

HEALTH AND STRESS

The Newsletter of The American Institute of Stress

Number 9

1997

REMINISCENCES OF HANS SELYE, AND THE BIRTH OF "STRESS"

KEY WORDS: Stress of Life Congress: From Molecules to Man, Hans Selye, General Adaptation Syndrome, Diseases of Adaptation, the distinction between stress and stressor

One can hardly go through the day without hearing or reading about "stress". Much of our puzzling preoccupation with stress stems from more and more research confirming its contribution to sudden death, heart attacks, hypertension, arthritis, gastrointestinal and skin diseases, depression, anxiety, insomnia, emotional disorders, infections ranging from the common cold and herpes to tuberculosis and AIDS, as well as immune system disturbances such as lupus and cancer.

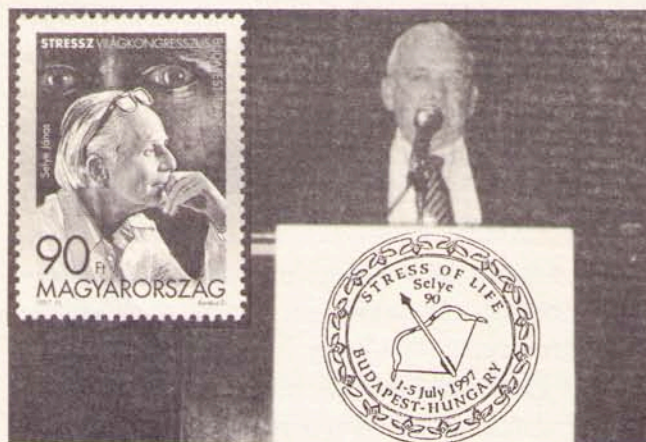
Stress has become such an ingrained part of our vocabulary and daily existence, that it is difficult to believe that our current use of the term originated only a little more than 50 years ago, when it was essentially "coined" by Hans Selye. How this came to pass because of a serendipitous laboratory accident is interesting, but not nearly as fascinating as the story of its discoverer.

ALSO INCLUDED IN THIS ISSUE

One Of The Most Unforgettable Characters I Have Ever Met.....	2
The Birth Of Stress And The General Adaptation Syndrome.....	3
The Novel Concept Of "Diseases Of Adaptation"....	3
Is Stress Cause, Effect, Or Both?.....	4
A Man For All Seasons.....	5
Some Personal Reminiscences.....	7

I was reminded of this recently, when invited to deliver a keynote address at the Stress Of Life Congress in Budapest, which had been specifically organized to commemorate the 90th anniversary of Hans Selye's birth.

Unfortunately, the dates happened to coincide with my own birthday. Two years ago I had spent it in Moscow at a World Health Organization Conference, and last year, in California at an Advisory Board meeting of The Institute of HeartMath, and I had promised to stay at home in 1997.



The circular logo of the Stress of Life Conference is a reproduction of the decoration found on a Hungarian silver bag plate 1100 years old, inside of which is a drawing of the IXth century Magyar Hungarian bow. Upper left, stamp of Hans Selye issued on the first day of the conference.

(Continued on page 2)

Health and Stress: The Newsletter of The American Institute of Stress is published monthly. Annual subscription rate \$35.00 (U.S.), \$45.00 (Foreign). Copyright © 1997 by The American Institute of Stress, 124 Park Ave., Yonkers, NY 10703. All rights reserved.

HEALTH AND STRESS

*The Newsletter of
The American Institute of Stress*

Paul J. Rosch, M.D., F.A.C.P.

Editor-in-Chief

Contributing Editors from The Board of Trustees of
The American Institute of Stress

Robert Ader, Ph.D., Rochester, NY
Herbert Benson, M.D., Boston, MA
Michael E. DeBakey, M.D., Houston, TX
Joel Elkes, M.D., Louisville, KY
Bob Hope, Palm Springs, CA
John Laragh, M.D., New York, NY
James J. Lynch, Ph.D., Baltimore, MD
Kenneth R. Pelletier, Ph.D., M.D., Berkeley, CA
Ray H. Rosenman, M.D., San Francisco, CA
Charles F. Stroebel, Ph.D., M.D., Hartford, CT
Alvin Toffler, New York, NY

(Continued from page 1)

However, I felt obligated to pay homage to my old friend and mentor, especially since I was one of the few survivors of those working in his laboratory during the early days of the formulation of the stress concept. In addition, because of our long and close personal and professional relationship, I was privy to a considerable amount of information not available to others, some of which I would like to share with you.

The Most Unforgettable Character I Ever Met

For those who knew him intimately, Hans Selye would easily qualify for the Reader's Digest "Most Unforgettable Character I Ever Met" classification. However, few individuals, especially those in the scientific community, ever enjoyed that privilege because of his apparently aloof attitude. His father, Hugo, was a surgeon in the Imperial Austro-Hungarian Army, and it was possibly his early upbringing that resulted in his stiff, authoritarian, Prussian demeanor, which many interpreted as an air of arrogance. He was born in 1907 in Komaröm, a small town, which at the time was divided by the Danube, in the Hungarian part of the Empire, midway between Vienna and Budapest.

He attended school at a Benedictine monastery, and since his family had produced 4 generations of physicians, entered the German Medical School in Prague at the age of 17, where he graduated first in his class, and later earned a doctorate in organic chemistry.

Selye once told me that he never felt he really had any nationality of his own. While his first name was Austrian, his surname was Hungarian. He was looked down on as an Austrian when he was in Hungary, and vice versa. When the Empire collapsed in 1918, he became Czechoslovakian without ever moving out of his house. The Czechs and the Slovaks had lots of disagreements with each other, but they unanimously detested both the Austrians and Hungarians. After he became an international celebrity, Czechoslovakia, Austria, and Canada, all wanted to claim him as their own. He readily accepted these accolades, but confided in me that he was most proud of his Magyar Hungarian heritage. He was particularly fond of Hungarian "Bull's Blood" red wine, and on occasion, we consumed liberal amounts of this, along with the superb Hungarian goulash he loved to make.

Because of his already obvious talent, Selye was awarded a Rockefeller scholarship to study in the U.S. He arrived at Johns Hopkins University in 1931, but was dumbfounded and dismayed by what he encountered. He had been reared in a formal academic European environment, in which 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 revered.

He was appalled at the sight of such distinguished middle-aged and older individuals playing charades, and acting in an undignified fashion at Faculty parties, to which underlings and even medical students were invited. Jackets and ties were discarded, everyone often seemed to be on a first name basis, and he suffered a severe case of culture shock. He thought of returning home, but had heard that Canada was more European and sedate, and decided to transfer his fellowship to McGill University in Montreal, because of their superb Department of Endocrinology.

(Continued on page 3)

(Continued from page 2)

He ultimately joined the McGill Faculty, became a Canadian citizen, and in 1945, moved to his own Institute of Experimental Medicine and Surgery at the University of Montreal.

The Birth Of Stress And The General Adaptation Syndrome

As a medical student, Selye had been impressed with the observation that patients suffering from very different diseases often exhibited identical signs and symptoms in the very early stages of their illness. All complained of low grade fever, feelings of malaise, fatigue, and generalized aching, and "they just looked sick". None of his professors could offer any explanation for this, and laughed at him when he said he would like to study this intriguing phenomenon. A decade later, while at McGill, he thought he had isolated a new female sex hormone. However, when he injected the preparation that presumably contained his discovery into his experimental animals, he was disappointed to find no evidence of any estrogen effects. What was worse, is that they became quite sick, and some died.

At autopsy, although there were no changes in the ovaries or breasts, all of them showed enlargement of the adrenal glands, shrinkage of lymphoid tissues, and stomach ulcers. This didn't make any sense at all, and he searched for some explanation. One possibility was that the changes were due to some contaminant in his chemical concoction. Formaldehyde is a toxic substance used to fix tissues in the laboratory, so that they can be studied under the microscope. There was a bottle right in front of him, and when he injected its contents into some animals, he was amazed to find that it produced identical results.

He began to wonder if other noxious substances or stimuli would also produce these same three findings, and what ensued is now history. He exposed rats not only to such chemical compounds, but also scorching heat, frigid cold, brilliant lights after their eyelids had been sewn back, deafening noise, strenuous exercise by making them continuously swim to the point of exhaustion, as well as intense psychological frustration.

Sure enough, all developed the same acute pathologic picture in the adrenals, lymph tissues and stomach. He termed this response, "The Alarm Reaction", and showed that it occurred not only in rats, but mice, rabbits, dogs, cats, and all other animals subjected to these acute insults.

He then studied the effects of longer exposure to noxious but not lethal stimuli, noting that this resulted in a "Stage of Resistance", during which the body's defense mechanisms seemed to adapt to these stimuli. However, if they persisted, a final "Stage of Exhaustion" ensued, with deterioration and death. He termed this three stage response, "The General Adaptation Syndrome". He performed numerous and detailed autopsies during the various stages of this syndrome, and was amazed to find with the naked eye as well as microscopic examination, changes in his laboratory animals identical to those seen in patients with arthritis, kidney disease, hypertension, coronary heart disease, and gastrointestinal ulcers.

The Novel Concept Of "Diseases Of Adaptation"

He suspected that perhaps "stress" might also cause these disorders in humans as well, and therefore considered them to be "Diseases of Adaptation". Actually, "Diseases of Maladaptation" would have been more appropriate. After thousands of additional experiments, he found that he could produce any one of these disorders selectively by sensitizing the animals through dietary or hormonal manipulation, and subjecting them to various distressful situations in experiments that would never be permitted today.

Selye subsequently traced the pathways and mechanisms that were responsible for these effects, demonstrating that they were due to increased pituitary stimulation of the adrenal cortex to produce steroids that would reduce inflammation. This explained why the adrenals were enlarged. Similarly, the stomach ulcers and lymph tissue shrinkage were due to the excess cortisone-like hormones. If the pituitary was removed, and he repeated the experiments, these manifestations of damage in different organs and structures did not occur. He

(Continued on page 4)

(Continued from page 3)

reasoned that if he could show how such injuries were caused, then perhaps he could also find a way to prevent them, or treat the diseases they were responsible for more effectively. These were entirely new and very radical concepts.

As a result of Pasteur's research and Koch's postulates, physicians had always 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 specific microorganisms etc.

What Selye was proposing was actually the complete reverse of this. He had now definitely proven 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 findings. While each of these had their own specific hallmarks, such as a burn, or frostbite, they nevertheless all showed the same non-specific changes of adrenal enlargement, stomach ulcers, and lymph tissue shrinkage he had originally seen with his presumably new ovarian hormone extract. Perhaps this also explained the curious, but very common early syndrome of "just being sick" he had observed as a medical student, in patients who later went on to develop quite different diseases.

Is Stress Cause, Effect, Or Both?

He chose the word "stress" to describe this phenomenon, defining it as "the non-specific response of the body to any demand for change". It turned out to be an unhappy decision that would haunt him the rest of his life. The term evolved from the Latin *strictus* (tight, narrow) and *stringere* (to draw tight). This became *estrece* (narrowness, oppression) in Old French, and *stresse* (hardship, oppression) in Middle English. From a practical standpoint, stress is generally viewed as a contraction or variant of distress, which would have been appropriate.

Unfortunately, Selye was 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 an external force, or stress, produces a proportional amount of deformation or strain. The maximum amount of stress a material can withstand before becoming permanently deformed is referred to as its elastic limit. This ratio of stress to strain is a characteristic property of each material, and is called the modulus of elasticity; its value is high for rigid materials like steel, and much lower for flexible metals like tin. Selye once 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 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. Twenty-four centuries previously, Hippocrates wrote 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's concept of stress and its relationship to illness quickly spread from the research laboratory to all branches of medicine, and stress ultimately became a "buzz" word in vernacular speech. However, the term was used interchangeably to describe both physical and emotional challenges, the body's response to such stimuli, as well as the ultimate result of this interaction. Thus, an unreasonable and over demanding boss might give you heartburn or stomach pain, which eventually resulted in an ulcer. For some people, stress was the bad boss, while others used stress to describe either their "agita" or their ulcer.

(Continued on page 5)

(Continued from page 4)

Because it was clear that most people viewed stress as some unpleasant threat, he had to create a new word, *stressor*, to refer to this, in order to distinguish between stimulus and response. Even Selye had difficulties when he tried to extrapolate his laboratory research to humans. In helping to prepare the *First Annual Report On Stress* in 1951, I included the comments of one critic, who, using verbatim citations from Selye's own writings, concluded that "Stress, in addition to being itself, was also the cause of itself, and the result of itself."

A Man For All Seasons

I first met Selye in 1949, when he was finishing his monumental tome, "Stress". He was already internationally regarded as one of the world's leading authorities, not only in endocrinology, but steroid chemistry, pathology, and experimental surgery. He had singly authored one of the first textbooks of Endocrinology, as well as a 27 volume Encyclopedia of Endocrinology, covering every conceivable aspect of this subject. To conduct his research, he needed to compare how animals responded to stress with and without the pituitary gland. The conventional operation for removal of the pituitary involved opening up the skull, required a skilled neurosurgeon, could take hours, and a significant number of animals died during or shortly after surgery. Selye developed a technique to remove the rat's pituitary through a small opening in the roof of the mouth in less than two minutes, with no mortality, and it only took him 15 minutes to teach each of us to do it just as well as he could. He discovered a way to remove two thirds of a rat's liver in less than a minute, which was necessary for other research studies, and invented the granuloma pouch technique to study the inflammatory process directly through a transparent window of tissue.

He spoke fluent German, Hungarian, Czech, Slovak, French, and English, since each had been his national language at one time or another. Based on personal experience, I can confirm that he was also comfortably conversant in Russian, Spanish, Italian, and Portuguese as well, and could understand Swedish and a few other languages if they were spoken slowly. While our staff meetings were

conducted in French, not all of us were proficient in this. Selye would go around the table explaining the highlights of what was being discussed in English, Spanish, Italian, German, or Czech, in an effortless fashion, until he was certain that each one of us had a clear comprehension of what was being discussed. If we responded with some question or suggestion in our own language, he repeated this process, to insure that everyone knew what was transpiring.

He was a voracious reader, consuming everything from the most technical and esoteric journals in 10 languages, to popular magazines and pulp fiction. He read as fast as most people could skim, and could skim a paper or book in almost the time it took to turn the pages. However, he retained as much from his skimming, as most of us would from reading, because of his amazing photographic memory. On occasion, he could quote almost verbatim, portions of an article he had seemingly only glanced at months before, sometimes even citing the page number!

He had a fetish about retaining copies of any article in any scientific or popular publication, in any language, that had even a remote reference having anything to do with stress. The problem was in deciding where and how to file this mountain of material. If an article dealt with cold stress in rats on a high sodium diet, with and without pituitaries, to determine the development of hypertension and/or heart enlargement, he would have had to make seven or more copies to store separately under each of these headings, to retrieve it by searching for that specific topic.

To overcome this problem, he devised his own symbolic shorthand system for classification, that made it possible to retrieve all reprints that dealt with a specific subject, or any possible combination of subjects. It was a vast improvement over the conventional Cutter and Dewey decimal systems, and while it looked strange and complicated, it was really quite logical and simple once you understood how to use it. Because of the great interest in this expressed by other scientists, Selye published a manual carefully explaining its details, which went through five editions until the computer made it obsolete.

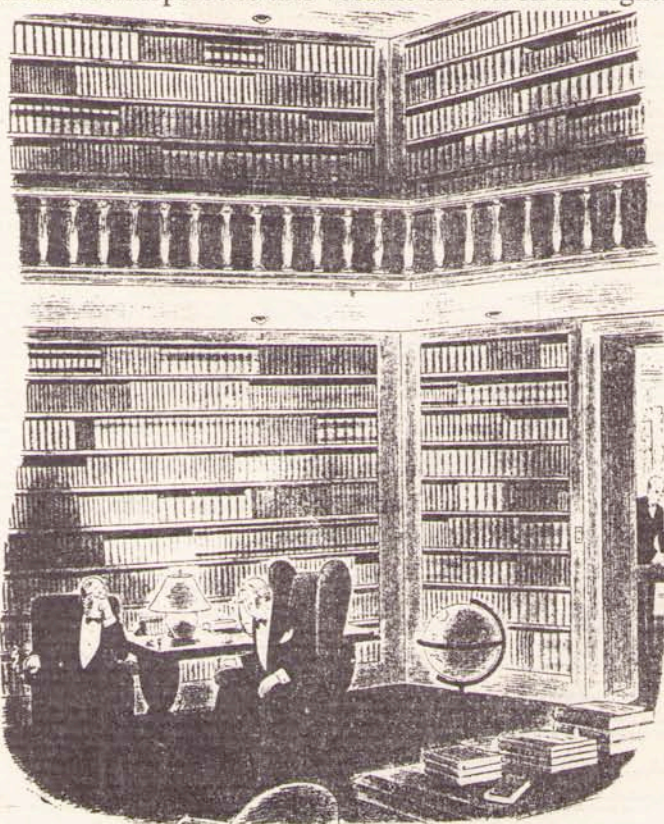
(Continued on page 6)

(Continued from page 5)

Megalomania Combined With A Sense Of Humor

Selye did everything on a grandiose scale. *Stress*, which was published in 1950, was a huge book of over 1000 pages containing more than 5000 references. However, it paled in comparison to his *Encyclopedia of Endocrinology*, where each of the volumes was the size of a telephone directory for a fairly large city. Some appreciation of this may be gained from Section IV, *The Ovary*. Volume VII, *Tumors Of The Ovary* actually consists of two mammoth books, the first of which contained detailed clinical descriptions, case reports, photographs of patients, X-rays, and numerous illustrations depicting the gross and microscopic pathology of every known tumor of the ovary. The second, consisted solely of over 18,000 references in different languages, with their symbolic shorthand label, as illustrated below on the left. Despite its stuffy, scholarly nature, Selye's sense of humor is evident from the frontispiece to this volume shown on the right.

- [illegible]



"I have a small confession to make - some of them I've only skimmed through."

Courtesy "The New Yorker" Magazine

Similarly, the frontispiece to the first volume read "*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 two large volumes entitled *The Steroids*, contained the formulae of all known chemical and biological activities of every steroid known in 1946. It was never completed, since Selye had to keep making additions as new compounds were discovered, and additional physiologic activities were delineated. When Kendall and Hench at The Mayo Clinic received the Nobel Prize for their discovery of cortisone and its dramatic effect on rheumatoid arthritis, there were many who felt that this honor should have gone to Selye, since he had predicted the existence of such a steroid as well as predicted its structural composition. He probably received more awards than any other physician, but was always bitter about not having received the Nobel Prize, although he had been nominated for it several times. This was particularly awkward when one of his students, Roger Guillemin, who worked right next door to me in 1951, later received the Nobel Prize for characterizing the endorphins, although this was not based on research done under Selye's aegis.

(Continued on page 7)

(Continued on page 7)

(Continued from page 6)

Selye's unusual wit and sense of humor was generally unappreciated, since he was perceived as being so stiff and formal, and it was often carefully concealed in his writings. Because of his obsessive-compulsive tendency to collect anything remotely dealing with stress, he would obtain all the pertinent citations listed in an article, and then retrieve the relevant references from those articles, which resulted in a never ending chain of requests. He was frustrated by the index of some pedantic texts, since when he sought details on a subject, he was often referred to another heading, which in turn, would suggest another topic, instead of identifying a page where the information could be obtained. Consequently, in the Index of his 1947 *Textbook Of Endocrinology*, there is an entry entitled, Selye; *see: what next?* If you follow this instruction, you will find, What next; *see: Selye*.

Another entry was, "O.K." rule, 816. The discussion on page 816 referred to the fact that conception is unlikely to occur around or during the menstrual period. Selye wrote, "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."

Some Personal Reminiscences

When I was at the Institute, Selye's average work day was 10 to 14 hours, including weekends and holidays. He habitually rose around 5:30, took a dip in the small pool in the basement of his house, and then rode his bike several miles to work. He was usually the first to arrive and the last to leave. On sunny days, he often put aside an hour or so after lunch to "take a nap in Miami". This was not Florida, but rather a solarium on the roof where he had the glass ceiling replaced with quartz, and could work on his tan, even during the winter.

As a result of his research on the experimental production of myocardial necrosis, and the benefits achieved by Sodi Pallares' polarizing solution in acute heart attacks, he filled all his salt shakers with potassium chloride. It tasted horrible, but he was convinced it would protect his cardiovascular system. He told me that he regularly took garlic pills, not only because of their health benefits, but because his breath discouraged prolonged, close conversations, especially with people he wanted to avoid, and he used this effectively.

His office was a real inner sanctum, guarded by an anteroom of protective secretaries and librarians. We had to make an appointment with these watchdogs if we wished to speak with him. There was a prominent green and red light over both sides of his entry door. When the red light was on, which was not infrequent, he was absolutely not to be disturbed by anyone, including these wardens. A green light indicated that he could now be approached with messages that had accumulated, or important incoming telephone calls. For some reason, I enjoyed a somewhat special relationship with him right from the start, possibly because he knew that I had been an English teacher before entering medical school. Although his command of the language was superb, he was concerned about the possible connotations of certain words or expressions that might have escaped him, and since most of his publications were now in English, wanted to make absolutely certain that they were letter perfect, and he had not overlooked anything.

He was extremely generous, inviting me to co-author the lead Chapter on Integration of Endocrinology for the AMA's *Textbook of Glandular Physiology and Therapy*, which included contributions from 32 leading authorities on various hormonal disorders. He had given a presentation for The New York Academy of Medicine in 1951, which they wanted to publish. However, it had been an extemporaneous speech, so he asked me to write something up from his notes, and to add anything I deemed appropriate, or that he might have neglected. When a preprint was submitted for his approval, he insisted that I be listed as a full co-author, explaining to them that the major portion of this was my contribution.

(Continued on page 8)

(Continued from page 6)

Selye's unusual wit and sense of humor was generally unappreciated, since he was perceived as being so stiff and formal, and it was often carefully concealed in his writings. Because of his obsessive-compulsive tendency to collect anything remotely dealing with stress, he would obtain all the pertinent citations listed in an article, and then retrieve the relevant references from those articles, which resulted in a never ending chain of requests. He was frustrated by the index of some pedantic texts, since when he sought details on a subject, he was often referred to another heading, which in turn, would suggest another topic, instead of identifying a page where the information could be obtained. Consequently, in the Index of his 1947 *Textbook Of Endocrinology*, there is an entry entitled, Selye; *see: what next?* If you follow this instruction, you will find, What next; *see: Selye*.

Another entry was, "O.K." rule, 816. The discussion on page 816 referred to the fact that conception is unlikely to occur around or during the menstrual period. Selye wrote, "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."

Some Personal Reminiscences

When I was at the Institute, Selye's average work day was 10 to 14 hours, including weekends and holidays. He habitually rose around 5:30, took a dip in the small pool in the basement of his house, and then rode his bike several miles to work. He was usually the first to arrive and the last to leave. On sunny days, he often put aside an hour or so after lunch to "take a nap in Miami". This was not Florida, but rather a solarium on the roof where he had the glass ceiling replaced with quartz, and could work on his tan, even during the winter.

As a result of his research on the experimental production of myocardial necrosis, and the benefits achieved by Sodi Pallares' polarizing solution in acute heart attacks, he filled all his salt shakers with potassium chloride. It tasted horrible, but he was convinced it would protect his cardiovascular system. He told me that he regularly took garlic pills, not only because of their health benefits, but because his breath discouraged prolonged, close conversations, especially with people he wanted to avoid, and he used this effectively.

His office was a real inner sanctum, guarded by an anteroom of protective secretaries and librarians. We had to make an appointment with these watchdogs if we wished to speak with him. There was a prominent green and red light over both sides of his entry door. When the red light was on, which was not infrequent, he was absolutely not to be disturbed by anyone, including these wardens. A green light indicated that he could now be approached with messages that had accumulated, or important incoming telephone calls. For some reason, I enjoyed a somewhat special relationship with him right from the start, possibly because he knew that I had been an English teacher before entering medical school. Although his command of the language was superb, he was concerned about the possible connotations of certain words or expressions that might have escaped him, and since most of his publications were now in English, wanted to make absolutely certain that they were letter perfect, and he had not overlooked anything.

He was extremely generous, inviting me to co-author the lead Chapter on Integration of Endocrinology for the AMA's *Textbook of Glandular Physiology and Therapy*, which included contributions from 32 leading authorities on various hormonal disorders. He had given a presentation for The New York Academy of Medicine in 1951, which they wanted to publish. However, it had been an extemporaneous speech, so he asked me to write something up from his notes, and to add anything I deemed appropriate, or that he might have neglected. When a preprint was submitted for his approval, he insisted that I be listed as a full co-author, explaining to them that the major portion of this was my contribution.

(Continued on page 8)