

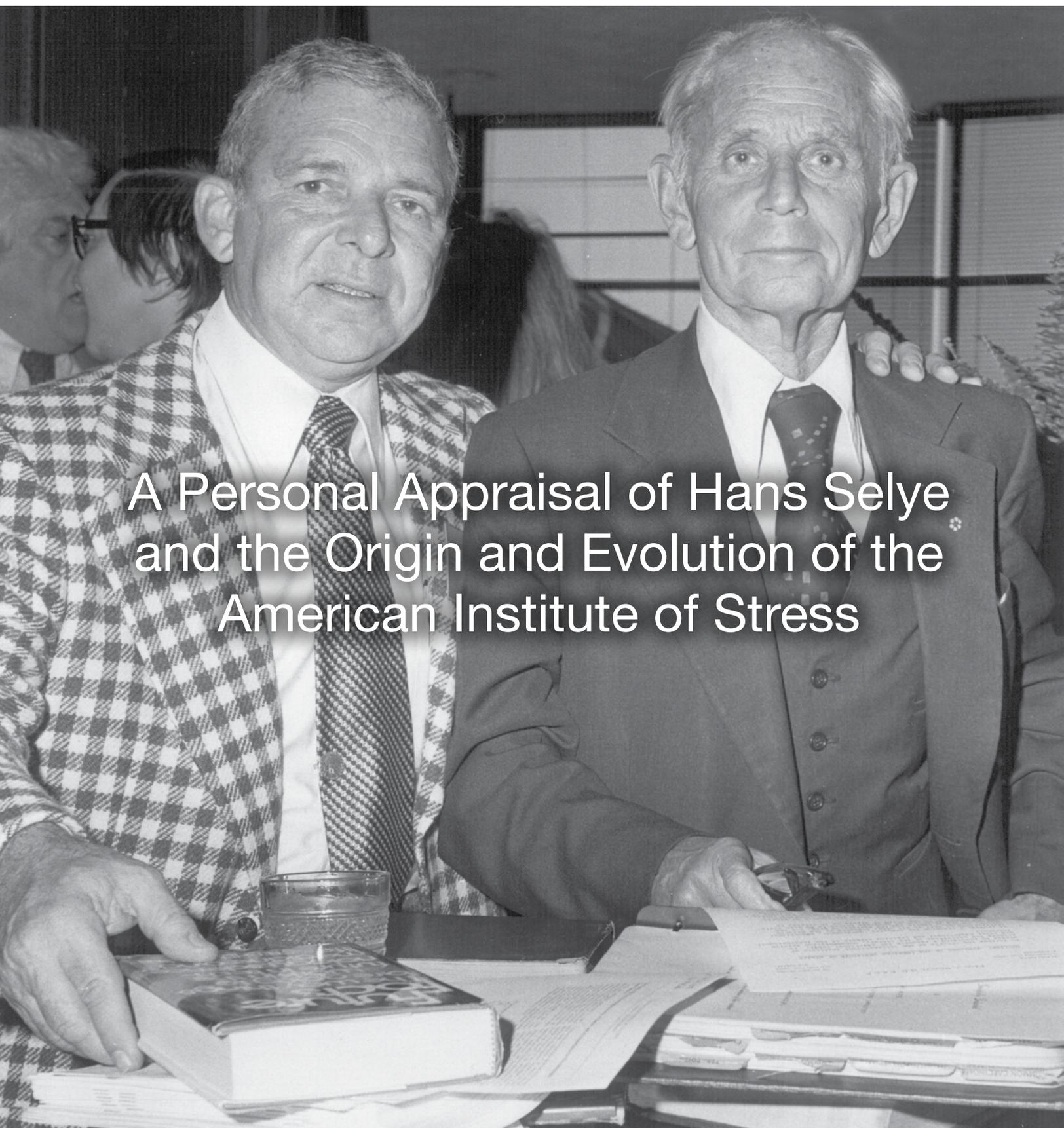
The American Institute of Stress

HEALTH AND STRESS

Your source for science-based stress management information

FINAL ISSUE

January 2018



A Personal Appraisal of Hans Selye
and the Origin and Evolution of the
American Institute of Stress

Your source for science-based stress management information

HEALTH AND STRESS

We value opinions of our readers. Please feel free to contact us with any comments, suggestions or inquiries. Email: editor@stress.org

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\$20 per issue or \$120 annual subscription rate.

Health and Stress appeals to all those interested in the myriad and complex interrelationships between health and stress because technical jargon is avoided and it is easy to understand. Health and Stress is archived online at stress.org. Information in this publication is carefully compiled to ensure accuracy.

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Health and Stress: The Final Issue

Paul Rosch, MD, FACP

About This Issue

A few months ago, Dr. Dan Kirsch asked me to contribute a monograph elaborating on how I became involved in establishing the American Institute of Stress (AIS), and to discuss some career highlights over the past 65 years. He also wanted to commemorate 28 years of *Health and Stress* Newsletters, which began as a monthly publication in 1988. Much of this information was already available in previous Newsletters and on our web site, as well as my editorials in *Stress Medicine* and articles in other publications. However, as I reviewed the contents of over 200 Newsletters, it was evident that some topics should be updated and that other important issues had been omitted. I have tried to rectify this in the following. References to validate any statements and/or to provide a link to additional information, as well as comments or questions, can be obtained by contacting prosch@stress.org.

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Part 1: Stress, Alcoholism, and Hans Selye— How it all Began

My interest in stress was kindled in 1949, when I was in charge of supervising the laboratory at a community hospital. This involved serving as bacteriologist, doing ECGs, drawing blood, overseeing or doing blood chemistries and CBC's, and helping the pathologist prepare slides. I was friendly with many of the attending physicians, especially one who had achieved success in treating alcoholism with injections of Eschatin, an aqueous solution of adrenal cortical hormones, along with a diet designed to prevent hypoglycemia. This was based on his theory that the stress of chronic alcoholism depleted adrenal cortical hormones, which resulted in recurrent episodes of low blood sugar that promoted the desire for alcohol.

I talked with several of his patients, all of whom who had successfully responded to this regimen, but later fell off the wagon when it was discontinued. Other physicians reported success and the World Health Organization also concluded that the basic cause of alcoholism was due to a congenital "slight deficiency of carbohydrate metabolism or of certain endocrine relations." I asked what led him to develop this treatment and he gave me a copy of a 1946 114-page article with 700 references by Hans Selye on "The General Adaptation Syndrome and the Diseases of Adaptation." This included Selye's classi-

fication of adrenal cortical hormones into glucocorticoids, which affected carbohydrate metabolism, mineralocorticoids that caused sodium and fluid retention and testoids, which had weak androgenic effects. It also confirmed that chronic stress eventually exhausted the ability of the adrenal cortex to make hormones.

Glucocorticoids like cortisone appeared to be the most important since they were essential to maintain life and also had powerful anti-inflammatory effects. This had first been demonstrated in 1948 at the Mayo Clinic in a patient with treatment-resistant rheumatoid arthritis who experienced dramatic relief from cortisone. It seemed to me that any benefits from Eschatin most likely came from its glucocorticoid content and that treatment results could be improved by administering more precise doses of cortisone, which could also be taken orally. I wrote to Selye and asked about this, and explained that I would be entering medical school in a few months and was interested in investigating this possibility. I also included a copy of a paper on "Endocrine Treatment of Alcoholism" that had just been published. I was surprised to receive a prompt and very cordial response as well as an invitation to pursue this at his Institute of Experimental Medicine and Surgery at the University of Montreal, if he could obtain funding. I was halfway through my first year when I

received a letter indicating that a suitable stipend had been arranged for a Fellowship starting in the summer.

I arrived at the University of Montreal in June 1951 and was surprised that there was hardly anyone around. I took the elevator to the Institute on the top floor, which also seemed deserted. There was a row of empty offices on each side of a wide corridor that led to a large glass enclosed office with several desks, only one of which was occupied by what appeared to be a secretary. I introduced myself and asked if I could see Dr. Selye. She identified herself as Miss Atkinson, Dr. Selye's personal assistant, and that they were the only ones there since it was St. Jean Baptiste day, a national holiday in Canada, and they had expected me the following day based on my last letter. She pointed to the door of his adjacent office, which had a bright red light over it that meant that he was not to be disturbed. She said that since the light had been on for over two hours, it was likely that he would soon take a break, and suggested I wait. She gave me a list she had prepared of nearby furnished apartments I could rent and their respective rates, as well as a map of the area showing their locations. After ten minutes or so, the red light went off and she informed Selye I had arrived. He immediately opened the door and greeted me warmly. He reiterated that I had been expected the following day, when arrangements had been made for me to be escorted on a tour of the Institute. He suggested I secure housing accommodations

as soon as possible and looked forward to meeting with me at noon after my tour.

My Introduction to The Institute of Experimental Medicine and Surgery

I found an inexpensive but well-furnished studio apartment quite close to the University and returned to the Institute the next morning, where I was greeted by Dr. Ernesto Salgado, a Fellow from Spain who spoke excellent English. He took me through the huge library and explained how to access its contents, showed me the laboratory facilities, conference rooms, and my office, which was next to Roger Guillemin's, who would later share a Nobel Prize for his discovery of the endorphins. He introduced me to Roger and some of the other Fellows, who also greeted me warmly. They were interested in learning more about my proposed project in the event they might be of assistance and also indicated the purpose of their own research. A few did not speak English and their responses in French were quickly translated by Ernesto. He also outlined what the usual schedule was with respect to laboratory work and periodic conferences with Selye, during which Fellows reported on the status of their projects.

I learned that Selye's average workday was 10 to 14 hours, including weekends and holidays. Ernesto said he habitually rose around 5:30, took a dip in the small pool in the basement of his house across from the McGill campus, and then rode his bike several miles to work. He was usually the

first to arrive and frequently the last to leave. On sunny days, he occasionally put aside an hour after lunch to “take a nap in Miami.” This was not Florida, but rather a solarium on the top floor, where he had the glass ceiling replaced with quartz so he could work on his tan during the winter. His office was a veritable inner sanctum, guarded by an anteroom of protective secretaries and librarians. We had to schedule an appointment with these sentries or Miss Atkinson if we wished to speak with him. There was a prominent green and red light over both sides of his office door. When the red light was on, which was not infrequent, he was not to be disturbed unless there was an emergency. A green light indicated that he could now receive messages that had accumulated and important telephone calls. If no lights were on, there was also the possibility of speaking with him without a prior appointment.

After my tour, I met with Selye at noon as scheduled to discuss the feasibility of my proposed project. He indicated that while there was no problem in finding a model of chronic alcoholism in rats, cortisone was not readily available and was expensive. When introduced the year before, the cost to synthesize cortisone was \$1,000/gram, and although the price had now plummeted, it was still prohibitive. A new method of synthesis from Mexican yams promised to vastly increase the supply at a drastically lower price, but not in time for me to finish my experiment. In addition, I had no experience at all in animal research, and

Selye felt this should be my top priority. He had previously demonstrated in several studies that steroids produced anesthesia when injected as a bolus intravenously or intraperitoneally. In addition, the degree and duration of anesthesia seemed to correlate with their potency. Testosterone was more effective than weaker androgens and he wanted me to investigate whether this was true for hormones secreted by the adrenal cortex. I agreed, but before describing what subsequently transpired, I believe it would be helpful to discuss Selye’s background, and what led to the establishment of his Institute of Experimental Medicine and Surgery at the University of Montreal.

The Rockefeller Scholarship, Johns Hopkins, and McGill University

Hans Selye was born in 1907 in Komarno, Slovakia, an area of Hungary midway between Vienna and Budapest. It was apparent early on that he was very bright and a quick learner, and his mother, who was well educated, forced him to speak four languages at home. He had no problem with Hungarian, Slavic or German, and was taught French and English by governesses. He attended school at a Benedictine monastery, and since four generations of physicians preceded him and his father was a surgeon in the Imperial Austro-Hungarian Army, he entered the University in Prague at the age of 17. He graduated first in his class from its medical school in 1929, attended universities in Paris and Rome, and obtained his Ph.D. in organic chemistry in 1931. Because of

his obvious talent, he was awarded a 2-year Rockefeller Foundation Scholarship to continue his research on steroid hormones at Johns Hopkins.

He arrived in Baltimore in 1931, rented an inexpensive room with a kitchenette near the University, and learned how to cook for himself so that he could save some money from his \$150 monthly stipend. He subsisted mostly on canned foods and later referred to this as his “sardine period,” since a large tin was a bargain at 10 cents, and he ate them daily. He was warmly accepted by the other postdoctoral students, and sympathetic faculty wives who felt sorry for “the poor lonely foreign students,” constantly arranged parties and social events where they could meet people. Although Selye spoke English fairly well, he quickly realized that Americans had their own jargon. On one occasion, he asked the very attractive daughter of a prominent professor if they could meet again to go to a movie or dinner, and offered to walk her home. Her response was “*Yes, but would you give me a ring first?*” Selye was petrified, since he thought she meant an engagement ring and had heard stories of the strict enforcement of “breach of promise” laws in the U.S. He congratulated another girl on her beautiful complexion by saying that her “hide” was of the finest quality, which she did not take as a compliment. Unfortunately, there was no distinction between hide and skin in any of the eight languages Selye spoke.

He also had difficulty adapting to this new situation at work, since he had been reared in a very formal academic environment where there were rigid class distinctions, much like the military. Full professors were respected and obeyed as if they were generals in the Army, and Department Heads were demigods. Selye was appalled at the sight of such distinguished middle-aged and older Faculty members playing charades and acting in an undignified fashion at parties to which underlings and even medical students were invited. Everyone seemed to be on a first name basis whereas this would have not been tolerated in Europe.

He recalled that as a medical student, patients suffering from very different diseases often exhibited the same signs and symptoms in the first days of their illness. They all had low-grade fevers, feelings of malaise, fatigue, generalized aching, and “they just looked sick.” He was excited about the possibility of studying the biochemical changes and mechanisms responsible for these common findings since he thought this might possibly lead to some form of treatment or relief.

He made an appointment to speak with the Chairman of the Department of Physiology to ask if he could study this in his laboratory on weekends or free time after school. The Chairman’s full name, including titles, was Hofrat Professor Doktor Armin Tschermak Edler (Nobleman) von Sysenegg. Since that was quite a mouthful, it was

concluded that at least his highest title should be used, and he expected to be addressed as “Herr Hofrat” Counsel to the Imperial Court. Selye, who was then 19 and unaware of this, innocently called him “Herr Professor”. Apparently, that was the only part of his enthusiastic presentation that made an impression, since after he had finished, the response was “*Well, if you are that chummy, why don’t you just call me by my first name, Armin.*” Even after profuse apologies, his request was rejected as being so juvenile that it was not even worth discussing. He was told that obviously, if a person is sick, he looks sick, just as if he is fat, he looks fat. He was warned not to bring the subject up again and to concentrate on studying for his exams.

Selye was so dismayed about the casual academic environment at Johns Hopkins he returned to Prague to continue his research on the structure and function of hormones with Professor Arthur Biedl, a distinguished endocrinologist, who had been his mentor at medical school. However, Biedl was retiring and had been replaced as Chairman of the Department of Pathology by a cardiologist who was not interested in Selye’s research project. A friend told him he could transfer his Rockefeller Scholarship to McGill University in Montreal, which had a more traditional European ambience. In addition, he could continue his research under the guidance of the renowned biochemist Bertram Collip, who discovered parathyroid hormone and ACTH, and had been a crucial member of the Banting and Best team respon-

sible for isolating insulin a decade earlier. When Selye arrived in 1932, McGill’s Biochemistry Department was the paragon of a modern endocrine research laboratory with all the latest equipment due to very generous funding from the Rockefeller Foundation. At the time, only two types of female hormones had been identified, but Professor Collip thought there was a third, and assigned Selye to this quest. He was sent to the slaughterhouses with a large bucket and told to retrieve as many cow ovaries as possible, which Collip then reduced to various extracts for Selye to inject into female rats for several days or weeks. The animals were later autopsied to look for any changes in their sex organs or other tissues that could be attributed to this presumed new ovarian hormone. However, no such effects could be demonstrated, and what was even more discouraging and depressing, most of the rats became severely ill, and some died.

Selye’s Concepts of Stress and the General Adaptation Syndrome

Selye was a meticulous pathologist, and although there were no changes in the ovaries or breasts, he noted that all his rats showed enlargement of the adrenals, shrinkage of the thymus and other lymphoid tissues, and ulcerations in the stomach. This made no sense, and he searched for some explanation. One possibility was that this was due to some chemical contaminant in Collip’s concoction. There was a bottle of formaldehyde, a toxic substance used to fix tissues for microscopic study, right in front of

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him. On a whim, he injected liberal amounts of it into several rats, and was amazed to find that this produced results identical to those observed with Collip's extracts. He decided to see what would happen if he injected other toxic chemicals and found that although they had effects on other organs and structures, there were always the same changes in the stomach, adrenals, thymus and lymphoid tissues previously noted.

Selye wondered whether a noxious physical stimulus would also produce these same changes and exposed rats to the frigid Canadian winter by leaving them on the windswept roof of the McGill Research Institute. He put some in a constantly revolving barrel-like treadmill driven by an electric motor so that they had to constantly run to stay upright. Others were dumped into a water barrel and had to keep swimming to prevent drowning. Sure enough, all that survived after a day or two of these physical torments showed the identical pathology produced with Collip's extracts and formaldehyde. Selye subsequently demonstrated that severe emotional threats could also do this in experiments that would be impossible to duplicate today, such as sewing back the eyelids of immobilized rats and exposing them to an extremely bright light, subjecting them to deafening and irritating noise, or intense psychological frustration that also bordered on torture. All of these also produced the same pathological triad. Prolonged exposure consistently resulted in pathologic changes in other organs and structures.

He decided to report these novel findings in a letter to the editor of *Nature*, a very conservative and highly respected journal. Letters to the editor today are usually limited to responses to articles previously published in that journal, but eighty years ago, they included short communications that were deemed to be important., Selye submitted his letter entitled "A Syndrome Produced by Diverse Noxious Agents," describing what he referred to as biologic stress. He went on to explain that this had three phases; the first being the changes in the adrenals, stomach, thymus and other lymphoid tissues that occurred within the first 48 hours. If exposure to the injurious agency continued, a second Stage of Resistance ensued that culminated in regaining normal defense mechanisms. Persistent exposure for 1-3 months resulted in a third Stage of Exhaustion in which the adrenal cortex failed to secrete hormones. He concluded that "*Since the syndrome as a whole seems to represent a generalized effort of the organism to adapt itself to new conditions, it might be termed the 'general adaptation syndrome.'*"

Although this letter is often cited as Selye's first use of stress, this word never appeared. The editor rejected stress since it was then commonly used as a synonym for distress, and most often referred to nervous strain in women. Instead, Selye called the first phase of the General Adaptation Syndrome the "Alarm Reaction," since he viewed it as a "call to arms" of the body's defense mechanisms.

Selye had originally written “noxious” agents, which implied something poisonous or lethal. However, since severe and protracted muscular exercise or extremes of temperature did not fall into this category, the editor substituted “nocuous.” Selye’s 74-line letter to the editor entitled “A Syndrome Produced by Diverse Nocuous Agents” appeared in the July 4, 1936 issue of *Nature*. What was unique about this syndrome was that it occurred following exposure to “*acute nonspecific nocuous agents such as exposure to cold, surgical injury, production of spinal shock (transcision of the cord), excessive muscular exercise, or intoxications with sublethal doses of diverse drugs (adrenaline, atropine, morphine, formaldehyde, etc.*” More importantly, “*the results were “independent of the nature of the damaging agent or the pharmacological type of the drug employed.”*”

This was quite radical. As a result of Pasteur’s research and Koch’s postulates, physicians had been taught that each disease had its own, very specific cause. Tuberculosis was caused by the tubercle bacillus, pneumonia by the pneumococcus, rabies, anthrax, and cholera by other microorganisms, and scurvy was due to lack of vitamin C. What Selye proposed was the reverse, since he had now demonstrated that very different and even opposite physical challenges, such as extremes of heat and cold, as well as severe emotional threats, could indeed produce identical pathological changes in certain organs and structures. While each of these hazards

might produce other damage, such as a burn, or frostbite, they all caused the identical nonspecific changes in the adrenals, stomach, and lymphoid tissues he had first seen following the injection of Collip’s extracts and formaldehyde. He also wondered whether stress might explain the common occurrence of “just looking sick” he had observed in the early stage of illness in patients who would later develop very different diseases.

Detailed autopsies performed during the various stages of the General Adaptation Syndrome revealed gross and microscopic changes very similar to those seen in patients with arthritis, kidney disease, hypertension, coronary heart disease, and gastrointestinal ulcers. Selye suspected that perhaps “stress” might also cause these disorders in humans as well, and referred to them as “Diseases of Adaptation.” After numerous additional experiments, he found that he could replicate many of these disorders selectively by sensitizing or conditioning the animals through certain dietary or hormonal manipulations. He subsequently traced the pathways and mechanisms that were responsible for the changes seen in the “Alarm Reaction” and demonstrated they were due to increased pituitary stimulation of the adrenal cortex to produce hormones that reduced inflammation. This explained why the adrenals were enlarged. Similarly, the stomach ulcers and lymphoid tissue shrinkage were due to the increased amounts of these cortisone-like hormones. If the pituitary or the adrenals were re-

moved, these manifestations of damage in different organs and structures did not occur. He reasoned that if he could show how such injuries were caused, then perhaps he could find a way to prevent or treat Diseases of Adaptation more effectively.

Since Selye's initial assignment at McGill focused on isolating what was believed to be a third ovarian hormone, he soon learned the best methods of preparing hormonal extracts from Collip. He was appointed Lecturer in 1933 and Assistant Professor of Biochemistry in 1934 at the age of 27. He also worked with an interdisciplinary group of other researchers like J.S.L. Browne and Eleanor Venning, who would later distinguish themselves because of their research on pituitary and adrenal cortical responses to stress. Under Collip's leadership, this prolific and talented team along with a rotating staff of three or four graduate students published nearly two hundred papers from 1934 to 1941, in what the historian Alison Li described as the "endocrine gold rush" of the 1930s. One reason for this was that the Rockefeller Foundation and other philanthropies were no longer awarding huge sums to institutions to fund basic science studies. Instead, they were now focusing on smaller grants to faculty members for specific research projects, especially those with the potential to provide clinical benefits in the near future. Due to the Great Depression, there were few other sources of support, and as faculty members were forced to compete for grants, they often had to revise their

research to attract funding. Studies dealing with new techniques and methodologies were most likely to attract funding and Selye took advantage of this. He continued to receive Rockefeller Foundation support, and by 1939. had secured additional funding from the Josiah Macy Jr. Foundation, the Markle Foundation, and the Commonwealth and Banting Funds. He also learned how to acquire laboratory supplies and research grants from pharmaceutical companies by emphasizing the cutting-edge nature of his research and its potential commercial rewards.

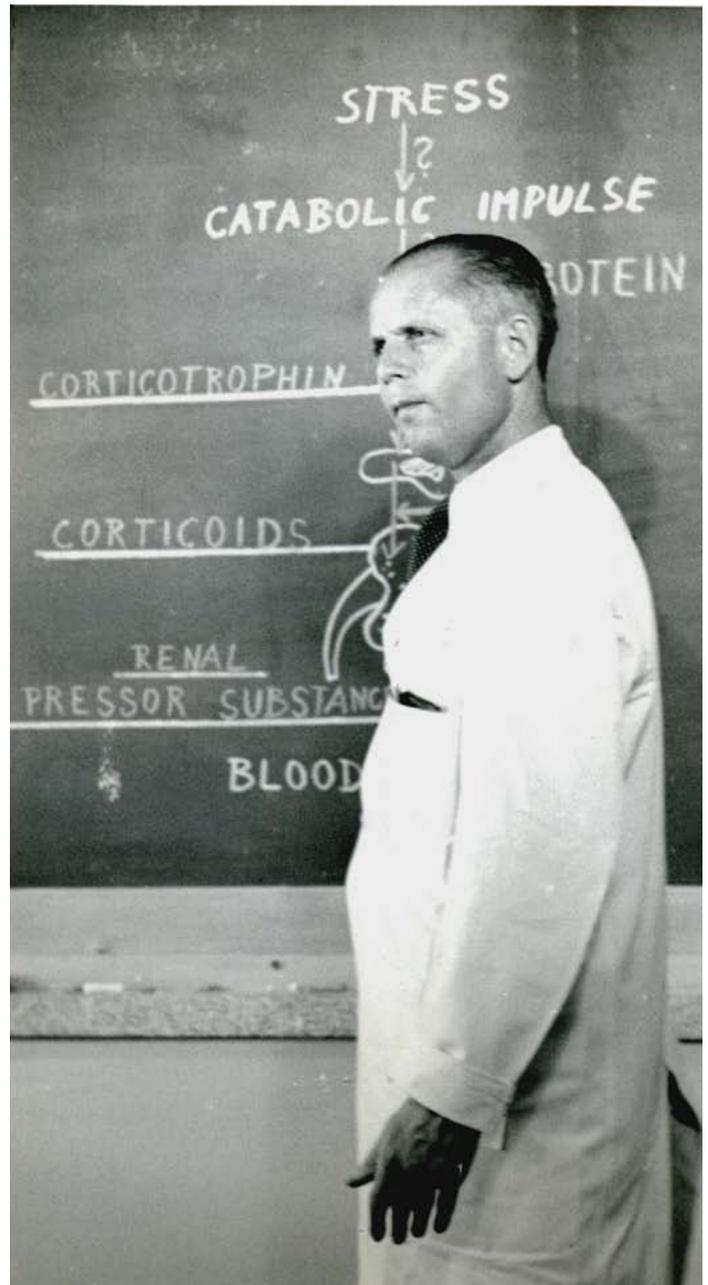
The Rockefeller Foundation's requirement that faculty terminate their private practices further separated clinical activities from academic research, which also reduced Selye's competition for funding. By 1943, he had received funding and supplies from Ciba, Des Bergers-Bismol, Merck, Smith, Kline & French, Pfizer, Hoffman-LaRoche and others to establish an independent Center at McGill that would focus on exploring steroid chemistry research. Frank W. Horner Ltd., a local pharmaceutical company, also presented him with the deed to a large Victorian house across from the McGill campus. This was to be converted into a state-of-the-art laboratory facility for the exclusive use of Selye's new Center, and to house his more than 50,000 reprints of relevant English and foreign language publications, many of which he had purchased from Dr. Biedl for \$1,000 (\$15,000 today). Selye's remarkable ability to attract funding was appreciated, but there were increas-

ing concerns about his independence from McGill University regulations, the nature of his collaboration with drug companies, and the tendency to promote his accomplishments through the media rather than the University. Several anonymous memoranda confirmed this resentment, and particularly a statement from William Hatcher, Professor of Biochemistry and Dean of Arts and Sciences. He indicated that not only was Selye's research not highly regarded in the United States by prominent authorities, but he was also "*perhaps serving the interests of drug companies under the University cloak, which is the very thing we have always tried not to do*" These internal disputes at McGill coincided with a very generous offer from the University of Montreal, which had not only developed a "magnificent new campus" on Mount Royal, but was also recruiting international researchers. However, it lacked the resources to rebuild multiple departments and decided to invest in developing at least one superlative, blue-ribbon division. Selye seemed admirably equipped to achieve this goal, since his revolutionary research results could attract funding from pharmaceutical firms, philanthropies, as well as governmental agencies.

Selye Called It Stress, But Was He Actually Describing Strain?

As a result, Selye transferred to the University of Montreal in 1945, where he rapidly established his Institute for Experimental Medicine and Surgery as one of the leading sites for studying interactions between environmental influences, endocrine function, and health. By 1949, he had

written over 450 scientific papers published in North and South America, Europe and Asia based on experiments in approximately 17,000 animals. When I arrived in 1951, there were well over two dozen other Fellows and researchers from fourteen different nations, as well as forty technicians and thirteen librarians. The *Reader's Digest* reported that his Institute was now funded by forty-five individual donors, drug companies, foundations and philan-



Dr. Selye at the chalkboard. Photo Credit: Paul J. Rosch, MD, FACP

thropies, as well as the U.S. and Canadian governments. His laboratory was reportedly “*financed almost entirely by grants from the United States Public Health Department*” with the National Heart Institute providing the bulk of his support. He had also been appointed expert consultant to the Surgeon General of the U.S. Army, possibly because his theory was considered to be the “*Greatest Concept Since Pasteur.*”

His *Textbook of Endocrinology* had become the standard text of most North American medical schools. First published in 1947, it went through five printings by the end of 1948 with a second edition in 1949. The first chapter outlined the basis of degenerative diseases by claiming that, “*the main, fatal syndromes of internal medicine (various cardio-vascular, renal, ‘rheumatic’ and old age diseases)... are probably byproducts of faulty hormonal adaptive reactions to a variety of non-hormonal pathogenic agents.*” As a result, most young physicians were already familiar with Selye’s theory and accepted it. In his Preface, the Argentinian physiologist Bernardo Houssay, who had received the 1947 Nobel Prize for discovering the role of anterior pituitary hormones on glucose metabolism, wrote that Selye’s Textbook was a “*volume of historic importance, since it is the most complete synthesis of endocrinological facts published up to date. In addition, Selye possessed ‘exceptional and probably unique conditions and abilities’ that enabled him to ‘dominate all aspects of endocrinology with equal competence;’ in addition to owning the ‘largest endocrinological library in the world,’ com-*

manding many languages, and being a ‘brilliant teacher.’” Selye’s colleague, J.S.L. Browne viewed the General Adaptation Syndrome as “*the pool of Bethesda,*” which, according to the Gospel of John, had remarkable healing qualities, with the following explanation:

It presents the picture of a basic pathologic process at work which, when it mounts to a certain magnitude, is the disease. And this idea, I may add, is completely at variance with the older views of scientific medicine. It is at variance with the ideas of compartmentalized disease, which is the central dogma of modern medical practice. Medical men who recognize the revolutionary and shattering nature of these developments realize that a great adjustment in our thinking has to be made. Here is the pool of Bethesda.

Nevertheless, several leading U.S. authorities continued to question Selye’s theories as well as the claim that he had coined the term “stress” as it was currently being used. Selye had first mentioned “stress” in a 1935 article to describe the adverse conditions to which rat placentas had been subjected. Stress did not surface again until his 1946 article “The General Adaptation Syndrome and the Diseases of Adaptation,” which was more than 100 pages and contained almost 700 references. In addition, Walter Cannon had used stress in a 1934 lecture that was published the following year (The Stress and Strains of Homeostasis) that clearly distinguished stress from strain. This was a problem that would continue to haunt Selye, who was also not aware that stress had

been used for centuries in physics to explain elasticity, the property of a material that allows it to resume its original size and shape after having been compressed or stretched by an external force. As expressed in Hooke's Law of 1658, the magnitude of stress, an external force, produces a proportional amount of strain, deformation, strain, in malleable metal. The maximum amount of stress a material can tolerate before becoming permanently deformed is its elastic limit. This ratio of stress to strain is a characteristic property of each material called the modulus of elasticity. Its value is high for steel and other rigid materials, and much lower for flexible metals like tin. Selye often complained to me that had his knowledge of English been more precise, he would have gone down in history as the father of the "strain" concept.

This also created considerable confusion when his research had to be translated into foreign languages. There was no suitable word or phrase that could convey what he meant, since he was really describing strain. In 1946, when he was asked to give

an address at the prestigious *Collège de France*, the academicians responsible for maintaining the purity of the French language struggled with this problem for several days, and subsequently decided that a new word would have to be created. Apparently, the male chauvinists prevailed, and *le stress* was born, quickly followed by *el stress, il stress, lo stress, der stress* in other European languages, and similar neologisms in Russian, Japanese, Chinese and Arabic. Stress is one of the very few words you will see preserved in English in these latter languages. As usual, "the Greeks had a word for it." Twenty-four centuries previously, Hippocrates had written that disease was not only *pathos* (suffering), but also *ponos*, (toil), as the body fought to restore normalcy. While *ponos* might have sufficed, the Greeks also settled on stress. Selye later sent me a post card from China indicating that their closest word for "stress" was Crisis, which contained two characters. In the hand-drawn diagram he included, the upper one signified Danger, and the lower represented Opportunity.



Chinese equivalent of Stress. Photo credit: Paul J. Rosch, MD, FACP

Part 2: My Professional and Personal Relationship with Selye

Getting back to my project, as previously indicated, Selye thought it was imperative for me to gain some experience with animal research by following up on the anesthetic effects of steroids. The degree of anesthesia appeared to correlate with the potency of the steroid based on studies comparing testosterone to weaker androgens. My assignment was to see if this also held true for adrenal cortical hormones, starting with deoxycorticosterone (DOC), a mineralocorticoid that causes sodium and fluid retention. However, anesthesia only resulted if the animal had very high blood levels, which meant injecting a large bolus of the steroid intravenously or intraperitoneally. After a few days of struggling to administer DOC intravenously to my rats, I adopted the intraperitoneal route, which was much easier and faster although it took more to achieve the same effect. I was able to adhere to the detailed protocol Selye had prepared, and was making some progress despite frequent interruptions to help with his numerous writing assignments.

Selye's Generosity, Alter Ego and Symbolic Shorthand System

For some reason, I enjoyed a special relationship with him, possibly because he knew that I had a Master's Degree in English literature and had taught English in college before entering medical school. I thought his

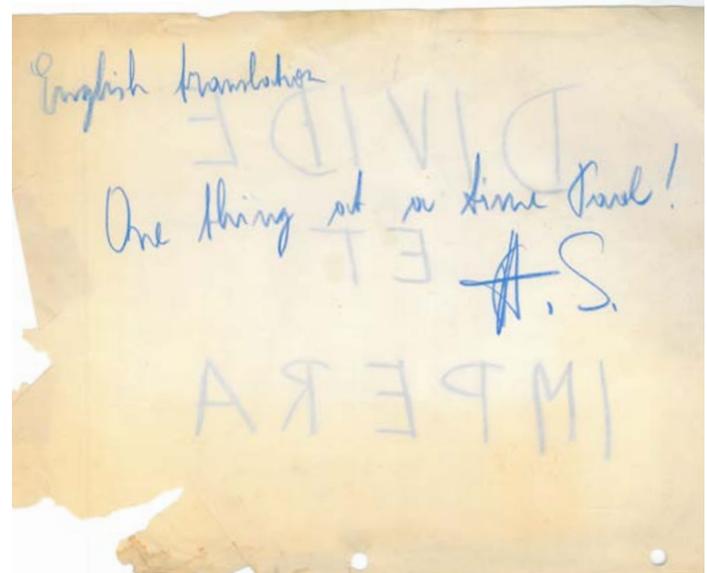
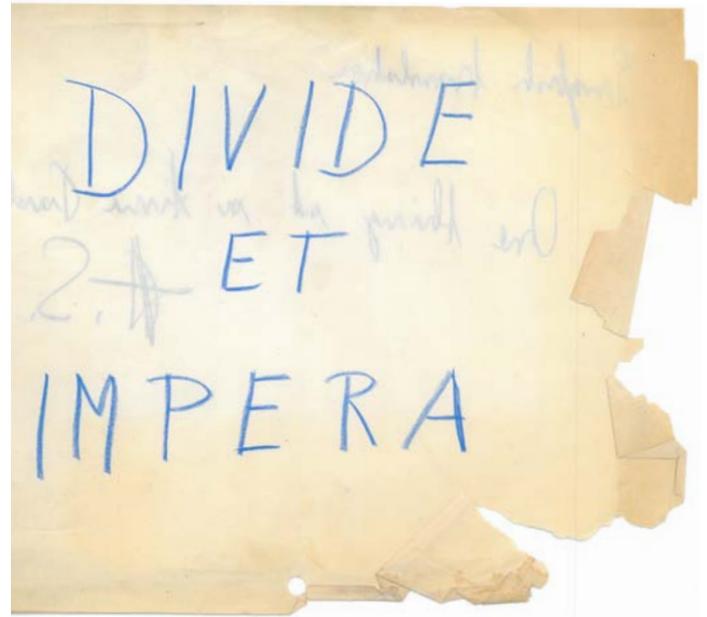
command of the language was superb, but he was still struggling with the confusion about what "stress" really signified to most people, especially doctors and scientists, and was concerned about the possible connotations of other terms and expressions that might have eluded him. Since most of his publications were now in English, he wanted to make absolutely certain they were perfect and that he had not overlooked anything. I proofed several of his manuscripts during my Fellowship and was occasionally asked to proof or critique other papers after I left to resume my medical studies.

He was extremely generous, and invited me to co-author the lead chapter "Integration of Endocrinology" for the AMA's *Textbook of Glandular Physiology and Therapy*, which consisted of contributions from 32 leading authorities on various endocrine disorders. He also asked me to conclude this by constructing a full-page color diagram showing all the endocrine glands and how they interacted. This book took almost four years to publish in order to ensure that it was accurate as well as up to date, and he was particularly pleased that our revised chapter required no changes. He had given a presentation for The New York Academy of Medicine in 1951, entitled "The Renaissance in Endocrinology" that would

be included in *Medicine and Science* along with chapters from Harold Wolff (Stress, Emotions and Bodily Disease), Norbert Wiener (Cybernetics) and other celebrities. However, this was an extemporaneous lecture, and since it was due in a week, he asked me to stop what I was doing and write something up from some notes he kept, and to add anything I deemed appropriate. When the proof of this chapter was returned for his approval, he insisted that I be listed as a full co-author by explaining that I had written a major portion of this version of his presentation. On one occasion when I had fallen asleep at my desk after a tedious session with my rats, I awoke in the morning to find a paper with the words DIVIDE ET IMPERA (Divide and Conquer) on the front in large blue letters. On the back he had written "English translation - One thing at a time, Paul - H.S."

Selye was perceived as being aloof and austere, especially at work, but a very different persona also surfaced at social occasions, where he could be very gregarious, friendly and less inhibited. Roger Guillemin's wife claimed that Selye was one of the best dancing partners she ever had. His personality and behavior also changed on those occasions when I was invited to his home for dinner, after which we chatted about everything ranging from nineteenth century English poets to criticisms of his Unified Theory. We usually had a few

glasses of "Bull's Blood," an inexpensive Hungarian red wine, along with the superb Hungarian goulash he was also fond of. He attributed these preferences to his early upbringing, although he told me that he was never quite sure of his nationality.



Divide and Conquer. Photo Credit: Paul J. Rosch, MD, FACP

While his first name was Austrian, his surname was Hungarian. He was looked down upon as an Austrian when he was in Hungary, and vice versa. When the Austro Hungarian Empire collapsed in 1918, he became Czechoslovakian without ever moving out of his house. The Czechs and the Slovaks had numerous disagreements but both of them detested the Hungarians and Austrians. After he became an international celebrity, Austria, Hungary, Czechoslovakia and Canada, all claimed him as their own and honored him in various ways. He enjoyed all of these accolades, but confided that he was most proud of his Magyar Hungarian heritage.

Our conversations were more formal when others were present and even when I was summoned to his office to discuss a paper or my project. It was a large, carpeted room and the shelves on the walls were filled with books, a few *objets d'art* and photographs of his four heroes; Claude Bernard, Louis Pasteur, Walter Cannon, and Arthur Biedl, his medical school mentor. Although I seldom saw him smoke, he also had an attractive rack of pipes on his desk, and presented me with a new meerschaum when I left as a going away gift "to remember me." His desk also had circular rotating shelves on both sides with large loose-leaf notebooks containing a list of subjects for the books and reprints on stress he had collected. He had a fetish about retaining copies of every paper or article dealing with stress, but it didn't stop there. He would request reprints of all the pertinent citations listed in an article, as well as re-

prints from all the relevant references from those articles. He repeated this process over and over, which resulted in a never-ending flood of reprints in different languages from all over the world.

As a result, he eventually accumulated a library of some 200,00 reprints and books. The problem was in deciding where and how to file this mountain of material so it could be readily retrieved. If it had to do with cold stress in hypophysectomized and/or adrenalectomized rats on a high sodium diet to determine the development of hypertension or cardiac enlargement, should he make seven copies to store separately under cold stress, hypophysectomy (removal of the pituitary), adrenalectomy, combined hypophysectomy-adrenalectomy, high sodium diet, hypertension, and cardiac hypertrophy? To overcome this problem, he had devised his own *Symbolic Shorthand System for Medicine and Physiology* (SSR) using mnemonic symbols and arrows that transcended language barriers. This allowed him to keep his library up to date since he could enter the SSR by hand under all of the relevant subject headings that were easily available in the carousels on each side of his desk. It was generally acknowledged to be a vast improvement over the conventional Cutter and Dewey decimal systems since it provided instant access of pertinent information on any stress related subject from any publication. It was later published for others to use and went through several editions until the computer made it obsolete. Although this huge library

was virtually destroyed by a fire in 1962, he was able to restore it by writing to everyone he knew requesting copies of all the reprints they had on any stress related topic. In many instances, they had originally obtained these from him during the course of their own research.

Selye's Unappreciated Surgical Skills and Dry Sense of Humor

Few people were aware of this achievement, or Selye's superb skills as an experimental surgeon. In order to trace the pathways of the response to stress, it was necessary to demonstrate the role of the pituitary and adrenal by studying the effects of removing these organs. Removing the adrenals required only an abdominal incision and a rudimentary knowledge of anatomy, but the pituitary posed a formidable problem. In humans, removing a pituitary tumor required opening the skull at a specific site, followed by five hours of painstaking surgery to go deep into the brain without damaging other vital structures. Save for Harvey Cushing and a few others, not many neurosurgeons were experienced in this transcranial approach, and morbidity and mortality rates were high. Removing a rat's pituitary without harm was equally difficult, and to obtain the dozen or more hypophysectomized but otherwise healthy animals required for each experiment would have taken weeks.

Selye devised a way to quickly remove the pituitary that was so simple and safe, all of us quickly learned how to do it on an assembly line basis. It

consisted of a rectangular block of wood with a one-inch staple partially embedded in it at the top, and a very strong rubber band to encircle and immobilize the body. To the right, we had a beaker filled with ether soaked balls of cotton, with an adjacent cage of rats to be operated on. We would put a rat in the beaker, and after a few minutes after it was anesthetized, we placed its upper teeth under the staple, pulled down on the body until the mouth was fully open, and maintained this position by snapping the rubber band over the lower portion of the body and the wooden block. We wore a flashlight on our foreheads and used magnifying spectacles, which allowed us to see clearly into the open mouth. Once we identified where the soft and hard palates met, we used a dentist's drill to make a small hole in the center of this junction that clearly revealed the pituitary and its stalk. Much like a cherry on a stem, it could easily be removed. The comatose rat was then put in an empty cage on the left to recover, a new anesthetized rat was taken from the beaker, attached to the block in the same fashion, and was replaced by another to be anesthetized in the beaker. We rarely lost an animal, and with a little practice, most of us could obtain up to six specimens in an hour. Selye told me that the renowned neurosurgeon Harvey Cushing, who had heard of this achievement, visited him to see how the procedure was performed. Today, removal of a pituitary tumor no longer involves opening the skull, but is done endoscopically through the nose or a sinus and usually takes less than 90 minutes.

In other experiments to study the role of the liver in responses to stress, it was necessary to demonstrate how removing a portion affected the metabolism of hormones. However, this had to be done in a standardized fashion without damaging other structures to obtain meaningful results.

Selye also discovered a way to accomplish this within a few minutes. Since the lobes of the rat's liver are well differentiated and readily apparent on opening the abdomen, it was simply necessary to tie a suture completely around two of them, which allowed their bloodless removal, resulting in a two-thirds partial hepatectomy that was identical for each animal. He also devised a unique technique for studying the inflammatory response to prove that hormones like cortisone reduced inflammation, while salt retaining steroids from the adrenal cortex had the opposite effect. This was much more complicated, since it required the ability to quantify how the body responded to a standard irritant. It was also necessary to accurately measure the two components of inflammation, the prompt production of fluid and the slower response of cellular tissue proliferation. He solved this in an ingenious fashion, by shaving the skin on the back of a rat, and then injecting air subcutaneously, so that a transparent sac resulted. Various irritants could then be injected and the amount of inflammatory fluid that was produced could be visualized and measured

on a daily basis by merely illuminating the sac with a flashlight. The effects of stress or injecting various steroids on fluid production were easily demonstrated, and the tissue response could be assessed by microscopic measurements of the sac wall thickness. This "granuloma pouch" technique was so useful, that one could only wonder why it had not been thought of previously.

Selye's most grandiose endeavor, which few people are aware of, was his 27-volume *Encyclopedia of Endocrinology* covering every aspect of this subject. Section I, entitled The Steroids, consisted of two huge volumes published in 1943 containing the formulae of all 728 steroids that had been identified, as well as the chemical and biological activities of each one. It was never completed, since he had to continually make additions as new compounds and their physiologic activities were constantly being discovered. Volume VII, *Tumors Of The Ovary* was published three years later but also required two mammoth books, since each was the size of a metropolitan telephone directory and a single volume would have been too heavy and unwieldy. The first included clinical descriptions, case reports, photographs of patients, X-rays, and numerous gross and microscopic illustrations of every known benign, malignant or cystic tumor of the ovary, with pertinent citations. The second consisted solely of 427 pages containing 15,000 references in eight different languages.

Selye's sense of humor was evident in both, despite their stuffy and scholarly nature. The first was:

Gratefully Dedicated to My Wife, The Motion Picture Industry and The New Yorker Magazine, without whose refreshing influence the boredom of this venture could not have been endured.

The frontispiece to the second with 15,000 references was this *New Yorker* cartoon:



Frontispiece to Volume 2. *"I have a confession to make—some of them I've only skimmed through."* Photo Credit: Richard Taylor, *"The New Yorker"* Magazine.

Selye's dry and witty sense of humor was also often unappreciated because of his formal and seemingly standoffish personality, although it is apparent in some of his books. He was frustrated by the indices of some pedantic texts, since when he looked up a reference, instead of citing a page number, he was often directed to some other heading, which on occasion would suggest looking under still another topic. As a result, the index of his 1947 *Textbook of Endocrinology* has an entry entitled, "Selye; see: what next?" If you follow this instruction, you will find, "What next; see: Selye." Another index entry was, "O.K." rule: 816. The discussion on page 816 noted that conception is unlikely to occur before or during the menstrual period. As Selye complained:

It is therefore customary to refer to the pre- and post-menstrual days as the 'safe period,' an expression which is perhaps not entirely beyond criticism, since it takes for granted that intercourse is decided upon for motives other than reproduction. This relationship between fertility and the phase of the menstrual cycle was mainly clarified by the Japanese physician Ogino and the Austrian investigator Knaus, and hence it is sometimes designated as the Ogino-Knaus or 'O.K.' rule. The writer disapproves of the use of an abbreviation in this instance.

Selye's First Annual Report on Stress and His Unified Theory of Medicine

As noted, progress with my project was interrupted by Selye's writing and editing assignments that were more

urgent. His 1950 1,000-page magnum opus *STRESS*, with 5,000 references had been widely praised, but there were also criticisms. He was anxious to respond to the latter in his forthcoming *First Annual Report on Stress* (AROS 1951), which he was able to promote vigorously, since he had become a celebrity. He had been awarded the 1950 prestigious Heberden Medal of the British Society for Rheumatology for his “research in the rheumatic diseases,” in London, after which he embarked from London on a whirlwind lecture tour that included presentations in Ireland, Holland, France, Germany, Austria, Italy, Spain, Switzerland, Portugal and Argentina, where he had an enthusiastic reception due to his friendship with their Nobel Laureate Bernardo Houssay. While in Rio de Janeiro, he also helped to organize a facility in experimental medicine and surgery modeled after his Montreal Institute.

He visited a total of sixty-seven universities and medical societies, and received honorary degrees from all five of the national universities of Argentina, the medal of the Florentine Academy of Medicine, and was named an honorary member of the National Academy of Spain. He promoted his forthcoming *First Annual Report on Stress* at all these events and on his return, he immediately started to assemble this. He had completed most of it, but was behind in fulfilling several other important obligations that had accumulated during his absence. Since the book was scheduled to be published

in two weeks, he asked me to hold off on my project to insure this, especially since there were important issues that were sensitive and had to be handled with discretion.

One of these was that the 1950 Nobel Prize in Physiology or Medicine had been awarded to Philip A. Hench, the Mayo Clinic physician who demonstrated the dramatic benefits of cortisone in rheumatoid arthritis, and Edward C. Kendall and Tadeus Reichstein, the chemists who isolated and identified the structure of cortisone. Both Kendall and Reichstein were well aware of Selye’s research in this area since they had sent him samples of DOC (desoxycorticosterone) and cortisone to use in his rat experiments. Selye frequently communicated with them as well as Hench, and sent them reprints of his papers. Although Hench’s 31-page Nobel acceptance speech contained 113 references, none of these included any of Selye’s previous pioneering publications a decade earlier on the anti-inflammatory effect of cortisone, or others specifically devoted to rheumatoid arthritis in *Lancet* and the *British Medical Journal*. Similarly, the Nobel Lectures of Kendall and Reichstein, which also discussed the anti-inflammatory effects of glucocorticoids, made no reference to Selye. This, despite the fact that Selye was nominated for the Nobel Prize in Physiology or Medicine, including twice in 1950 and fifteen other times between 1949 and 1953 for his “work on endocrinology and the adaptation syndrome,” for his contributions to

the “isolation of steroid hormones,” and for his formulation of “stress reactions.” And, he had also been awarded the 1950 Heberden medal for these achievements. Moreover, Kendall, who received the Heberden Medal in 1951, not only made no mention of this, but specifically dismissed Selye’s adaptation syndrome as an explanation for the role of cortisone in arthritis in his acceptance speech by stating that “*The nature of this agent is unknown, but I agree with Professors Pickering and Meiklejohn that the hypothesis of the adaptation syndrome of Selye is not acceptable.*”

Selye was obviously disappointed that he was not included as a recipient of the 1950 Nobel Award, especially since Morris Fishbein, the powerful editor of the *Journal of the American Medical Association* had publicly gone on record as saying Selye was an “odds-on favorite.” He was hurt even more by the failure of the recipients to mention or cite his contributions and their disparagement of his theory. However, it was necessary to comment on the 1950 Nobel Prize, and he did not want to seem like “sour grapes” by complaining about how he had been treated. After careful consideration, none of the above was mentioned. Instead, we had a paragraph congratulating the three Nobel Prize recipients on their achievements and thanking them for inspiring him and stimulating his own relevant research. Selye was also insistent that we include all negative commentary so that this first report did not seem biased. As a result, I inserted the comments of F. F. Roberts, a British

physician, who pointed out that many of the diseases and pathology Selye attributed to the General Adaptation Syndrome could also be caused by exposure to x rays, and asked, “Are we to conclude that x rays act not directly but through *the intermediation of the hypothalamus-hypophysis system?*” More importantly, using verbatim citations from Selye’s papers, one would conclude that “*Stress, in addition to being itself, was also the cause of itself, and the result of itself.*”

The First Annual Report on Stress was completed on time and Selye and I celebrated with champagne. I was also listed in the dedication along with the other Fellows, but was the only one from the U.S. As with his *Textbook of Endocrinology and STRESS*, it was published by Acta Inc., a Montreal company that he owned and controlled. Ten thousand books were printed with the same rich red buckram leather binding as *STRESS*, and despite the \$14.00 cost (about \$140 today), they sold out quickly due to the heightened interest Selye had created here and abroad. In point of fact, the *First Annual Report on Stress* outsold all other scientific books in 1951 and 1952 save for the Kinsey Reports on sexual behavior. It also presented the rudiments of his proposed Unified Theory of Medicine as follows:

Whenever a large number of facts accumulates concerning any branch of knowledge, the human mind feels the need for some unifying concept with which to correlate them. Such integration is not only artistically satisfying, by



Celebrating the completion of the 1951 First Annual Report on Stress with some Champagne. Photo Credit: Paul J. Rosch, MD, FACP

bringing harmony in what appeared to be discord, but also practically useful. When surveyed from a great elevation some details in the landscape become hazy, or even invisible; yet, it is only from there that we can see the field as a whole in order to establish where more detailed exploration of the ground would be most helpful for its further development.

He provided additional details in his 1952 *The Story of the Adaptation Syndrome*, an informal series of illustrated lectures, and in subsequent Annual Reports on Stress.

In January 1953, he sent me a draft of what he was planning to include about this in that year's *Third Annual Report on Stress*. He asked me to critique this as an adversary and "not to pull any punches." I found much of it difficult to comprehend, especially the six or more complicated illustrations and diagrams in his concluding "Sketch for a Unified Theory of Medicine." It was obvious that he had spent a great deal of time on this as he considered this theory to be extremely important and it was awkward for me to be completely candid. I made some grammatical corrections and suggestions

in a four-page response, which also recommended including a glossary to explain some of his abbreviations and acronyms that many readers would find obscure. In addition, I felt he should consider publishing it in a journal that would reach a larger audience of interested researchers and scientists, and listed some possibilities. He thanked me and indicated he would consider my suggestions along with others he had received. It was subsequently published in an obscure journal I had never heard of with a glossary and other embellishments, but most reviewers still found it difficult to comprehend.



Autographed photo presented to me at the end of my Fellowship. Photo Credit: Paul J. Rosch, MD, FACP

Mounting Criticisms of Selye's Theories

Most criticisms dealt with his reaction theory, which conceptualized all life as a series of adaptive reactions. He proposed that the basic building blocks of life were not molecules, but what he termed “reactons,” subcellular but supramolecular structures that were the “*smallest biologic target which can still respond selectively to stimulation.*” Reactons, not cells or molecules, were the elementary keys of living matter, and all the manifestations of healthy and pathologic conditions depended on when, where, and how many groups of reactons were stressed and how much “adaptation energy” they possessed. This referred to the energy available to allow adaptation to stressors that threatened the status quo. He suggested that disease, health and life itself were all determined by the organism’s available adaptation energy.

His rationale was that since stress contributed to so many diseases and could affect all organs and tissues, it was tempting to propose it as the basis for his Unified Theory of Medicine. He did this very effectively in books for lay audiences, particularly his 1956 *The Stress of Life*. It was extremely popular in North America, was translated into Afrikaans, Danish, Czech, French, German, Italian, Polish, Russian, Portuguese, Serbo-Croat, Slovak, Spanish and Swedish, and quickly rose on best-seller lists throughout the western world. By the end of 1958, *The Stress of Life* had sold out five editions that allowed him to convince the public of the validity of his

stress theory by providing supportive clinical studies and compelling diagrams that made complex topics easy to comprehend. Selye was hailed as “The Einstein of Medicine” and “The American Pasteur.” Even Einstein sent his congratulations, comparing Selye’s Unified Theory of Medicine with his own efforts toward a unified field theory of the physical world.

Many more had reservations. As Roger Guillemin, who shared a 1977 Nobel Prize for discovering the endorphins explained:

What was so appealing about it was its intellectual simplicity and the fact that it addressed itself to sociologically important diseases, which were apparently reproduced in the laboratory with great ease. Few, if not none at all, of these speculations have survived studies which were more extensive and critical than those of Selye’s over the next 20 years or so.

Sandor Szabo, another Fellow who also admired Selye, noted:

Since his experimental work was heavily descriptive, often not analytical enough by modern criteria, his students often learned not only the creative aspects of research and how to explore those routes, but also what not to do after becoming independent.

The comprehensive 1953 Symposium on Stress conducted at Walter Reed Army Medical Center was chaired by John C. Whitehorn, Chair of Psychiatry at Johns Hopkins, who warned,

Stress is a rather broad conceptual term—like a tennis racket—with which we can manage to bat about, like tennis balls, some other concepts which are concerned with the more sharply definable reaction processes...We may be able to get some use out of the term stress even if it is left vague and not very clearly defined, provided we succeed in specifying fairly sharply some of the aspects of the biological reactions to stress, in which I think we are actually more deeply interested.

Rachmiel Levine, Chair of the Department of Medicine at Chicago’s Michael Reese Hospital, focused his criticism on the specific and diverse responses to stress rather than alleged general or nonspecific responses.

We tend to forget the specific changes which tissues and organs in the body as a whole undergo as a result of specific stimuli, in favor of a generalization which we have termed and accepted as “the” stress reaction...Such generalization has a most inviting ring. It has stimulated a good deal of valuable work, both in the experimental and in the clinical domain. However, has too much attention been lavished on the non-specific generalized reactions to a variety of stimuli, at the expense of looking for specific responses which characterize the reactions to a particular stimulus, and which may serve to distinguish them?

Curt Richter, the distinguished psychobiologist from Johns Hopkins, argued that there are also behavioral adaptations the organism can make when it attempts to counteract stressors and maintain homeostasis based on his animal studies. These and criticisms from the Mayo Clinic's Dwight Ingle and other authorities are covered in depth in Tulley Long's comprehensive review of this Symposium.

Selye was understandably upset by these and other attacks, but took comfort in the knowledge that his heroes, Claude Bernard and Louis Pasteur and others who proposed radical changes in medicine were severely criticized initially. However, after their research and hypotheses were confirmed, they were celebrated and honored.

I must admit that here disagreements were many and sometimes formulated with great violence and emotion Being quite emotional myself, I cannot claim to have registered such attacks with complete equanimity, but I tried to find consolation in the thoughts expressed almost a hundred years ago, by the father of experimental medicine: 'As all those who have had the joy of introducing into science unexpected facts or new ideas, I have been, and still am, the object of much criticism'.

The concluding quotation is from Claude Bernard's *Introduction to the Study of Experimental Medicine*. Selye subsequently reiterated this as follows:

When Pasteur proclaimed that infectious diseases were due to germs, when Clemens P. Pirquet and Charles R. Richet discovered allergy, the literature was full of biting, hostile remarks, in which those who did not have the originality of creating - or even understanding - new concepts in medicine, tried to compensate by displaying their wit.

Nevertheless, it was difficult to counter numerous later attacks that were based on solid scientific experiments by leading authorities. In 1958, I contributed a chapter to *Modern Trends in Endocrinology* on "The Growth And Development Of The Stress Concept And Its Significance In Clinical Medicine." The editor indicated he had initially asked Dr. Selye to provide this, but Selye was overwhelmed with other obligations and suggested they contact me. So much additional information had accumulated in the seven years since I had been at the Institute that covering everything proved to be a formidable task, especially since much of this consisted of additional criticisms of Selye and his theories. It was necessary for me to include some of these, such as Frank Engel's assertion that glucocorticoids did not cause disease, but merely had to be present. Engel, who headed the department of Endocrinology at Duke had previously stated, "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, Dwight Ingle

at the Mayo Clinic had demonstrated 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, since they acted as catalysts. He referred to this as 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. He used the analogy of putting grease on an axle wheel to explain the role of hormones in the response to stress. Without grease (corticoids), 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 related diseases were modulated by hormone levels that were largely determined by pituitary-adrenal axis activities. Fortunately, Selye was not offended by my references to these criticisms since he recognized that I was simply fulfilling my assignment.

Altruistic Egoism and Conflicts with Psychosomatic Medicine

The controversy over his theories continued since Selye now proposed that stress caused or influenced the course of all diseases. In addition, he had discovered a novel approach to understanding the “mosaic of life in health and disease,” that supported his Unified Theory of Medicine. The crux of this was that each of us has a limited amount of “adaptation energy” to buffer stress that is gradually reduced by the “wear and tear of life.” This eventually resulted not only in Diseases of Adaptation, but also premature aging and death. “Every stress leaves an indelible scar, and the organism pays for its survival after a stressful situation by becoming a little older.” It therefore followed that we could enjoy longer and much healthier lives by minimizing this progressive depletion of adaptation energy, and the best way to accomplish this was by “living wisely in accordance with natural laws.” This would allow us to “derive some general philosophic lesson, some natural rules of conduct in the permanent fight between altruistic and egotistic tendencies, which account for most of the stress in interpersonal relations.” He believed the most important lesson we could learn from Nature was altruistic egoism, since “by helping others (altruism) and “earning their love,” while at the same time recognizing our own needs and enhancing ourselves (egoism), we can enjoy a rewarding lifestyle free of disabling stress, especially since we have a natural biological drive for self-preservation.”

Selye's concept of altruistic egoism led him to suggest that the Golden Rule "Do unto others as you would have them do unto you," as well as "Thou shalt love thy neighbor as thyself" should be revised, as follows:

'Love thy neighbor as thyself' is a command filled with wisdom, but as originally expressed it is incompatible with biologic laws; no one needs to develop an inferiority complex if he cannot love all his fellow men on command. Neither should we feel guilty if we work for treasures that can be stored to ensure our future homeostasis. Hoarding is a vitally important biologic instinct that we share with animals such as ants, squirrels and beavers.

He suggested that it would be preferable to advise people to "Earn thy neighbor's love," since this would be more apt to promote altruistic egoism since it instilled feelings of appreciation, and especially gratitude, in both the recipient and donor. Selye considered gratitude to be the healthiest emotion because he believed it conserved adaptation energy more than any other attitude and would therefore reduce stress related complaints and diseases. He claimed his philosophy was derived from natural laws and was shared "by all living beings." There were examples of altruistic egoism in mammals, birds and fish, and even "multi-cellular organisms, in which individual cells prioritize their own survival for the good of the entire organism."

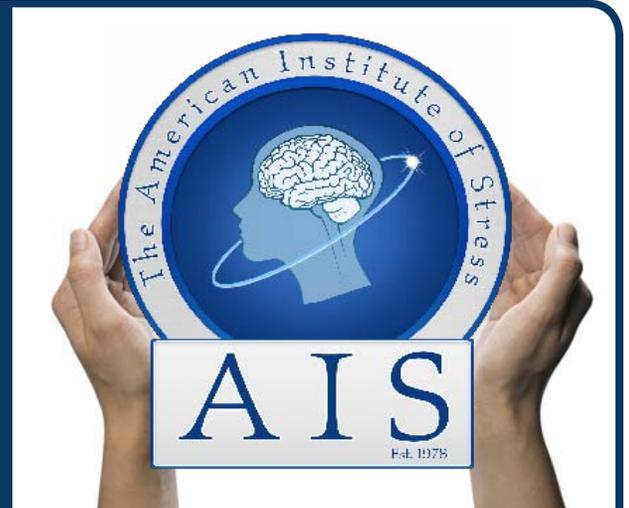
Consequently, it seemed quite plausible that:

The same principles must govern cooperation between entire nations: just as a person's health depends on the harmonious conduct of the organs within his body, so must the relations between individual people, and by extension between the members of families, tribes, and nations, be harmonized by the emotions and impulses of altruistic egotism that automatically ensure peaceful cooperation and remove all motives for revolutions and wars.

Most physicians did not agree that Selye had linked hormonal stress responses to psychosomatic medicine, and many felt he had actually created a schism. His stature and the popularity of his books actually contributed to efforts to redefine "psychosomatic diseases" as "stress diseases." For example, "Stress is a short, positive and provocative word which we believe would serve us better than the familiar term psychosomatic." Some also combined these by referring to "psychosocial stress." The problem was that this was difficult to define, much less measure, since stress had become an ambiguous abstraction and a metaphor for anxiety and tension. Stress was also often a euphemism for alcoholism, substance abuse and other personality or mental disorders, as well as a synonym for strain, anxiety or exhaustion. This also made it difficult to determine if stress was an internal, external, physical or emotional phenomenon, as it could apparently be all of these.

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The term “psychosomatic” was introduced into American medicine by Flanders Dunbar in her more than 600-page scholarly treatise, *Emotions and Bodily Changes: A Survey of Literature on Psychosomatic Interrelationships, 1910-1933*. As indicated in the subtitle, it was a comprehensive review of the literature from 1910–1993 that provided evidence of the diseases and somatic perturbations that could result from emotional stress and strain. She also emphasized the multidisciplinary nature of psychosomatic medicine by drawing together mind/body research from psychiatry, neurology and physiology. There was no reference to Selye in her magnum opus, since this was published a year before his first description of what he would later call stress.

It was Dunbar’s training in psychoanalysis that had the greatest influence on her philosophy of medicine. Talk therapy that focused on each patient’s unique history could uncover subconscious or suppressed memories that were the likely cause of their neuroses and complaints. Based on her emphasis on individual personality, she was subsequently able to correlate different personality types with hypertension, coronary heart disease, rheumatoid arthritis, diabetes, and even fractures in patients who were accident prone. Some of these were also Selye’s Adaptation, but did not appear to be mediated by hormonal responses. Dunbar recognized that many people with the same personality type were quite healthy, but insisted that disease could not be comprehended

without analyzing the patient. She later went on to found the American Psychosomatic Society in 1942 and was the first editor of its journal. I met her shortly after I entered practice since she was interested in Selye and attended a talk I had been asked to give on “Stress, Behavior and Coronary Disease.” She invited me to come to her office to discuss how I might treat some of her patients with angina, asthma and rheumatoid arthritis based on my knowledge of stress. It was a very stimulating meeting and we became good friends. She subsequently referred several patients to me and asked me to contribute a chapter on Regulators of Homeostasis for her 1959 book *Psychiatry In the Medical Specialties*, which I co-authored with her.

Franz Alexander, another psychosomatic medicine pioneer, emphasized the need to understand the mechanisms that explained how various personalities caused different diseases. He focused on emotional states and how patients adjusted to environmental changes rather than Dunbar’s personality types or Selye’s preoccupation with stress. With respect to Dunbar’s profile of the coronary disease prone individual, who had most of the traits that would later be called Type A behavior, he warned:

It might well be that a certain type of living, certain types of mental exertion, create somatic conditions conducive to certain progressive changes in the vascular system resulting ultimately in coronary disease. The true correla-

tion may be not between personality make-up and coronary disease but between the mode of living and disease.

John Mason, who was doing his “executive monkey” studies at Walter Reed, was one of Selye’s severest critics. He objected to Selye’s repeated references to emotional factors in these experiments as “mere nervous stimuli,” and repeatedly challenged Selye to acknowledge the importance of psychological factors in stress and disease as well as other flaws in his theory. A half dozen of his criticisms included: 1) Stress has too many ambiguous meanings and Selye should have coined a new word rather than selecting an existing one; 2) stress is an abstraction since it has no real independent existence; 3) stress has been applied to both the agent and its consequences; 4) the stress response cannot be both specific as well as nonspecific; 5) there have been few attempts to arrive at a consensus definition and operationalization for the term stress; 6) the stress definition and General Adaptation Syndrome fail to consider cognition, perception, or how the individual interprets the stimulus. These comments appeared in the June 1975 Journal of Human Stress, and were followed by Selye’s rebuttal paper “Confusion and Controversy in the Stress Field,” which explained:

An attempt is made to further clarify present areas of controversy in the stress field, in response to a two-part article by Dr. John W. Mason which concludes in this issue of the Journal of Human Stress. The author tries to

elucidate each source of confusion enumerated by Dr. Mason. The continued use of the word ‘stress’ for the nonspecific response to any demand is deemed most desirable. The once vague term can now be applied in a well-defined sense and is accepted in all foreign languages as well, including those in which no such word existed previously in any sense. Subdivision of the stress concept has become necessary as more recent work has led to such notions as ‘eustress,’ ‘distress,’ ‘systemic stress’ and ‘local stress.’ Confusion between stress as both an agent and a result can be avoided only by the distinction between ‘stress’ and ‘stressor.’ It is explained that the stress syndrome is - by definition - nonspecific in its causation. However, depending upon conditioning factors, which can selectively influence the reactivity of certain organs, the same stressor can elicit different manifestations in different individuals.

This explanation did not address the significance of psychological stress and other controversial issues. In addition, the FDA had approved meprobramate (Miltown, Equanil) for the short-term treatment of anxiety in 1956, and the response was overwhelming. Although there had been no advertising, by 1957, “Americans had filled 36 million prescriptions for Miltown, more than a billion pills had been manufactured, and these so-called ‘peace pills’ accounted for one third of all prescriptions” The ability of a pill to rapidly reduce anxiety and tensions blurred the distinction between psychological anxiety and physiological stress.

Stress was no longer a syndrome in laboratory rats subjected to uncontrollable and often life-threatening challenges, but was increasingly viewed as an interaction between people and their environment that could be controlled by numerous methods.

The term stress has become a rallying cry and the anti-stress industry has become immense. The current vogue of stress-reduction clinics, physical fitness classes, yoga sessions, meditation lectures, various forms of psychotherapy, prescription drugs, and so forth - each with its unique view of stress and coping - is ever expanding.

This was written well over 30 years ago, and interest in stress and the market for stress reduction techniques has escalated since then. Selye recognized that his definition of stress had little to do with its use by the public as well as physicians, and explained:

It was only gradually, through habit rather than logic, that the term stress, employed in my sense, slipped into common usage, as the concept itself became a popular subject for research. There were numerous other criticisms about his Diseases of Adaption and Unified Theory of Medicine that Selye could not refute, and both gradually faded into oblivion

Selye's Promotion of Cigarettes, Cognitive Decline and Paranoia

In 1964, the US Surgeon General released a Report on Smoking and Health delineating the scientific evidence linking tobacco smoking with

lung cancer, cardiovascular disease, bronchitis, emphysema and psychosocial problems. As a result, public health campaigns were initiated in the United State and Canada to impose regulations on tobacco sales as well as cigarette advertisements. The tobacco industry countered by claiming the lack of proof of any causal relationship between smoking and disease.

They pointed out that the Surgeon General's report had listed various factors that encouraged smoking, such as type A coronary prone behavior and high levels of anxiety and stress, which also increased the risk of heart attacks and cardiovascular disease. And since the report also noted cigarettes helped many to alleviate stress, the emphasis should be on reducing stress rather than smoking. Nobody could do this better than Hans Selye, since in 1959, he had been liberally compensated for preparing two memoranda on the relationships between cigarettes and lung cancer for a prominent New York law firm. It emphasized that a statistical correlation did not prove a causal effect and that cigarettes offered benefits that might outweigh their risks

The CTR (Council for Tobacco Research), the purportedly independent research wing of the powerful tobacco industry trade association, obtained these memos, and in 1966, key officials flew to Montreal to discuss with Selye the possibility of recruiting him as an expert witness and spokesperson. Selye was very receptive to their public relations predicament and pointed out that even though there

was likely some link between smoking and cancer, this was not much of an indictment against cigarettes since *“you can produce cancer with anything... and almost anything will be toxic to some people under some circumstances.”* He also noted that experiments showing cigarette smoke to induce cancer in animals do not establish a strong causative relationship, just as experiments showing that alcohol was harmful for dogs did not establish that it was also a danger to human health. More importantly, he emphasized that there were benefits to smoking that could outweigh any risks, such as *“a very stressful individual is better off for smoking because, if the person did not smoke, he ‘might pop a blood vessel.’”* In such a case, cigarette smoking was *“a reasonable risk to take,”* compared to the consequences of further increased stress, and that *“there would be no great problem in convincing the public of the importance of stress in disease because the public already has been conditioned to accepting it.”* (The above and subsequent quotes and details are referenced in Burrows’ comprehensive review.)

Selye agreed to write an updated memorandum containing these and other supportive comments within a month, for which he was paid \$5,000 (about \$35,600 today). He also agreed to serve as a spokesperson, write supportive articles, and testify at Congressional hearings against regulatory efforts to restrict smoking if he was adequately compensated. What he proposed was \$100,000 per year for three years (\$650,000 per

year today) with the CTR and Canadian Tobacco Manufacturers Council splitting the bill, which they agreed to. In subsequent testimony before the Canadian Senate, Selye stated that *“man will always seek gratifying relief from stress,”* and warned that *“our responsibility is not to lock up all avenues that may be dangerous, but to determine as objectively as possible which are the most and which are the least dangerous in proportion to their benefits.”* He claimed that banning smoking could lead to choosing even riskier diversions, since those fearful of cancer from smoking cigarettes might turn to illegal drugs instead. Because every person is different in their response to stress, they also gain relief from very different diversions and *“did not think that government should mix into the private predilections of individual citizens... if somebody wants to smoke, despite the fact that he knows what dangers may be or may not be involved, that is his private business.”* And since cigarette smoke was no more harmful than industrial smog or automotive exhaust, he claimed *“singling out of this particular activity seems to me not to be based on logic.”*

Between 1969 and 1974, Selye also received \$50,000 annually (about \$280,000 per year today) for two research projects on *“Cross-Resistance and Beneficial Effects of Deviation,”* and *“Stress and Relief from Stress,”* that resulted in two scholarly publications on behalf of the CTR, and four others for the Canadian Tobacco Manufacturers Council. In 1972, the CTR conducted a *“Conference*

on the Motivational Mechanisms of Cigarette Smoking” in St. Maarten that was funded by seven major tobacco companies. They invited experts in the life, behavioral and social sciences to mount “*a renewed scientific attack upon a question that in recent years has not been accorded the priority that it rightfully merits.*” In Selye’s keynote address “Smoking as a Defensive Response to the Effects of Stress” he argued that depriving cigarettes from smokers could cause them “*to overeat, to drink, to drive on polluted and crowded highways, to fret and bite their fingernails to avoid boredom and to give vent to pent-up energy. Man must weigh the pros and cons of any diversional activity; he must undertake his own benefit/risk analysis, and act accordingly.*” He claimed that therapies like insulin shock, metrazol shock, electroshock, or extreme hot or cold baths were unpleasant or even highly dangerous, but were used because they obtained the best results. Since there was good evidence that tobacco industry lawyers helped with the wording and content of some of these claims, Selye’s comments were cited as an example of racketeering in the successful anti-racketeering case brought by the US Department of Justice against seven tobacco companies in 2009.

I had tried to politely warn Selye that these statements could damage his reputation and credibility, since there was now overwhelming evidence of the dangers of cigarettes and nothing to support any presumed benefits. He did not dis-

pute this, but explained that he desperately needed funding and some sacrifices were necessary. In addition, he was entitled to his opinion and did not care if I or others had opposing views. During the St. Maarten conference, Selye learned that the position of Scientific Director of CTR was vacant, and he told senior officials that he intended to soon retire from the University of Montreal and was interested in this since he was looking for a new position in the United States. However, they saw no advantage in this over their existing arrangement. After Selye retired, he applied to CTR in 1976 to help fund his newly formed International Institute of Stress. It was denied because “*his budget was more than twice the necessary amount, and his request was inspired by hubris rather than genuine need.*” In addition, it was no longer wise to invest in his work as he seemed “*to be showing some signs of advancing senility, and had contributed very little new to the study of stress over the past 10 or 15 years.*”

I had also noted some cognitive decline and personality changes. In addition to his 1975 International Institute of Stress, he created the Hans Selye Foundation in 1976 and the Canadian Institute of Stress in 1978 to preserve and protect his status as the preeminent expert on stress. He had hired various individuals to obtain funds for these organizations and suspected that they were diverting large amounts of what was received for their personal use. I received several calls complaining about this with frantic and urgent requests for me to come to Montreal

to evaluate what he had uncovered. I finally acquiesced, and was appalled at his changed living conditions. The first floor of his spacious Milton Street home across from McGill campus was crammed with his massive library of reprints and books, save for the kitchen and a small dining area. So was most of the second floor, except for a room he had converted into an office, and a small bedroom that he shared with his secretary, Louise Drevet, whom he later married. Although he was now undoubtedly a millionaire due to the huge fees he charged for lectures as well as royalties from his numerous books, he had developed a paranoid attitude and a preoccupation with money. I examined the incriminating documents he had assembled and could understand why he was so upset. I was also reminded of the old saying, "There is nothing worse than being paranoid and being right." I suggested he contact a lawyer, since in establishing these organizations, no provisions had been made for him to fire key officers, and I suspected it would be difficult for him to do this as it did not appear that they had violated their contracts.

The Second International Symposium on Stress and Our Breakup

Our close relationship really disintegrated when I was asked to give a keynote address at the 1979 Second International Symposium on Stress in Monte Carlo organized by the Hans Selye Foundation. I was to receive what would be the equivalent of \$5,000 today, and First Class Airfare and accommodations for my wife and myself. Other speakers included

Nobel Laureates Linus Pauling, Jonas Salk, Roger Guillemin, Christian de Duve, and Hans Krebs as well as AIS Fellows. There were also several speakers who were neither scientists nor researchers, but represented companies that sold various stress reduction products and services. In addition, the symposium was co-sponsored and funded by Dr. Alfred Sapse's International Health Resorts, which had developed the Kronas formula. This consisted of a combination of vitamins, minerals, liver extract and a local anesthetic that was administered by injection for two weeks, and then orally for a year. Kronas purportedly not only reduced stress, but prolonged life and "had FDA approval with a national drug code number."

However, I checked with the FDA and was told that there was no such approval and that national drug code numbering merely monitors the sales of all drugs and does not imply any approval or clearance. I also learned that the anesthetic was procaine, which Sapse, an unlicensed Romanian ophthalmologist, had previously included in his Gerovital, another anti-aging drug that was later banned. What was worse was that the company's literature, brochures and press releases were replete with Selye's endorsements for the \$3,000 year-long Kronas executive health program (\$10,500 today) and that he was being paid over \$100,000 (\$350,000 today) for this, as well as serving as the Scientific Director of Kronas.

The conference was also supported and held under the auspices of the royal family of Monaco, that now included Princess Grace Kelly, and there were other inducements, such as a color illustration of the event created and signed by Salvador Dali. As can be seen, it shows bloodless faces and skulls with a mountainous landscape and a setting sun in the background. The title stress is scribbled in the foreground. There was also a 24K gold plated medallion which reproduced Dali's rendition of stress on one side, and referred to this event as "The 2nd International Symposium on the Management of Stress," listing the dates and venue. This implied that it was an ongoing event despite the lack of any evidence that there had been any previous symposium. Both sides indicated The Hans Selye Foundation Montreal, Canada and International Health Resorts, Inc. Beverly Hills, CA U.S.A. as sponsors.

The Aims of this 2nd International Symposium on Stress were purportedly:

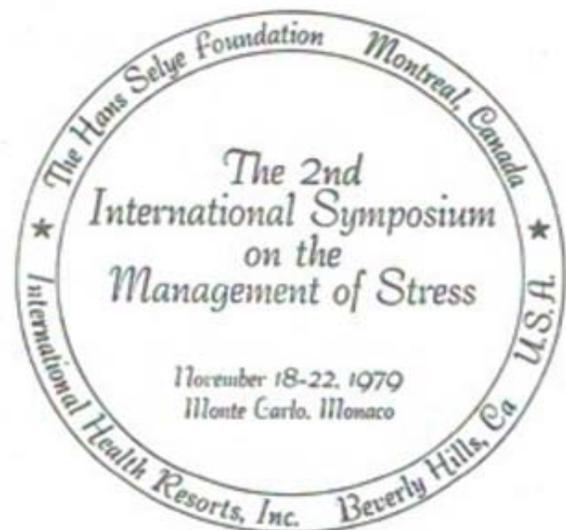
1. To draw attention to the inability of many people in our society to cope with stress.
2. To describe ways of increasing resistance to stress or reducing its harmful effects in our daily lives.
3. To present stress management techniques as a valuable type of preventive medicine.

I doubted that these issues fell within the areas of expertise of the various celebrities listed and it appeared

to me that the purpose of this symposium was to imply their endorsement of Sapse's Kronas therapy. I refused to participate and explained why in a letter to Selye, as well as Joel Elkes, Herbert Benson, Nelson Hender, John Laragh, Kenneth Greenspan and Norman Cousins, American Institute of Stress Board members who had also been listed as speakers. It expressed my concerns that



A Salvador Dali 24K Gold Plated Medallion



Salvadore Dali 24K Gold Medallion for Congress. Photo Credit: Paul J. Rosch, MD, FACP

participation implied an endorsement of Sapse's Kronas formula and "executive health" program, as well as other stress reduction products and services about which we knew nothing. It seemed likely that arrangements would be made to have photos taken of these vendors with Nobel Laureates and other celebrities to imply their endorsement. Other questions about the professionalism and integrity of this event surfaced in advertisements, such as one in the *Wall Street Journal* indicating that registrants would receive "AMA accreditation for CME credits." This claim was not possible since conferences are never accredited unless they are developed by Institutions that are authorized to do this or are conducted under their auspices. All of the American Institute of Stress speakers subsequently decided not to participate in this event. *Medical Tribune*, a highly respected weekly newsletter that reached over a million physicians and scientists in 20 countries and seven languages, subsequently devoted a full-page article discussing this entitled, "Monaco Stress Meeting a 'Promotion' Charge Stay-at-Homes," which included photos and the Salvatore Dali portrait of stress.

Selye was furious, and I received phone calls and letters from Jonas Salk and Roger Guillemin asking me to change my decision. They agreed that it was an unfortunate situation, but their consensus was that Selye's reputation was too great for this Congress to do any lasting damage. Moreover, he would be hurt much more by my refusal to participate and acting

like a "dog in the manger" by encouraging AIS Fellows to do the same. I pointed out that I had never suggested this, but merely listed the reasons for my refusal. Others had made their own decisions, although as detailed in the *Medical Tribune* article, some cited poor health and other excuses to avoid antagonizing Selye. I indicated that I might reconsider if the conference was clearly separated with a scientific session followed by another that dealt with various commercial interests. Salk and Guillemin felt this was a reasonable solution, but later informed me that even if Selye agreed, Sapse, who had the final say, refused to consider this. Salk was married to Picasso's widow, who was very friendly with Dali, and most likely had asked him to create something special for the symposium. Guillemin told me that his participation in this event also allowed him and his wife to spend some time in Dijon, the region in France where he had been born and raised, so both had other agendas.

Dr. William Barclay, editor in chief of the *Journal of the American Medical Association*, had been invited so he could report on and possibly promote this star-studded event. He was very charitable when he summarized it as "disappointing" in his subsequent editorial.

MONACO, a tiny principality that mixes a certain medieval charm with 20th-century avarice, was the site of the Second International Symposium on Stress held in November 1979.



STRESS

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Invitation

Salvatore Dali Portrait of Stress. Photo Credit: Paul J. Rosch, MD, FACP

Organized in honor of Hans Selye, MD, and planned for a large attendance, it attracted a disappointingly small group of approximately 200. Perhaps a few famous experts including several Nobel Laureates, speaking on a subject in which they had no special expertise could not compensate for a group of relatively anonymous speakers addressing subjects they apparently knew a lot about. In any event, it was a small, and in my judgment, a disappointed audience.

Other reviewers and registrants, who had not been hired by Sapse, called it a disaster and a fiasco. The Nobel Laureates and other prominent speakers, including Selye, had nothing new to offer, and others promoting Kronos and other stress reducing therapies had no scientific support for their claims. Barclay went on to confirm that the real purpose of the symposium was a lengthy description of the Kronos stress management program and emphasized *“the impracticality of this approach for treating the millions of poor souls stressed by the hundreds of stressful circumstances that daily beat on their physical and psychic selves.”* He also noted that the Third International Symposium on Stress was scheduled for Tokyo in October 1980, but like the First International Symposium, this never took place. Sapse was subsequently sentenced to 17 years in federal prison and ordered to pay over \$1 million in restitution for a subsequent fraud involving stem

cell injections to retard aging. In the court proceedings, the judge called him a “modern Dr. Frankenstein.”

Selye never forgave me and I never had any contact with him after that. It did not appear that he had any friends or close relationships other than a few dedicated employees who had assisted with his research and activities. His first wife, Frances Rebecca Love, resented the lack of attention due to his preoccupation with work, and divorced him after the birth of their daughter Katherine. The decree included abolishing Katherine’s use of her father’s surname. He had four children with his second wife, Gabrielle Grant, a scientist, but after 28 years, he left her. There was no divorce since it was determined that they had never been legally married. He did not have any children with his third wife, Louise Drevet. To the best of my knowledge, his children never visited him and he rarely contacted them. I was told that he was rather lonely and bitter when he died from a heart attack in 1982. The year before his death, Selye had been audited by the Canadian Revenue department because of discrepancies and omissions in his tax returns. They searched his house and university office and seized some of his files. According to his widow, Louise Drevet Selye, the ordeal was very stressful. In a bizarre twist, she sued the Canadian government for \$700,000, claiming that his death was due to the stress of their harassment, which had also sullied Selye’s reputation as a renowned researcher.

Part 3: The Origin and Evolution of The American Institute of Stress

Stress and Cancer, and Why The American Institute of Stress Was Formed

I kept in touch with Selye during my internship and residency at Johns Hopkins, where I was friendly with superb endocrinologists, including John Eager Howard, Lawson Wilkins, Harry Klinefelter and Sam Asper, and often helped to organize their endocrine clinics. Although they were all very interested in Selye, most disagreed with or did not understand his concepts, and asked if I could invite him to give an update on his research. Selye gladly accepted this opportunity to return to his old haunts, showed me where he used to live and shop, and his lecture was surprisingly well received. At the time, all physicians were required to enlist in the Armed Services for two years due to the Korean War. Because of my background, I was fortunate to obtain a Fellowship at Walter Reed Army Hospital where I headed the Endocrine Division of the Department of Metabolism. John Mason, who would later be one of Selye's severest critics, was conducting his famous "executive monkey" experiments at the adjacent Walter Reed Army Institute of Research, so it was an interesting experience. After I entered private practice, Selye and I often met when

he was in Manhattan, where I had an office in the Waldorf Astoria Towers.

On one of these occasions, he told me that his Institute was co-sponsoring a conference with Sloan-Kettering on Stress and Cancer in Montreal. He recalled that 25 years previously, in one of our after-dinner conversations, I had suggested that some cancers might be "Diseases of Adaptation" and he wanted me to contribute a presentation supporting this. It was difficult for me to refuse anything that Selye requested, but I politely pointed out a variety of potential pitfalls in attempting to accomplish this. It was impossible to determine when a malignancy developed as opposed to when it was diagnosed, different cancers such as brain tumors and malignant melanoma likely had different causes, etc. In addition, I had been completely involved in clinical practice for the past 20 years, and no longer had the time, training or resources to adequately address this subject. We reminisced about other things, and I assumed the matter was closed. However, two weeks later, I received a large parcel filled with assorted reprints, on many of which he had written comments to support the role of stress in cancer, the efficacy of stress reduction in treatment, as well as questions designed to pique my curiosity.

I was intrigued, since in looking into this more carefully, I was impressed with the observation that as one descends the phylogenetic scale; the incidence of malignancy decreases progressively and disappears. Conversely, the ability of the organism to regenerate injured or lost tissues increases proportionately. Simple organisms have the ability to sever parts of their anatomy when they are injured. This capability would have survival value only if the animal possessed an equally remarkable ability to regenerate the cast-off portion from available cell remnants. A starfish can restore a lost appendage, and the newt will grow a new tail or leg if it is amputated. This restorative capability is not retained in humans, although the spleen does possess unusual regenerative potential. It is also the only organ in humans that does not give rise to spontaneous cancer, suggesting that its response to loss has been preserved as purposeful regeneration. In addition, if a child under the age of two severs a fingertip, it will grow back completely, nail and all.

This suggested that some malignant responses in man might represent an atavistic, vestigial remnant of this primordial, purposeful, regenerative trait. When we suffer a loss or injury, attempts at replacement could well be activated as they are in lower life forms, but this new growth (neoplasia) may be more harmful than purposeful. The leap from physical to emotional

loss should not be too troublesome. The ability to regenerate lost or injured tissue in lower forms of life obviously involves something more than a simple local response. The message that tissue has been lost, irritated or damaged must be relayed to higher central nervous system centers that initiate coordinated restorative activities involving neurohumoral and immune system mechanisms. Because of our highly developed cerebral cortex, a significant emotional loss may well be perceived as even more stressful than physical loss of a body part. The same reparative signals may be activated, but responses designed to stimulate purposeful replacement are futile, and any resultant new growth is apt to be malignant. And when chemicals that are carcinogenic in humans are injected into the limb of a newt, it grows an accessory limb at that site. If injected into the iris of the eye, it grows a new lens.

The presentations at the conference were published in the 1979 Sloan-Kettering Cancer Series and Selye was very pleased with my chapter on cancer as a disease of adaptation. In his Foreword, he explained that he had a very personal interest in this subject, since five years previously, he had a tumor in his thigh that was diagnosed as a histiocytic reticulosarcoma. This is usually a fatal malignancy that is resistant to treatment. He attributed his complete recovery to a fierce desire to continue his research, since he had refused

surgery and chemotherapy. He also singled out my chapter as follows:

Perhaps, has Paul Rosch of New York has suggested, cancer might even be an attempt by the human organism to regenerate tissues and organs and even limbs, as lower animals are able to do spontaneously. Going further, one might say that the ultimate health of the organism, like that of society, appears to depend on how well or appropriately its constituent units communicate with one another.

There were numerous other fascinating examples to support a stress-cancer link, especially the stresses of civilization, that I later detailed in a Newsletter, and subsequently updated in a lengthy book chapter with over 250 references.

Selye continued to recommend me for important writing assignments, such as a chapter on “Stress: Its Relationship With Illness” in the 12-volume *Traumatic Medicine and Surgery For The Attorney*. I subsequently served as an expert witness in a variety of stress related lawsuits, particularly those involving heart attacks or deaths due to job stress. Although he was besieged with requests for advice on how to reduce stress and could have charged huge sums for a consultation, Selye never treated a patient. However, he referred many to me, including celebrities like Joseph Karsh, the famous photographer, who had been commissioned

to do a portrait of Selye. I also participated in Selye’s care when he had his hip replacements and later obtained the required blood test for his marriage license to Louise Drevet, his personal secretary who had been living with him.

Why and How The American Institute of Stress was Formed

After retiring from the University of Montreal, Selye was concerned about losing control over his creation, and in 1975 established his International Institute of Stress in Montreal to sponsor stress research, hold conferences and to keep physicians and the public advised on advances in measuring and treating stress. To attract funding, his Founding Board of Trustees included Nobel Laureates Linus Pauling, Jonas Salk and Hans Krebs, as well as Alfred Toffler, Buckminster Fuller and other celebrities. He subsequently recognized that it was difficult for Canadian organizations to receive financial support from U.S. philanthropies, organizations, drug companies and other potential donors, and that an American Institute of Stress was needed.

The subject of Stress has become so significant that numerous charlatans and unscrupulous and ill-informed individuals have attempted to capitalize on it, and there is great danger that the significance and importance of the concept will be jeopardized or distorted. There is a need for an organization such as this [the American Institute of Stress] to monitor such activities.

Selye's supporters were invited to a 1977 exploratory meeting at Nelson Hendler's Mensana Clinic for the diagnosis and treatment of pain located in the lush Greenspring Valley suburb of Baltimore. They included Joel Elkes, Emeritus Professor and Chair of Psychiatry at Johns Hopkins from 1966 to 1974, Jim Goddard, former FDA Commissioner and a half dozen or more other prominent physicians. Hendler, an Assistant Professor of Psychiatry at Johns Hopkins, also invited several colleagues and Selye insisted that I attend. This subsequently led to the formation of The American Institute of Stress in 1978. Many of the Founding Trustees of his International Institute of Stress agreed to serve in a similar capacity and Joel Elkes was elected President. At the time, Joel was revising the Department of Psychiatry at McMaster University, and after a month or two, asked me to replace him because of his numerous other obligations. Selye, who had invited me to serve on the Board of his International Institute of Stress, was adamant that I accept this position so that these two groups would be firmly linked. I told both that my time was consumed with a very demanding practice and raising five children, but agreed to take on this additional responsibility on a temporary basis.

However, it was not clear how our new Institute would be funded or where it would be located, since one of its purposes was to organize conferences dealing with advances in stress

research. Bob Schwartz, a patient, good friend and entrepreneur, who developed and owned the Tarrytown Conference Center, came to my rescue. It was the first conference center in the U.S. and its 28 acres included several majestic buildings containing 30 meeting rooms and offices of various sizes, over 200 guest rooms and suites, a first-class dining facility and recreation area, indoor swimming pool, conference rooms that could accommodate 50 to 350 people, and was only 8 miles from my home. Bob said I could have an office there and hold conferences at no charge, since he was fascinated by Selye and thought it would be a good advertisement for his Conference Center. I invited Selye to our inaugural event there in 1978, which included Board Members like John Laragh, Alvin Toffler, Joel Elkes and Norman Cousins, as well as Governor Nelson Rockefeller, who lived nearby, and other dignitaries. Although not specifically invited, two officers from the International Institute of Stress, Marie Gibeau and Dr. Pierre Hogue, who had learned of the event, also attended.

Selye was apparently unaware of this, and while initially cordial, after talking with these two officers, quietly told me he would not participate until he or his International Institute of Stress received a check for \$50,000, which Nelson Hendler, our Vice President, had previously promised. To emphasize this, Selye abruptly closeted himself in a downstairs bathroom and refused to

come out until his demand was met. We had received no outside funding, and while Nelson had previously written to Selye that he hoped to personally raise \$1,500,000, there was no specified timetable for this. After an embarrassing ten minutes, Bob Schwartz came to my rescue again by producing a blank check that was allegedly from The American Institute of Stress for \$5,000 that I signed. Bob delivered the check and explained that this was all we had in our bank account. Selye accepted it and promptly returned to the festivities as if nothing had

happened. He was as witty and charming as ever and made a short speech thanking me profusely for organizing this event, and praising me for all my hard work and serving as President. He notified me the following week that the check was bogus, but I suspect he knew this all along, and accepted it to avoid embarrassing himself more than me.

Although Selye originally indicated that the American Institute had been established for educational purposes, it became apparent at our Tarrytown



Drs. Rosch & Selye at Tarrytown Inaugural. Photo Credit: Paul J. Rosch, MD, FACP

inaugural meeting that his primary goal was to provide income for the International Institute of Stress. He offered to make available experienced fund raising personnel to enable us to obtain government grants and financial support from philanthropies that were limited to U.S. organizations. His International Institute of Stress would assist in complying with any requirements associated with these bequests and in return, they would receive 25% of our annual income. This essentially meant that instead of being autonomous, The American Institute of Stress was merely a subsidiary of his International Institute, since we had no resources that would allow us to fulfill any government grants or philanthropic funding. Nor did we have any other significant source of income, and his proposal was ignored. Instead, we began to publish and sell a monthly newsletter on advances in stress research and therapy, that was also available to our members and those who qualified as Fellows, in return for a modest annual fee.

The Montreux International Congress on Stress and Selye's Legacy

We struggled along, and in 1982, I was invited by Dr. Claude Rossel to serve as a consultant to his Biotonus Clinic in Montreux, Switzerland. An M.D. with a Ph.D. in physics, he had previously been Director of Research at a Swiss pharmaceutical company, but had received a huge grant to establish a first-class facility that would incorporate promising alternative medicine

approaches with the latest advances that modern medicine could provide. Since its main focus was to retard the aging process, he had studied with Paul Niehans, the Swiss urologist who developed cellular rejuvenation therapy; investigated Anna Aslan's procaine therapy in Rumania; and was familiar with the Russian ophthalmologist Vladimir Petrovich Filatov's placental therapy, which was being promoted by French physicians he respected. However, Claude felt that stress played a major role in accelerating aging, and since he did not consider himself to be a clinician and I had been highly recommended, wanted to enlist me in his quest, and to help evaluate a novel radio frequency wave stress reduction device to treat insomnia.

I gladly accepted his generous offer, and he indicated that there were undoubtedly stress reduction or anti-aging therapies in other countries we knew nothing about. He had investigated this and urged me to help organize and preside over a conference that would amalgamate these random efforts. I subsequently chaired a 1983 three-day "Conference on Stress and Aging" sponsored by Biotonus Clinic, which was conducted at the adjacent Five Star Grand Hotel Excelsior that the Clinic owned. Claude had attracted two Nobel Laureates and several other distinguished scientists as well as an array of obscure researchers working in disparate areas that seemed to have little relevance.

However, as the conference unfolded, it became obvious that this was to provide a platform and forum for unorthodox studies that could be critically evaluated to determine whether any should be further explored for use at the Biotonus Clinic. These included hyperbaric oxygenation, with which I was familiar, but others like placental therapy that I knew little about, save for its rich content of hormones and growth factors. Claude had already begun studies on the use of placental extracts in rheumatoid arthritis at the University of Geneva, and laboratory studies confirmed they produced a significant increase in immune system responses, as measured by rises in interleukin-2 and T-cell mitogenic activity. The conference was both stimulating and successful, since I suspect that everyone learned something new that was of interest. In addition, several new associations and friendships were formed. As a result, Claude asked me to organize a similar event dealing with advances in stress research and therapy.

Our First Montreux International Congress on Stress in 1988 was a three-day conference that followed the same format of an eclectic mix of distinguished authorities reporting on advances in their areas of expertise, and researchers who were relatively unknown but had exciting presentations. A major goal of this event was to pay tribute to Hans Selye by presenting the Hans Selye Award to an outstanding researcher and the

first recipient was Stewart Wolf, whose Hans Selye lecture was a 25-year review of the results of his renowned Roseto research. This Congress was also held at the majestic 5-star Grand Excelsior hotel, famed for its fabulous cuisine and white glove service. Its location on Lake Geneva also provided every room with a panoramic view of the French, Italian and Swiss Alps, and Evian, which is only a few miles directly across the lake. Faculty and registrants dined together and met in the main salon after dinner to renew old friendships and make new ones. This elegant but informal ambience fostered the development of close personal as well as professional relationships, and the response was so enthusiastic that I was invited to continue the Congress on an annual basis, and it quickly grew into a five-day event. Claude gave me carte blanche with respect to the selection of speakers and subjects that were often unrelated to the interests of Biotonus Clinic. Although Biotonus was listed as a sponsor in the Congress program, there were never any advertisements or promotional activities, since he insisted that these events should be strictly educational. However, participants could elect to take a guided tour of Biotonus to learn about its programs and services, use their exercise facilities, or take a dip in its Olympic sized heated swimming pool. Another unique feature of these events was the ability to include presentations from scientists in Eastern Europe, Russia and elsewhere who could not partici-

pate because of financial constraints. In some instances, airfare alone would have consumed three months' salary. Claude not only subsidized hotel expenses for all speakers but provided airfare and honoraria for those who could not afford to attend.

We had increasingly successful and cutting edge annual Congresses until Claude Rossel's untimely death in 1999. These events attracted international interest and established the American Institute of Stress as the preeminent stress organization in the world. Our 11th and last Congress in 2000 was held in Hawaii, and was funded entirely by Earl Bakken, who founded Medtronic, the \$28 billion global leader in electric and electromagnetic therapies. The contents of each Congress and a profile of Hans Selye Award recipients is available on our website, www.stress.org as well as www.swissrev.org, a group that is trying to reestablish the Montreux Congresses. The American Institute of Stress is also attempting to revive these events in the U.S, under the leadership of Dr. Daniel L. Kirsch, who succeeded me as President, his wife Tracey Kirsch, a successful medical entrepreneur and Member of the AIS Board of Directors, and AIS Executive Director Dr. Heidi Hanna, an acclaimed author and lecturer. Along with a dedicated and enthusiastic staff, the new AIS leadership has organized virtual stress conferences and are planning live conferences soon. Our website has been revised

and updated, and continues to have one of the highest rankings on Google and other search engines for inquiries on stress and stress related topics. There are now two additional free quarterly publications; *Contentment* magazine to report on the latest advances in stress research that provide assistance in finding which stress reduction strategy works best for you, and *Combat Stress*, which focuses on the unique stresses faced by military service members and their families.

There are also plans to provide educational programs and services that will attract members and Fellows as well as funding. I will remain as Chairman



Dr. Paul J. Rosch confirming incoming American Institute of Stress President Dr. Daniel L. Kirsch. Yonkers, New York, 2012.

to provide advice if requested, but am no longer involved with daily activities, since I am a dinosaur with respect to Facebook, Twitter, LinkedIn, Instagram and other social media that facilitate immediate interaction with large numbers of people. I look forward to a productive and bright future.

Selye was a genius and visionary, and his curiosity, stamina and dedication to deciphering the causes and consequences of stress made an indelible impression on me. With respect to his legacy, as a Google search will quickly confirm, his theory has essentially been discarded or forgotten. Selye also seems to have abandoned it, since it is not mentioned in his 1300-page *Stress in Health and Disease*, nor is it even cited in the hundreds of annotated references in the 228-page section discussing Theories. His concept of altruistic egoism by earning your neighbor's love also never caught on, and he is most likely to be remembered for his aphorisms and advice, such as:

- *Stress can be the spice of life or the kiss of death.*
- *Adopting the right attitude can convert a negative stress into a positive one.*
- *To remain healthy a man must have some goal, some purpose in life that he can respect and be proud to work for.*
- *Man should not try to avoid stress any more than he would shun food, love or exercise.*

- *It's not stress that kills us, it is our reaction to it.*
- *Fight for your highest attainable aim but never put up resistance in vain.*

Nevertheless, as the Bible reminds us in Ecclesiastes 1:9, "*there is no new thing under the sun.*"

Over 2,000 years ago, the Greek stoic philosopher Epictetus also advised:

- *There is only one way to happiness and that is to cease worrying about things which are beyond the power of our will.*
- *It's not what happens to you, but how you react to it that matters.*
- *Men are disturbed not by things, but by the view which they take of them.*

The Roman Emperor Marcus Aurelius similarly suggested, "*If you are distressed by anything external, the pain is not due to the thing itself but to your own estimate of it; and this you have the power to revoke at any moment.*" And more recently, Eleanor Roosevelt similarly pointed out that "*Nobody can make you feel inferior without your consent.*"

Selye's legacy also consists of his more than 1,700 publications that include 15 monographs and 40 books, 7 of which were targeted to a lay audience. However, few of these are popular today. He was also responsible for creating The Internation-

al Institute of Stress, The American Institute of Stress, the Hans Selye Foundation and the Canadian Institute of Stress. Some of these are still active several decades after his death and provide a variety of services. The Hans Selye Foundation offers a certification program for “Stress & Wellness Consultants,” and after Selye’s death, was moved from Montreal to Toronto where it became affiliated with the Canadian Institute of Stress, which concentrates on problems related to job stress. In 2004, the Vital Corporation Inc. was formed as a joint venture between the Canadian Institute of Stress and the Self-Management Group Inc., which had over 30 years of experience in reducing and alleviating job stress. Their focus is on helping companies attract and retain key executives as well as increasing employee productivity by improving the quality of life in the workplace. Services include providing assessment and coaching for executives and corporate training for health care and human resource personnel, especially in dealing with downsizing and hostile takeovers. The Vital Corporation now has a Tokyo-Selye Center branch in Japan, and similar facilities in Dammam, Saudi Arabia, and Madison, Wisconsin in the U.S. They plan on opening additional branches, and recently proposed establishing a new Hans Selye Montreal Stress Institute. A Selye-Toffler University was organized in 1994 with the usual distinguished Board of Governors. It would have been the first “Third Wave” edu-

cational institution, since there were no courses. Registrants who wanted to learn how to reduce job stress and improve performance, were required to have at least five years of work experience before they could access the interactive online college and web sites. Despite all the initial hoopla, it apparently never materialized. On the other hand, at least one new organization honoring Selye has emerged. The Selye International Institute for Advanced Studies has conducted its “Selye Symposium” in Budapest under the auspices of the Hungarian Academy of Sciences every year since 2012. It features lectures on advances in stress research and therapies from international authorities.

As noted previously, The American Institute of Stress has an auspicious and promising future, and may be Selye’s greatest legacy as it continues to memorialize him with an annual Congress that features a Hans Selye Award and Hans Selye Lecture. Some credit Selye’s success to luck, particularly the serendipitous bottle of formaldehyde sitting on his laboratory table at McGill in 1935. From my perspective, he illustrates Armand Hammer’s observation that “*When I work fourteen hours a day, seven days a week, I get lucky,*” as well as Pasteur’s opinion that “*Chance favors the prepared mind.*”

Selye theorized that stress caused disease and premature aging because of failure to adapt to pituitary-adrenal

cortical stimulation. However, he was unaware of telomeres or telomerase, which influence the aging process, or that stimulation of the amygdala activates the autonomic nervous system and produces the behavioral changes seen in response to stress, especially fear. Sophisticated imaging studies now confirm that stimulation of the amygdala also increases inflammation and cardiovascular disease. Other studies show that the cannabinoid system inhibits these amygdala responses, whereas CRF (corticotropin releasing factor) has the reverse effect. These and other investigations into how we adapt or respond to stress, or how stress contributes to cardiovascular and diverse diseases are not mediated by stress hormones, and appear to contradict Selye's theory. DNA research may reveal the role of heredity and other influences in the pathogenesis of certain disorders that he also failed to consider. Few physicians and researchers doubt that stress can contribute to or influence the course of a disease or accelerate aging, but not necessarily through the hormonal responses specified by Selye.

In that regard, it is not possible to prove a theory, since it would then become a fact. In contrast, Hypotheses and theories are not difficult to discredit. As Thomas Henry Huxley noted, "*The great tragedy of science is the slaying of a beautiful theory by an ugly fact.*" I suspect that Selye recognized this, since he often reminded me that the-

ories don't have to be correct, only facts do. Many theories are valuable simply because of their heuristic effect, in that they encourage others to discover new facts, which then lead to better theories. This appears to have been prophetic, since it seems to epitomize and predict the fate of his own theories.

Physical/Atomic Energy Versus Chemical/Molecular Communication

Good health depends entirely on good communication – good communication between the constituents of an organism as well as with the external environment. Progress in our understanding of how to maintain health when it has been threatened by various stressors has always depended on advances in physiology, biochemistry, and other agencies that are activated by stress. Claude Bernard, the 19th century "father of modern physiology," emphasized that good health depended on preserving the stability of the *milieu interieur* (internal environment). By this, he meant maintaining the concentrations of glucose, electrolytes, oxygen, temperature, blood pressure etc. within specific limits. This was enlarged upon a half century later by Walter B. Cannon at Harvard, who coined the term homeostasis to describe "*the maintenance of steady states in the body and the physiological processes through which they are regulated.*" Cannon attributed his "fight or flight" responses to severe stress to the secretion of what he called "sympathin" from the adrenal

medulla, since little was known about the role of the pituitary and adrenal cortex at the time. A few decades later, Hans Selye provided this information, and subsequent researchers delineated the hypothalamic-pituitary pathways responsible for initiating the response to stress, as well as the participation of the endorphins and a host of other neuropeptide chemical messengers.

The integration and coordination of all the above constituents requires good communication, but how does communication take place in the body? The role of the central nervous system with its sympathetic and parasympathetic components that maintain homeostasis is fairly well delineated. The endocrine system has its own balancing mechanisms, in which the secretion of hormones is regulated by feedback from target glands or metabolic consequence. Much less is known about how equilibrium is maintained in neurotransmitter networks or in the immune system, which has both hardwired and humoral central nervous system connections. In addition, our current concept of how communication takes place in the body is at a chemical/molecular level as we visualize small peptide messengers fitting into specific receptor sites on cell walls much like keys that fit into certain keyhole sites on cell walls. Such physical structural matching, which could occur only on a random-collision basis, does not explain the myriad instantaneous and

constantly changing reactions that occur in “fight or flight” responses to severe stress.

There is an emerging paradigm of communication at a physical/atomic level that may not only provide some answers, but also insights into widely acknowledged but poorly understood phenomena such as the placebo effect, the power of prayer and a firm faith, as well as the benefits of therapeutic touch, and acupuncture. EEG waves may not merely reflect the noise of the machinery of the brain, but signals being sent to specific sites on cell walls. As with neuropeptide stimulation, these send a nonthermal energy signal to the interior of the cell to activate various enzyme systems or to replicate itself. Thus, in addition to being a protective shield, the cell wall can be a powerful amplifier for subtle electromagnetic forces. All communication in the body ultimately takes place at a physical/atomic level via weak electromagnetic signals.

Why Doctors May Soon be Prescribing Frequencies Rather Than Pills –LEET, PST and CES Stimulation

This model of communication at a physical/atomic rather than a chemical/molecular level has important implications for preventing and treating stress related damage. Hans Selye demonstrated that in myocardial infarction produced by ligation of the coronary artery, the amount of damage following stress could be significantly reduced or prevented by ad-

ministering potassium. The eminent Mexican cardiologist, Demetrio Sodi Pallares, confirmed this, and also showed a clear and consistent correlation between the degree of damage and intracellular concentrations of sodium and potassium as one progressed from the area of necrosis, to zones of lesser tissue damage and healthy muscle. The higher the concentration of sodium in the cell, the greater the degree of damage but the reverse was true for potassium. He showed that a low sodium high potassium diet was effective in treating a variety of cardiovascular complaints. In addition, an intravenous solution designed to force potassium in and sodium out of the cell when administered promptly to heart attack patients, significantly reduced myocardial damage as well as arrhythmias, congestive failure, and other complications. The efficacy of this polarizing solution of potassium chloride, insulin and glucose was confirmed by others, including Eugene Braunwald's group at Harvard, and was widely adopted. G.N. Ling proposed that these benefits were due to increasing the mitochondrial production of ATP, the source of energy in all cells, and that polarizing solution could be used to treat other conditions. Sodi Pallares subsequently found that electromagnetic fields could also increase ATP, and added this to his low sodium-high potassium regimen, which he referred to Magneto-Metabolic therapy. This was found to be effective not only in cardiovascular disease, including pa-

tients with terminal cardiomyopathy waiting for heart transplants, but pancreatic and other cancers with widespread metastases.

More relevant are the observations of Boris Pasche and coworkers on the biological effects of low level radiofrequency electromagnetic fields. Ross Adey had shown that very low levels of amplitude-modulated electrical fields could alter EEG activity and the release of ions and neurotransmitters from the brain in experimental animals. Pasche et al. demonstrated that certain radiofrequency fields well below the international standards of safety were effective in treating stress related insomnia, and this was confirmed by polysomnography. Subsequent double blind studies revealed that other LEET (Low Energy Emission Therapy) radiofrequency fields could relieve chronic anxiety states. Treatment is administered by the patient using the hand held Symtonic energy emitting device, with a coaxial cable attached to an electrode that is applied to the roof of the mouth for 15 minutes in the morning and 30 minutes at night. Treatment is painless, there are no side effects, improvement is seen in the majority of patients after a week, and is successful in 90% of patients within three weeks.

More recently, Therabionic LEET using a different frequency range has been demonstrated to be more effective and much safer for treating hepatocellular carcinoma than chemo-

therapy, radiation and surgery. It also benefits patients with other malignancies based on the observation that different tumors respond to different frequencies. Therabionic therapy utilizes the Oncobionic device, which is similar to Symtonic, but uses an entirely different range of frequencies that are specific for different cancers. The electrode is placed in the mouth for one hour, three times a day, during which patients can read a book or watch TV at home. Over the course of the one-hour treatment, the Oncobionic RF generator runs through 194 different modulations, beginning with 410 Hz and rising to 21 kHz. Each one lasts three seconds, and at the end of the cycle, the sequence keeps repeating itself. As with Symtonic, treatment is painless and has no immediate or long term side effects since the dose the body receives is estimated to be 100 to 1,000 times lower than that from a cell phone. Healthy tissue is unaffected since only cancer cells with specific frequencies are inhibited. For additional information, see www.therabionic.com. How these beneficial LEET effects are mediated is not clear, but the authors suggest that undiscovered receptor mechanisms may be involved.

Richard Markoll's PST (pulsed signal therapy) for the treatment of osteoarthritis and a host of other disorders is also based on stimulating or simulating the piezoelectric signal that promotes the growth of connective tissue and cartilage. It is available at over

500 clinics and hospitals around the world, and its success in veterinary medicine confirms this is not a placebo effect. Additional information can be obtained at www.pst-global.com. In addition, Björn Nordenström had demonstrated an electrical circulatory system in the body that is contained in the walls of blood vessels. He proposed that the energy flowing through this system is analogous to chi, and that yin and yang may represent positive and negative charges. He also demonstrated that specific DC microcurrents are an effective and safe treatment for eradicating or preventing the growth of cancer, and particularly pulmonary metastases, which has been verified by others.

All organs and structures in the body vibrate, but at different frequencies. As illustrated by Therabionic and PST, the ability to simulate, stimulate or restore this frequency when it has been altered by disease can provide therapeutic rewards. Further support comes from a very recent study showing that a neural network of the brain called the dorsal stream is responsible for remembering words and music. Inside the dorsal stream are rhythmic electrical pulses called theta waves, but it was not known if they played a role in auditory memory. To explore this, researchers used MEG (magnetoencephalography) and EEG (electroencephalography) recordings to measure the amplitude and frequency signatures of theta waves in the dorsal stream, while the subjects performed

auditory memory tasks. These also revealed where the theta waves originated in the brain. Based on these findings, researchers then applied TMS (transcranial magnetic stimulation) at the identical theta frequency, and found that it significantly improved auditory memory. However, this occurred only when the TMS matched the rhythm of natural theta waves. Different rhythms had no effect, suggesting that it was enhancement of theta waves rather than TMS that improved memory. As the lead author concluded, *“This study shows that human behavior can be specifically boosted using stimulation that matched ongoing, self-generated brain oscillations. Even more exciting is that while this study investigated auditory memory, the same approach can be used for multiple cognitive processes such as vision, perception, and learning.”* This approach might also be utilized to improve our ability to respond to stress if the mechanisms that mediate this can be identified.

I have long believed that the future of stress therapy lies not in drugs, but research into electromagnetic and subtle energy therapies that might provide insights into mechanisms of action. I presented the first report on Symtonic LEET therapy in 1984, at an Electromagnetic Fields and Neurobehavioral Function conference in Belgium. Our First International Congress on Stress in Switzerland in 1988 was a 3-day event that had sessions chaired by Ray Rosenman (Stress and Cardiovascular Disease), Charles D. Spielberger (The Effect of Stress and

Emotions on Health), Herbert Benson (Stress Reduction in Theory and Practice) and Paul J. Rosch (Psychosocial Stress and Executive Health). These included presentations by eminent stress researchers like Han Eysenck, Daniel Goleman and Tores Theorell. But it also featured one on “Electromagnetic Energy Effects on Psychophysiological Functions” chaired by Björn Nordenström, who explained his theory of an electrical circulatory system and demonstrated how electrical energies could reduce or remove metastatic lung and other malignancies. Boris Pasche discussed “The Physiological Effects of Low Energy Emission Therapy (LEET)” with the Symtonic device demonstrating its efficacy and safety for treating insomnia. Saul Liss presented his data on “The Effect of Electromagnetic Energy on Brain Neurotransmitters” with Shealy-Liss cranial electrotherapy stimulation (CES). Some were curious as to why I had included this session and I explained my belief that the future of stress therapy would be in such nondrug approaches. Since then, we have had presentations by other electromedicine pioneers, including Demetrio Sodi Pallares on his Magneto-Metabolic therapy for cancer and cardiovascular disease, Daniel Kirsch on Alpha-Stim CES for neuroregulation and the treatment of anxiety, depression, insomnia, cognitive dysfunction and pain, and Rollin McCraty on heart rate variability (HRV) biofeedback for reducing stress and preventing sudden death.



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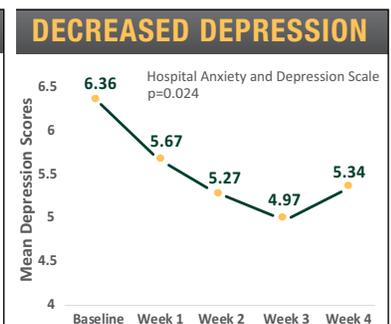
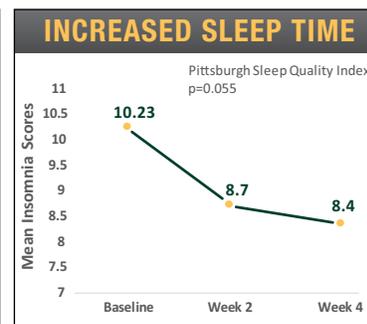
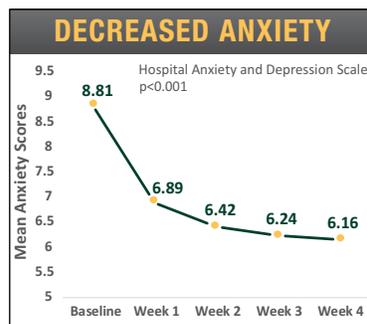
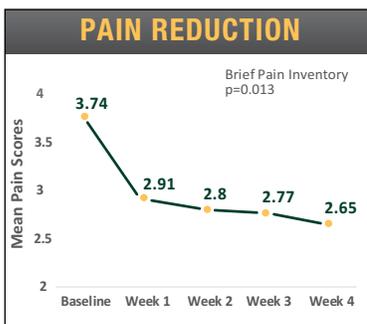


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REFERENCE

Yennurajalingam S, Kang D-H, Hwu W-J, Padhye NS, Masino C, Dibaj SS, Liu DD, Williams JL, Lu Z, Bruera E. Cranial electrotherapy stimulation for the management of depression, anxiety, sleep disturbance, and pain in patients with advanced cancer: a preliminary study. *Journal of Pain and Symptom Management*. E-published ahead of print, September, 2017.

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Many of the above modalities are safer and more effective than drugs but their wider use has been curtailed by other factors, especially vested interests. For example, repetitive transcranial stimulation (rTMS) is approved for treating drug resistant depression, but is expensive and requires administration by a physician. In contrast, CES has long been FDA cleared for treating depression and other stress related complaints, can be used by patients at home, and is very cost effective, especially for long term use. It is also so safe that it does not require a prescription in other countries. In contrast, antidepressants, which are not significantly superior to placebos in some studies, can have severe withdrawal and other adverse side effects, including increased risk of suicide. In that regard, the only drugs approved for treating post-traumatic stress disorder (PTSD) are two selective serotonin reuptake inhibitor (SSRI) antidepressants, and many believe they are contributing to the alarming increase in suicide in PTSD veterans. Over 20 veterans a day commit suicide, and these two drugs are associated with higher rates of suicide than other antidepressants. They are also contradicted or banned in patients 18 and under in the U.K. and elsewhere, and have a black box warning in the U.S. Unfortunately, things are not likely to change due to the tremendous influence powerful pharmaceutical companies have on the FDA, Congress and other regulatory authorities, academia, the media, as well as prominent medical organizations and physicians who are the recipients of their largesse.

There is also evidence that CES can significantly improve PTSD. But CES does much more than this, and also differs from other technologies in that it uses a smaller dosage of current. One company, Electromedical Products International, Inc., was formed in 1981 to manufacture Dr. Kirsch's invention, the Alpha-Stim, which utilizes a patented waveform of frequencies delivered in microcurrent similar to those that occur naturally in the body to promote health. It has waged a 35-year uphill battle to have unfair FDA restrictions changed, including a successful lawsuit against the FDA. Dr and Mrs. Kirsch also published a detailed analysis of problems they and others have encountered with the FDA's classification of this and other devices. They were featured in the 2017 documentary film, *The Body Electric*, by Justin Smith, where they spoke out about FDA bias and dishonesty as well as discussing how their technology works, and its safety and efficacy profile. Ironically, the US Government is also the largest consumer of Alpha-Stims which is widely utilized by the Department of Defense and Veterans Affairs Medical Centers.

Dramatic improvement has been achieved in rheumatoid arthritis by vagal nerve stimulation, (VNS) which also may be effective in treating obesity, and by deep brain stimulation (DBS) for treatment resistant depression and obsessive-compulsive disorder, and especially Parkinson's disease. See http://www.youtube.com/watch?v=uBh2LxTW0s0&feature=player_embedded for an incredible illus-

tration of immediate relief of all signs and symptoms in this devastating disorder. No drug can replicate this since DBS targets only the source of the problem. Although brain surgery is required, some of these benefits can now be reduplicated by noninvasive deep transcranial magnet brain stimulation (dTMS). Significant weight loss may also be achieved by dTMS by applying electromagnetic coils to the scalp, according to a presentation at the 2017 meeting of the Endocrine Society. Numerous other examples could be cited, but there are equally impressive results from ultrasound, which may replace surgery and radiation for treating various disorders. Focused ultrasound therapy concentrates the acoustic energy of ultrasound waves over 20 KHz, which cannot be heard by humans, to deliver heat to a target area in the body without affecting overlying skin and normal tissues. This noninvasive, bloodless and painless procedure is effective for treating benign uterine fibroids, relieving bone pain due to metastatic disease and has proven helpful for treating patients with movement disorders. Focused ultrasound surgery for uterine fibroids takes 2 or 3 hours, after which patients can resume normal activities without the need for hospitalization. For a compelling video of this, see https://www.youtube.com/watch?v=8EdFNm610Bw_

Unlike light, sound is not transmitted as an electromagnetic wave. Although both sound and electromagnetic waves have frequency, velocity and

specific wave lengths, they are completely different phenomena, Sound waves transmit mechanical energy using the elastic properties of matter and require a physical medium for energy transmission. Electromagnetic waves transmit electrical (magnetic) field energy from one place to another but do not require any material medium. Ultrasound is particularly useful in medical imaging since it is portable, relatively inexpensive and there is no harmful ionizing radiation and has been approved for healing fractures that have failed to unite after nine months or more. Echocardiograms use ultrasound waves to detect blockages in the coronary arteries, evaluate abnormalities in heart valves and heart failure. It is likely that electromagnetic, sound, light and other energies will be developed to treat numerous other disorders because they are safer and more effective than drugs or surgery.

Why Electromagnetic Therapies Have Difficulty Being Approved or Accepted

But it is even more likely that they will have difficulty gaining FDA approval for several reasons, such as the reluctance of physicians to admit they were wrong. Over 75 years ago Sidney Burwell, Dean of Harvard Medical School, told his students *“Half of what we are going to teach you is wrong, and half of it is right. Our problem is that we don’t know which half is which.”* More recently, David Sackett, often referred to as the “father of evidence-based medicine,” similarly

warned “*Half of what you’ll learn in medical school will be shown to be either dead wrong or out of date within five years of your graduation.*” This is supported by a review of studies for one year that “made some claim with respect to a medical practice” in the prestigious *New England Journal of Medicine*. Thirteen percent, almost one in eight, were complete reversals of what had originally been stated. John Ioannidis has also demonstrated that most published research findings are false.

Practicing physicians are also reluctant to embrace new therapies unless they have been firmly established as superior, or they provide some financial gain. In many instances, the mere mention of homeopathy, acupuncture, magnetic or “energy healing” is like waving a red flag in front of a bull, and the reaction from some doctors is “I wouldn’t believe it even if it were true.” In contrast, magnetic and electrical therapies were extremely popular in the U.S. at the end of the 19th century and the beginning of the 20th, when over 10,000 medical practitioners were administering some type of electrotherapeutic modality for every conceivable complaint. The Dynamizer was a radio-like device that could allegedly diagnose any disease by analyzing a drop of blood. It was not necessary to examine a patient, since simply sending a drop or two of dried blood on a piece of paper through the mail was sufficient to obtain a diagnosis and treatment recommendations. This was followed by the Oscilloclast

and Radioclast devices that were so powerful, a diagnosis could be made by talking to a patient over the phone in order to determine their personality. There were also a variety of less expensive “Violet Ray” devices that not only promised to provide “Health, Power and Beauty,” but could also quickly and safely cure almost anything painlessly, as illustrated by the advertisement for the following conditions;

Problems with circulation of the blood, the heart’s action, bumps of the funny-bone, germ infections, weakness, the waste of the body, congestion, impaired physical development, pains and aches, complexion and skin diseases, facial and body blemishes, hair loss, headaches, inflammation of joints, muscles, nerves, atrophy, circulatory disorders, constipation, deafness, goitre, high blood pressure, arteriosclerosis, insomnia (sleeplessness-Brain Fog), indigestion, dyspepsia, neuritis, nervousness, hysteria, melancholia, neurasthenia.

Since most of these were stress-related subjective complaints, it is likely that some patients had experienced transient relief because of a placebo effect, and their enthusiastic endorsements were repeatedly touted to increase sales. Permanent magnets were an even more popular scam. The Sears Roebuck catalog advertised magnetic boot soles for 18 cents a pair, as well as genuine magnetic rings, belts, girdles, caps, jewelry and other apparel and accessories to treat

everything from menstrual cramps and impotency to baldness. Traveling magnetic healers sold their own versions of these paraphernalia in addition to home-made magnetic salves and liniments.

As might be suspected, the quality of health care in the U.S. was appalling at the time because of the lack of regulation not only with respect to devices, drugs and food safety, but educational and licensure standards. In 1906, President Theodore Roosevelt signed the Pure Food and Drug Act that required labeling of the contents of all drugs, and in 1908, the AMA asked the Carnegie Foundation to survey the status of North American medical education and to make recommendations based on their findings. Abraham Flexner, a prominent educator who was selected to conduct this investigation, personally visited each of the 155 medical schools and found that many were small trade schools owned by one or more doctors for profit. They had no college or university affiliation and the Faculty consisted of local part time doctors whose own training was minimal. A degree was typically awarded after only two years of study that did not include any laboratory work or dissection, and regulation of the medical profession by state governments was minimal or nonexistent. There was no control over patient medicines containing narcotics or medical devices making exaggerated but unproven claims.

The 1910 Flexner report resulted in major changes. One third of medical schools were immediately shut down, and others that could not adhere to new four-year requirements soon followed. In 1910, only 16 out of the 155 medical schools required applicants to have completed two or more years of university education. By 1920, 92 percent of U.S. medical schools had a four-year course that included anatomical dissection and laboratory training. The Flexner Report was also the death knell for electrotherapy as state licensure and regulations not only became much stricter, but were also more vigorously enforced. Because there was no scientific basis to support electrotherapy, it was now excluded by law from the practice of medicine and was considered to be fraudulent for the next six decades. This is not too surprising, since the Carnegie family was heavily invested in the young pharmaceutical industry, which still continues to thwart the approval of anything that might replace drugs. This continues to be the major impediment.

Epilogue – What Does the Future Hold for Stress Research?

In 1992, J. Andrew L. Bassett, one of the early advocates of the use of electromagnetic fields to unite nonunion fractures that failed to heal after a year or more, made the following prophecy:

In the decade to come, it is safe to predict, bioelectromagnetics will assume therapeutic importance equal to, or greater than, that of pharmacol-

ogy and surgery today. With proper interdisciplinary effort, significant inroads can be made in controlling the ravages of cancer, some forms of heart disease, arthritis, hormonal disorders, and neurological scourges such as Alzheimer's disease, spinal cord injury, and multiple sclerosis. This prediction is not pie-in-the-sky. Pilot studies and biological mechanisms already described in primordial terms, form a rational basis for such a statement.

That was over 25 years ago, when electromagnetic bone growth stimulators for fractures had already been successfully used for well over a decade in tens of thousands of patients whose fractures failed to heal with other treatments. Nevertheless, it has been tough sledding since then to obtain approval for electromedical devices that are also safe and effective for numerous other indications.

Eventually, "truth will out," but as the distinguished physicist and Nobel Laureate Max Planck observed:

A new scientific truth does not triumph by convincing its opponents and making them see the light, but rather because its opponents eventually die, and a new generation grows up that is familiar with it.

William James, "Father of American Psychology" similarly noted:

First, you know, a new theory is attacked as absurd; then it is admitted to be true, but obvious and insignificant; finally, it is seen to be so impor-

tant that its adversaries claim that they themselves discovered it.

This helps to explain why it takes so long and is so difficult for valid electromagnetic and other therapies that threaten to disrupt the drug monopoly to be approved and accepted. It also explains why the establishment resists the incontrovertible fact that extremely weak nonthermal electromagnetic fields can have significant biologic effects. It is important to re-emphasize how little we know about how communication takes place within the body and between the body and its external environment. There are more questions than answers, and the great obstacle to discovery is not ignorance, but the illusion of knowledge. In that regard, it would be prudent, especially for stress researchers, to remember the following advice that Albert Einstein prominently displayed in large type on the wall of his office in Princeton:

Not everything that can be counted counts, and not everything that counts can be counted.

About the Author

Dr. Paul J. Rosch is Chairman of the Board of The American Institute of Stress, Clinical Professor of Medicine and Psychiatry at New York Medical College, Honorary Vice President of the International Stress Management Association and Chairman of its U.S. branch. He graduated from Albany Medical College, completed his internship and residency training at Johns Hopkins Hospital, and subse-

quently at the Walter Reed Army Hospital and Institute of Research, where he was Director of the Endocrine Section in the Department of Metabolism. He had a Fellowship at the Institute of Experimental Medicine and Surgery at the University of Montreal under the supervision of Dr. Hans Selye, the founder of the Stress Concept, and has co-authored works with Dr. Selye as well as Dr. Flanders Dunbar, who introduced the term, "psychosomatic" into American medicine.

Dr. Rosch was the 1998-99 President of The Pavlovian Society, an organization of distinguished international scientists devoted to integrating basic and clinical research and has been the recipient of many honors, including the Outstanding Physician's Award of the New York State Medical Society, Man of the Year Award with a Congressional Citation, the Schering Award, and the International Distinguished Service Award of the American Rural Health Association. In 1985, he received an award from Dr. Michael E. DeBakey, President of the American Society for Contemporary Medicine and Surgery for "contributions to our understanding of stress, health, and disease." The Russian Academy of Medical Sciences bestowed the I.M. Sechenov Memorial Medal on him in 1993 and he is one of the few foreign members ever elected to full Fellowship in this prestigious organization. He was also the recipient of the 2001 annual Innovation Award of The International Society for the Study of Subtle Energies and Energy Medicine.

Dr. Rosch has served as President of the New York State Society of Internal Medicine, Chairman of the International Foundation for Biopsychosocial Development and Human Health, Expert Consultant on Stress to the United States Center for Disease Control, President, Westchester Diabetes Association, and President, Yonkers Academy of Medicine. He is a member of the Honorary Advisory Board of the Reflex Sympathetic Dystrophy Association, Board of Governors of Northwood University, The American Academy of Experts in Traumatic Stress, Scientific Advisory Council of the Alzheimer's Prevention Foundation, and has served as Consultant to the Mensana Clinic, Biotonus Clinic in Switzerland, and other organizations involved in the delivery of health care. He is a Fellow and Life Member of the American College of Physicians, Diplomate of the National Board of Medical Examiners, Emeritus Member of The Endocrine Society, Emeritus Member of The Bioelectromagnetics Society, Fellow of the Council of Epidemiology of the American Heart Association, Fellow of the Society of Behavioral Medicine, Fellow of the Council on Geriatric Cardiology, Fellow of the World Academy of Art and Sciences, and Fellow of The Royal Society of Medicine. He was recently unanimously elected as a Full Member of the prestigious Russian Academy of Medical Sciences, one of only six foreigners who have received this honor in the past twenty years. Dr. Rosch is Senior Consultant in Internal Medicine and Honorary Emeritus Physician at St. John's Riverside Hospital

in Yonkers, New York, and has a Workers Compensation Subspecialty Rating in Cardiology, Endocrinology, and Metabolic Diseases.

Dr. Rosch is Editor of Stress Medicine, published by John Wiley & Sons in England, Associate Editor of The International Journal of Emergency Mental Health, and International Journal of Stress Management, and has served or serves on the Editorial Board of many publications including the Journal of Human Stress, International Journal of Psychosomatics, Cardiovascular Reviews and Reports, Comprehensive Therapy, Journal of Human Behavior, and Health Inform; Essential Information on Alternative Health Care. He has organized and presided over the annual International Congress on Stress since 1988, which has featured state of the art presentations on all aspects of stress, as well as cutting edge research in relevant areas of Bioelectromagnetic and Alternative Medicine. For further information on this, visit www.stress.org.

Dr. Rosch authored the Wellsprings of Health section of Creative Living and Health and Stress, the monthly Newsletter of the American Institute of Stress for 29 years. He has written extensively on the role of stress in health and illness, with particular reference to cardiovascular disease and cancer, and problems associated with job stress. In recent years, much of his

attention has focused on the psychophysiological effects of subtle energies as well as the clinical use of pulsed electromagnetic fields and heart rate variability feedback. He is co-author of The Doctors Guide To Instant Stress Relief, Magnet Therapy, DeStress, Weigh Less, senior editor of Bioelectromagnetic Medicine and editor of Bioelectromagnetic And Subtle Energy Medicine. He has appeared on numerous national and international television programs such as The Today Show, Good Morning America, 60 Minutes, Nova, CBS, NBC, PBS, BBC and CBC network presentations. His editorials and comments have been published in every major medical journal including the New England Journal of Medicine, Annals of Internal Medicine, Journal of The American Medical Association, British Medical Journal and The Lancet. He has been interviewed and widely quoted in Time, Fortune, Newsweek, The Reader's Digest, The Wall Street Journal, New York Times, USA Today, The Washington Post, The London Times, and numerous other publications here and abroad. The annual Paul J. Rosch Award was established by the Brazil branch of The International Stress Management Association, he is a member of the International Advisory Committee School of Psychology and Social Science, Universidad de Flores in Buenos Aires, and an International Institute of Stress Medicine is being established in his honor in Mexico (Instituto Internacional de Medicina del Estrés Dr. Paul J. Rosch).

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ISSN # 108-148X