophils. Thorn later developed a test to diagnose adrenal insufficiency based on the inability of ACTH to cause a disappearance or significant drop in circulating eosinophils. Since ACTH was often not readily available and costly, adrenaline was sometimes substituted.

It was thought that eosinophils, (so named because they pick up the red dye eosin during the staining process for examining white blood cells under the microscope) might provide a method to measure the glucocorticoid activity of various steroids. However, this was a tedious process, since although easily identified by their red color, eosinophils normally comprise only up to 3% of total white cells. Franz Halberg, who had been assigned to this assay project, also found that in animal studies, eosinophil levels varied with the time of day, calorie restriction, diet, genetic factors and gender. More importantly, he demonstrated that even after removing the adrenals and all visible ectopic tissue that resembled the adrenal cortex, adrenaline still caused a significant drop in eosinophils. This could not be duplicated by others in Thorn's group and was thought to have little clinical significance, but it was subsequently confirmed by others and the adrenaline test for adrenal insufficiency was abandoned. Halberg, who coined the terms circadian and chronobiology, later showed the importance of these influences on human diseases and their treatment, especially hypertension. He is still going strong at ninety, and more information about his many achievements will be provided in a future Newsletter interview.

As Thomas Huxley noted, **"The great tragedy of science is the slaying of a beautiful theory by an ugly fact."** and there were others that Selye would have to contend with. As Frank Engel acknowledged in 1956, "Selye's theory of stress and the diseases of adaptation 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." However, Engel, who headed the department of Endocrinology at Duke, did not believe that glucocorticoids caused disease, even though luminaries like Fuller Albright had endorsed Selye's claim. Dwight Ingle at the Mayo Clinic had shown that adrenalectomized animals showed the same responses to stress if they were on maintenance doses of glucocorticoids. In other words, these hormones needed to be present, but it was not their increased production that caused pathology, which he called a **"permissive" effect**. Engel subsequently confirmed this, and also demonstrated that the metabolic response to stressors in animals with intact adrenals occurs much more rapidly than does the response to either ACTH or glucocorticoids, even when these hormones were administered intravenously. Engel used the analogy of putting grease on an axle wheel to explain the role of hormones in the response to stress. Without grease (hormones), the wheel was difficult to turn. A certain amount is necessary to allow the wheel to turn freely and

the grease must be replenished as the wheel is used. The more rapidly or continuously the wheel turns, the greater the need for supplying grease to the axle. But too much grease could make the wheel slip; respond to forces that previously had no effect; or to revolve more rapidly than usual. This permissive effect was not compatible with Selye's contention that stress responses and stress related diseases were modulated by hormone levels, which were largely determined by pituitary-adrenal axis activities.

One of his severest critics was John Mason, who complained in a lengthy 1971 article that the General Adaptation Syndrome was incompatible with the concept of homeostasis, no attempts had been made to evaluate its three phases with biochemical measurements of pituitary and adrenal activity that were now available, and especially lack of acknowledgement of the influence of emotional factors on the pituitary. He proposed that only marked anxiety or fear was responsible for similar neuroendocrine responses to different stressors, but that this did not apply to other emotions. Selye subsequently countered this by proposing that most stressors induced two types of responses: 1) a general stress response, which is common to all and involves the release of ACTH and adrenal glucocorticoids, and 2) individual stress responses mediated by "conditioning factors, such as genetically determined predispositions. In other words, stress can sensitize the organism to respond to normal or near normal amounts of adrenal hormones. As he explained, it is "proper to designate a manifestation of stress as due to hypercorticism whether it results from an actual increase in corticoid production or from sensitization of certain target organs to these hormones." As an analogy, he pointed out "A room may become overheated either because more heat is produced by the furnace or because an increase in the outside temperature lessens heating requirements. In either case, it is quite correct to say that the heating system is overworking."

There have been numerous other objections, criticisms and modifications of Selye's concept of stress over the past four decades, the most recent being allostasis, the process of achieving homeostasis through physiological or behavioral change. Homeostasis was coined by Cannon from the Greek *homeo*, meaning "same," and *stasis*, or "stable;" thus, remaining stable by staying the same. Allostasis was derived from the Greek *allo*, which means "variable;" thus, remaining stable by being variable. But there was nothing very new about this. Claude Bernard had written in the 1850's, "*La fixité du milieu intérieur est la condition de la vie libre*" (The stability of the internal environment is a condition for a free life). But he had carefully noted that this stability was due to a continual equilibration or variation in numerous systems, in order to maintain relative constancy. Cannon called this "the steady state" and also emphasized that homeostasis was dynamic and "admits some variation" around different metabolic "set points".

How Will Hans Selye Be Remembered In 2036 And Beyond?

Stress is not a useful term for scientists since it cannot be accurately defined or measured, nor is it a disease. As Selye was fond of saying, "**Everyone knows what stress is but nobody really does.**" Nevertheless, stress somehow seems to encompass the variegated and poorly understood interrelationships between emotions and health. It is not likely to be replaced by any other term or phrase that is more meaningful in the foreseeable future. I suspect that it will continue to be a popular "buzz" word 100 years after Selye introduced it in 1936 and that he will be indelibly linked with stress. He may have been wrong in assuming that his stress related Diseases of Adaptation in animals applied to humans. However, there is increasing evidence that "stress" can have a significant influence on the development and course of coronary disease, hypertension, diabetes, gastrointestinal, dermatologic, mental/emotional and other disorders like obesity that are often associated with civilization. Advances in psychoneuroimmunology and neuroendocrine research are now delineating some pathways that may mediate these effects.

My own lasting memory of Selye would be what he often reminded me and others, namely, that **theories don't have to be correct - only facts do.** He emphasized that many erroneous theories are still valuable because of their heuristic merit, in that they encourage others to discover new facts, which then lead to better theories. Perhaps he sensed that his theories might suffer this fate and there is little doubt that his revolutionary ideas were responsible for an explosion of research into how hormones functioned. Selye did not endorse any particular type of stress reduction technique, but he recognized the benefits of meditation and correctly predicted that how these were achieved would be discovered. He advocated "altruistic egotism", doing something you enjoy that benefits others, and that the "Golden Rule" should be "Earn thy neighbor's love" (rather than "Do unto others" etc.). Another of his aphorisms was, "Fight for your highest available aim but do not put up resistance in vain." His advice to researchers was "Neither the prestige of your subject and the power of your instruments, Nor the extent of your learnedness and the precision of your planning, Can substitute for the originality of your approach and the keenness of your observations." Much more could be said about this remarkable man – so stay tuned. In the interim see some relevant comments and illustrations on the next page.

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In *The Structure of Scientific Revolutions*, Thomas Kuhn argued that science rarely progresses in some sort of logical stepwise fashion as is commonly believed. This is because it is often portrayed in that fashion by historians who cherry pick what they present to give that impression. Scientists do not always incorporate new data that is pertinent, especially if it does not fit into existing paradigms or contradicts their theories. Many are more concerned with "Who is right", rather than "What is right". Selye could never be accused of this. He reported everything objectively, responded to all criticisms, and in some instances, seemed to relish his skill in explaining why they were not necessarily inconsistent with his concepts and theories.

Paul J. Rosch, MD, FACP
Editor-in-Chief



Above: With Norman Cousins, who along with Linus Pauling, Alvin Toffler, Bob Hope, and Michael DeBakey, were Founding Trustees of The American Institute of Stress.

Below: With Hans Selye at the 1978 Founding Ceremony in Tarrytown, New York.

