HEALTH AND STRESS

The Newsletter of
The American Institute of Stress

Number 2 February 2012

STRESS & HEALTH UPDATES FOR THOSE STAYING TUNED

KEYWORDS: Social media, Alzheimer's disease, amyotrophic lateral sclerosis, Coenzyme Q10, tricyclic antidepressants, Prozac, selective serotonin reuptake inhibitors, ECT, DBS, rTMS, CES, psychoneuroimmunology, placebo - nocebo effects, Nicholas Cohen, CRH, GRF, Nobel Prize for endorphins, Roger Guillemin, Daniel Weiss

I frequently ask readers to "stay tuned" for updates on controversial topics, and have done so for many of these, especially when new findings furnish support for the opinions expressed, or tend to refute them.

Also Included In This Issue

However, there has been such an explosion of interest in stress over the past few years in so many diverse areas, that it would take several issues of the Newsletter to comment on all of those that are relevant. In addition to thousands of articles, Amazon predicts that **in 2012, there will be at least two new books published every week on stress-related topics.**

As some subscribers may have noticed, we have expanded from the traditional 8 pages of previous print issues, to 12 or more, in order to provide updates, as well as new and interesting subjects in a comprehensive fashion. We would also plan to include more references, book reviews and news about our Fellows. The American Institute of Stress is currently undergoing a major transition in an effort to provide the above and other services utilizing blogs, Facebook, Linkedin, Twitter and other social media. This will encourage more active participation by our membership and attract new Fellows and Members. Although our website is still **#1 or in the top 3 out of several hundred million for "stress" inquiries on Google** and other search engines, it is now undergoing a major restructuring to include additional topics and services to make it more user friendly. We will also

expand our efforts to evaluate new products in an effort to separate the wheat from the chaff. Stay tuned for more on this, but in the interim, here are this month's updates and other news.

Neuropathy, Memory Loss, Diabetes and Other Sinister Statin Side Effects

I developed a personal interest in the suppressed side effects of statins about a dozen years ago, when my wife, Marguerite, was placed on Lipitor. Like many others of Mediterranean extraction, her cholesterol had always been well over 300, and although most of it was "good" HDL that put her at low risk for a heart attack, her physician felt she should be placed on statins in accordance with current guidelines. Although I had written extensively about the non-role of cholesterol in the pathogenesis of coronary heart disease, statins were touted at the time as having a superb safety record, and rare complications like muscle or liver disease were presumably readily avoided by monitoring routine blood tests. Some authorities felt they were so effective, that not prescribing them for high-risk patients was tantamount to malpractice, so I acquiesced. She started with 10 mg. of Lipitor daily, which resulted in a slight lowering of cholesterol, and since she had no apparent adverse effects, the dosage was increased.

Marguerite was an excellent and avid golfer, being Class A Ladies Champion at two different clubs to which we belonged. She played 4-5 days a week, often 36 holes, and still had enough energy to prepare dinner. However, after being on Lipitor for seven months, she noted that she became fatigued on the back nine and that her muscles ached. I joined her whenever I could, and noticed that she had lost 30-50 yards on her drives. She also complained of occasional memory lapses or "senior moments", although she was well below Medicare eligibility. Physical examination and blood tests were normal, but by this time, I had become aware of increasing reports of memory loss, amnesia and muscle weakness due to statins, some of which appeared to be due to their suppression of Coenzyme Q10, which is vital for the formation of ATP, the source of all cellular energy. I convinced her to stop the statins and started Q10 supplementation, with dramatic results. Within 6-8 weeks, she was hitting the ball farther than ever, could play as many holes as she wanted, and no longer had memory problems recalling familiar names or what she went to the supermarket for.

I was reminded of this by a recent report indicating that statins caused definite but silent damage to peripheral nerves when taken for more than two years. There are at least 88 studies linking statins to nerve damage, and 12 showing a direct connection to peripheral neuropathy.[1] The NIH describes this statin type of nerve damage and peripheral neuropathy as follows:

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1. Neuro Endocrinol Lett. 2011 Sep 3;32(5):688-690

Symptoms are related to the type of affected nerve and may be seen over a period of days, weeks, or years. Muscle weakness is the most common symptom of motor nerve damage. Other symptoms may include painful cramps and fasciculations (uncontrolled muscle twitching visible under the skin), muscle loss, bone degeneration, and changes in the skin, hair, and nails.

Peripheral neuropathy describes damage to the peripheral nervous system, the vast communications network that transmits information from the brain and spinal cord (the central nervous system) to every other part of the body. Peripheral nerves also send sensory information back to the brain and spinal cord, such as a message that the feet are cold or a finger is burned. Damage to the peripheral nervous system interferes with these vital connections. Like static on a telephone line, peripheral neuropathy distorts and sometimes interrupts messages between the brain and the rest of the body. Because every peripheral nerve has a highly specialized function in a specific part of the body, a wide array of symptoms can occur when nerves are damaged.

Some people may experience temporary numbness, tingling, and pricking sensations (paresthesia), sensitivity to touch, or muscle weakness. Others may suffer more extreme symptoms, including burning pain (especially at night), muscle wasting, paralysis, or organ or gland dysfunction. People may become unable to digest food easily, maintain safe levels of blood pressure, sweat normally, or experience normal sexual function. In the most extreme cases, breathing may become difficult or organ failure may occur. Some forms of neuropathy involve damage to only one nerve and are called mononeuropathies. More often though, multiple nerves affecting all limbs are affected-called polyneuropathy.

National Institute of Neurological Disorders and Stroke (NINDS)

In addition to peripheral nerves, statins also damage the brain. One study reported statin-induced cognitive impairments such as confusion, memory loss, or inability to concentrate to be quite common along with four other complaints when these were specifically inquired about in a questionnaire.[2] Patients usually do not report such symptoms since they come on gradually and are assumed to be due to aging. **90 percent of patients reported improvement when statins were stopped, sometimes within a few days, with the median time being 2.5 weeks. "In some patients, a diagnosis of dementia or Alzheimer's disease reportedly was reversed."** Whenever patients whose symptoms had disappeared or improved significantly, following cessation of a particular statin, later received another brand, their symptoms recurred, and in some cases, this happened on multiple occasions. **One web site lists over a dozen studies**

[2] Pharmacotherapy. 2009 Jul ;29(7):800-11

specifically linking statins to significant memory problems, and more than 300 complaints and disorders associated with statins.[3]

Some of these, such as diabetes, have long been suspected based on findings that were obscured or ignored in drug company sponsored trials. A 2010 meta-analysis of 13 statin trials, consisting of over 91,000 participants, found that statin therapy was associated with a 9 percent increased risk for diabetes onset.[4] A 2011 analysis of data from 5 statin trials involving 32,000 patients reported that high-dose statin therapy was associated with an increased risk of new-onset diabetes when compared to moderate doses.[5] And a few weeks ago, **a follow-up of over 160,000 postmenopausal women found that statins increased the risk of diabetes by almost 50 percent!**[6] These reports are alarming, since diabetes is a risk factor for heart disease and statin proponents maintain that all diabetics should be placed on statins regardless of their cholesterol or LDL levels. A high blood sugar, along with its various glycation products, damages the inner lining of arteries, causing endothelial dysfunction and diminished blood flow to muscles and nerves. Statins also increase insulin resistance that promotes inflammation, which contributes to coronary heart disease. Ironically, preventing this is the major reason for taking statins.

ALS (Amyotrophic lateral sclerosis) or Lou Gehrig's Disease, is a rare but fatal disorder due to progressive destruction of nerve cells in the brain and spinal cord that control voluntary muscles. The cause is unknown, but it tends to affect middle-aged and older individuals and is more common in men. Diagnosis can be difficult since sophisticated imaging studies and laboratory tests show no abnormalities, but may help rule out multiple sclerosis, Lyme disease, HIV and other disorders that mimic the early stages of ALS. Subsequent symptoms depend on which muscles are affected, but it is often weakness or twitching of an extremity or difficulty in speaking. Electromyography, nerve conduction velocity and muscle biopsy can provide additional information, but the diagnosis is usually suggested by evidence of progressive loss of control of all muscles throughout the body. Ninety percent of all patients die within 3 to 5 years, usually from respiratory failure. The ability to see, smell, taste, hear, and feel pain is usually not affected. Up to 20 percent of patients contemplate or seek physician-assisted suicide to escape from what some describe as "living in Hell."

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[3] www.GreenMedInfo.com
[4] Lancet. 2010 Feb; 375: 735-742
[5] JAMA. 2011 Jun 22;305:2556-64
[6] Arch Int Med. 2012 Jan 23;172:1-12

A front page July 3, 2007 *Wall Street Journal* article attracted national attention by suggesting a link between statins and ALS like symptoms.[7] A WHO monitoring center had reported an unusually high incidence of this in patients taking statins but not other drugs. The center director was reluctant to report this because of fears of an unwarranted drug panic, but changed his mind after discussing the data with experts and reading a study showing that some neurodegenerative effects of statins might be halted or reversed. His report was rejected by the *British Medical Journal* and *Lancet*, which is not surprising, since many journals tend to reject anti-statin reports that might decrease lucrative advertising revenues. It was eventually published in *Drug Safety*, a smaller New Zealand journal.[8] Since then more convincing evidence has accumulated. One physician who provided details on 35 cases not previously reported, noted that ALS symptoms often began shortly after statins were started, and in some cases, regressed when they were stopped, suggesting a causal relationship.[9] As noted above, there was also evidence that Co-enzyme Q10 might improve symptoms, as had been shown in statin induced muscle complaints and Parkinson's disease. In addition to blocking cholesterol synthesis, statins also inhibit the production of Q10, a crucial component of the mitochondrial electron transport chain that provides energy for all cellular functions. Defects in mitochondrial function have been incriminated as contributing to both ALS and Parkinson's.[10]

Proving that statins cause ALS is difficult since the diagnosis is not always clear; ALS starts in an age group likely to take statins as well as other drugs. Physicians seldom ask patients about statin side effects, and are likely to disregard a link when such a question is raised, even when there is supportive literature.[11] Studies just published show that patients rarely recognize that muscle pain or cramps could be due to statins[12] and statin induced mitochondrial dysfunction can be demonstrated in patients without any muscle discomfort or other symptoms.[13] More importantly, probably 95% of adverse drug reactions that occur outside a hospital or health facility are not reported, in addition to many more that are never even recognized.[14]

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7 Wall Street Journal. (2007) July 3 A risk in cholesterol drugs is detected, but is it real?

8 Drug Safety. (2007) 30: 515-25 Statins, neuromuscular degenerative disease and an amyotrophic lateral sclerosis-like syndrome: an analysis of individual case safety reports from Vigibase.

9 Graveline D. www.spacedoc.net

10 Neurodegen Dis. (2004) 1: 245-254 Dupuis L. Mitochondria in ALS: a trigger and a target

11 Drug Safety. (2007) 30: 669-675 Physician Response to Patient Reports of Adverse Drug Effects

12 The American Journal of Medicine (2012) 125: 176-182

13 Toxicol. Appl. Pharmacol. (2012) Jan. 25 (e-pub ahead of print doi:10.1016)

14 Avorn J. (2004) Powerful Medicines:The Benefits, Risks and Costs of Prescription Drugs. Knopf, New York

Unraveling The Statin → Low Cholesterol→ Cancer Conundrum

As indicated in a previous Newsletter, Uffe Ravnskov, Kilmer McCully and I wrote a paper with a similar title that was published in the *Quarterly Journal of Medicine* three months ago to call attention to the possibility that statins might cause cancer in humans. It had over 40 supportive references from clinical and animal studies that discussed the association of low cholesterol with cancer, the likelihood that statins were carcinogenic, why meta-analyses of drug company sponsored trials failed to support this hypothesis, plausible mechanisms of action and other pertinent issues. It is difficult to prove that statins cause cancer, and to add to the confusion, some reports have suggested they might prevent or help to treat malignant growths. I was reminded of this by **"Study Hints That Statins Might Fight Breast Cancer"** the title of a January 20, 2012, lead story in *USA Today*. **"Cholesterol-Lowering Statins May Treat Breast Cancer"** was the *Medical World News* headline. Presswatch, a news reporting service in the U.K. was even more emphatic the following day, as it triumphantly trumpeted **"How Statins Beat Cancer"** with the following explanation.

> A study on breast cancer by researchers at New York's Columbia University has found that the cholesterol-busting drugs called statins can block the growth and spread of tumors. **The findings could revolutionize treatment of cancer, and it is believed that statins could be effective against many other types of the disease.**

There is no way of estimating how many breast cancer patients may have shown their doctors such articles and asked them to prescribe statins, even though it has been established that statins provide no benefits to women, save for those who have had a heart attack or other coronary event. And confused physicians who made the effort to investigate this soon discovered it was a misleading hoax. What the Columbia researchers had reported in the current issue of *Cell*, a highly technical journal, was that in test tube studies, statins could influence a mutant p53 suppressant gene that inhibits malignant growth. This may or may not have relevance for a very small percentage of women with breast cancer, and **no cancer patients had been treated.** No mention was made in the media that statins **might actually cause breast cancer**. In the CARE trial, **there was a 12-fold increase in the incidence of breast cancer in postmenopausal women treated with Pravachol after only 4 to 6 years** when compared with placebo.[15] Another study reported a **15% increase in breast cancer in patients on statins**.[16] Similarly, press reports with headlines such as **High Blood Cholesterol Levels Accelerate The Growth Of Prostate Cancer** (which indirectly promotes statins) refer to test tube experiments in mice

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[15] N Engl J Med (1996) 335:1001–1009

[16] JCE (2005) 56: 280-285

force fed a high cholesterol diet, that are not relevant to humans. No mention is made of studies showing an increase in prostate cancer that correlated with increasing statin dosages[17] or the duration of therapy.[18]

With respect to criticisms that our paper discussing the possible link between statins and/or low cholesterol with cancer was of little interest because of its low priority, consider the following. As with smoking and lung cancer, it may take decades before a carcinogenic effect can be identified. There are few statin follow-up studies of that duration, and in many instances, patients may have stopped taking them because of other adverse side effects. **Over a million prescriptions for statins are written each week, and one in four Americans over the age of 45 is now taking a statin,** which in most cases is not justified, especially for primary prevention. Statins are available without a prescription in the U.K., where proponents feel they are so safe and effective, they should be put in drinking water, given to children, and taken by everyone over the age of 55 along with other drugs in a "polypill" to prevent cardiovascular disease. While they are not yet over the counter here, anyone hoodwinked by advertising hype can easily obtain statins without a prescription through the Internet. Many fear this could result in a major public health disaster of unprecedented proportions.

The Serotonin Scam: Will Electromagnetic Therapies Replace Antidepressants?

Antidepressants are now the third most commonly prescribed drugs in the U.S., with sales of over $11 billion in 2010.[19] As with statins, this is largely due to massive direct to consumer TV advertising, as well as claims that they are effective and safe in a wide variety of disorders for which they were originally not approved. Four out of five antidepressant prescriptions are from primary care physicians who increasingly use these drugs to treat nonpsychiatric conditions such as fatigue, nonspecific pain, smoking cessation, headaches, strange sensations and premenstrual tension.[20] Not all of these are "off label", since drug companies have managed to get FDA approval for some antidepressants to treat premenstrual dysphoric disorder, smoking withdrawal symptoms, fibromyalgia, diabetic neuropathy and chronic muscular pain. In some instances, the trade name is changed so patients will think they are receiving a brand new drug. Patients often have a tendency to assume that newer drugs will be more effective. Thus, Sarafem was approved for premenstrual problems, although it is identical to 30-year-old Prozac.

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[17] Prostate (2011) 71:1818–24
[18] Am J Epidemiol (2008) 168:250–60
[19] Health Aff. (2011) 30:1434-42
[20] Am J Psychiatry (2011) 168:1057-65

Prozac is the reason all this serotonin stupidity started. Up until the late 1950's, the only drugs to treat depression were opiates and amphetamines, and electric shock therapy was used for severe cases. The notion that depression was due to some deficiency or imbalance in brain chemicals began when a Swiss psychiatrist gave a new tricyclic chemical to 10 patients who had been disabled by deep depression for years. He was amazed to see how they became more energized and interested in their surroundings over the next three or four weeks, and tricyclic drugs like Elavil and Sinequan quickly became the first antidepressants. No one had an explanation for why they worked until several years later, when it was found that Parkinson's disease was due to a deficiency of dopamine, a brain neurotransmitter. It was speculated that depression might be due to a similar lack of some mysterious chemical in the brain but which one remained a mystery until Prozac was introduced in 1987, and promptly became wildly popular. This was not because it was more effective than trycyclics, but it had fewer side effects. More importantly, since it boosted levels of serotonin, a neurotransmitter, it was assumed that depression was due to low serotonin. People were no longer "loony"; they simply had a deficiency disease that could now be corrected. There were cover stories in major magazines, songs and books were written about it and serotonin became as familiar as Kleenex. It was a popular subject at cocktail parties, where many were taking Prozac not for depression, but rather because it made them feel happier or better in some way. There was not only no stigma attached to this, but it was also sometimes made available at such events for the curious to try. For some, enthusiasts, Prozac had the social status and safety of healthy spring water.

But there was little scientific support for all this hoopla. There were no studies that convincingly demonstrated any serotonin deficiency in depressed patients. Pedro Delgado, chairman of the Psychiatry Department at the University of Texas Health Science Center at San Antonio, depleted normal individuals of serotonin and none became depressed or had significant mood changes. Nevertheless, the serotonin hypothesis still prevails, due to persistent TV promotion of SSRIs (selective serotonin reuptake inhibitors) and because portraying depression as a deficiency disease, that can now be corrected, makes patients more willing if not anxious to take the drug – and more likely to get positive results. As previously emphasized, antidepressants are not much better than placebos in most studies. As a result, in new drug applications, **another antidepressant rather than a placebo is used as a control, since it is only necessary to show an equivalent effect in two studies.** Trials failing to show this don't have to be reported, even if there are many more.

Providing a convincing explanation can be crucial, since, as Delgado pointed out, "When you feel that you understand it, a lot of the stress levels are dramatically reduced. So stress, hormones and a lot of biological factors change." The focus on serotonin has also stifled research in other areas, although that hasn't reduced the influx of new drugs that target other neuropeptides in addition to serotonin. This shotgun approach also has no rationale to support it, and may have long-term side effects not evident in clinical trials that are frequently of fairly short duration. In a recent interview, Joseph Cole, Professor of Psychiatry and Neuroscience at Harvard Medical School and an expert in the field commented, "Chemical imbalance is sort of last-century thinking. It's much more complicated than that. It's really an outmoded way of thinking."

In that regard, a pertinent new paradigm of how communication takes place in the body at a physical/atomic rather than the current chemical/molecular level is emerging. While we think of communication in terms of neuropeptides and small chemical messengers fitting into or stimulating specialized receptor sites on cell walls, like keys in a keyhole, the ultimate stimulus to the interior of the cell is a feeble electrical signal. It has been proposed that EEG waves are not merely the noise of the machinery of the brain, but rather similar signals that are transmitted to cells much like radio waves reach receivers tuned to specific frequencies. Similarly, externally applied electromagnetic fields with certain frequencies and other characteristics may have a similar effect if they are able to stimulate sites that are "tuned in" to them. There is little doubt that various types of electrical stimulation of the brain can relieve depression, including ECT (electroconvulsive therapy), DBS (deep brain stimulation with implants), rTMS (repetitive transcranial stimulation), VNS (vagal nerve stimulation) and CES (cranial electrotherapy stimulation). Of these, CES is by far the safest, least expensive and most cost effective. It is cleared by the FDA not only for the treatment of depression, but also insomnia and pain, which are often concomitant complaints and can contribute to depression. CES has had an unblemished safety record in the U.S. for thirty years. Unlike antidepressants, which are banned in some countries because of suicidal tendencies, it is not addictive and not associated with deadly serotonin syndrome. It is so safe that it does not require a prescription in other countries. Yet its use continues to be curtailed here, and many believe this is because it is a threat to powerful drug companies. Critics complain that the mechanism of action is unknown, but that's also true for antidepressants. ECT has been used effectively for over six decades, and we still don't know why it works. The FDA is conducting a hearing on February 10 to discuss revising current CES classifications – so stay tuned for more on this.

In Memoriam: Robert Ader (1932-2011) And Wylie Vale (1940-2012)

Two giants and pioneers in stress research passed away recently. Bob Ader, who, together with Nicholas Cohen at the University of Rochester coined the tongue twisting term psychoneuroimmunology in 1975, died in December after a long illness. As his lengthy obituary in the *New York Times* noted:

His initial research, in the 1970s, became a touchstone for studies that have since mapped the vast communications network among immune cells, hormones and neurotransmitters. It introduced a field of research that nailed down the science behind notions once considered magical thinking: that meditation helps reduce arterial plaque; that social bonds improve cancer survival; that people under stress catch more colds; and that placebos work not only on the human mind but also on supposedly insentient cells. At the core of Dr. Ader's breakthrough research was an insight already obvious to any grandmother who ever said, "Stop worrying or you'll make yourself sick." He demonstrated scientifically that stress worsens illness — sometimes even triggering it — and that reducing stress is essential to health care.

Like Selye's discovery of stress, Ader's epiphany that the brain influenced the immune system resulted from a serendipitous laboratory accident. He was conducting a classical conditioning experiment in which one group of rats was given saccharine sweetened water along with an injection of a drug that caused stomach pain. A control group of littermates received only the sweetened water. After the series of injections stopped, the rats refused to drink the sweetened water, as expected, and had to be force fed with an eyedropper to complete the protocol. What was not expected, however, was that forcing the rats to continue to drink the sweetened water would eventually kill them, which it later did. He reasoned that the drug must have been responsible, and while any medication causing stomach ache without producing any other damage, he had selected Cytoxan, which is widely used to treat certain cancers because it suppresses the immune system. He thought that perhaps the rats had died from an overdose, but the amount they received was much too low, and rats receiving the identical number of injections and dosage had no problems.

He consulted Nicholas Cohen, an immunologist, who scrutinized the protocols and they hypothesized that the rats died because the taste of the sweetened water alone was able to trigger signals that suppressed the immune system just as it would have been had they been overdosed with Cytoxan. This was supported by the observation that deaths were due to

bacterial and viral infections their immune system could no longer fight off. In humans, the placebo effect fools the brain into believing it is receiving something beneficial, but this was an opposite nocebo effect. Subsequent investigations by Ader and Cohen as well as others provided solid confirmation that they were correct, and a new era of mind-body medicine and the burgeoning field of psychoneuroimmunology were born.

Bob was a good and very generous friend, and AIS Board Member who participated in and enriched our conferences. Because of my interest in stress and cancer and had written a lengthy book chapter on this that he found stimulating, he invited me to speak at the University of Rochester. It was like bringing coals to Newcastle, since Art Schmale, Howard Iker, Bill Greene, whom I had cited for their seminal contributions in this area, were in the audience. I also had the privilege of meeting George Engel, Chairman of the Department of Psychiatry, a towering figure in the field of stress. George drove me back to the airport, where we talked about his twin brother Frank, a severe critic of Selye's theories and head of endocrinology at Duke, as well as my good friend Stewart Wolf. All three of these stress superstars had been classmates at Johns Hopkins. Bob was later appointed George L. Engel Professor Of Psychiatry at the University of Rochester Medical Center, along with numerous other honors **that are listed in an attachment to this Newsletter**. A few years ago, I asked Bob why, after all this time, there were apparently no studies demonstrating the practical application of psychoneuroimmunology. Nick Cohen had expressed a similar view at one of our conferences. Bob told me to wait, since he was doing a study on psoriasis. My August 2010 Newsletter interview, the last medical article he wrote, describes this study. I was reminded of this by the following e-mail.

> Dear Paul,
> I'm sure you've heard the sad news that Bob Ader died on Dec. 20. We've both lost a very good friend and colleague. I just finished reading your interview with Bob in the AIS newsletter. I only learned about that interview after reading the University of Rochester press release/obit, which I've attached. I finally read the interview last night. The interview in the newsletter is absolutely wonderful. I can hear Bob talking when I read his words and I must say, it evokes a strong emotional response that is bittersweet.
> I've had the difficult task of writing two memoriam pieces. The first one in now in press in Brain Behavior and Immunity, the journal that Bob started. I've attached this "article" as well. Had I known about your published interview with Bob before I submitted my tribute, I would have included it as a reference. It certainly highlights Bob's legacy to science and illustrates at the end how Bob thought about the future of the field. I will see if I can add the reference when I receive the proofs.
> Warm regards,
> Nick
>
> Nicholas Cohen, Ph. D.
> n.cohen@rochester.edu
> Professor Emeritus of Microbiology & Immunology and of Psychiatry at the
> University of Rochester Medical Center

Wylie Vale, who died unexpectedly last month, may not be as well known outside of endocrine circles, but he was responsible for crucial advances in our understanding of how we respond to stress. Walter Cannon had shown the role of the adrenal medulla and adrenalin in "fight or flight" responses and Hans Selye subsequently demonstrated that his "Alarm Reaction" was due to the secretion of cortisone-like hormones from the adrenal cortex due to stimulation by ACTH from the pituitary. But what triggered the pituitary to do this was a mystery that eluded him and other researchers. In 1939, he noted that although ACTH was increased during emergencies, other pituitary hormones like the gonadotropins were suppressed, and suspected that these responses were regulated by hypothalamic factors. Selye and many others tried in vain to identify these, but it was not until 1981, that Wylie Vale was able to prove that the on-off switch for stress was CRH (corticotropin releasing hormone). Accomplishing this feat was an arduous technical challenge his colleagues described as like "trying to climb Mt. Everest". The following year, he discovered GRF (growth hormone releasing factor), which controls the body's growth, and along with his team, later identified over a dozen neuropeptides and their signaling mechanisms.

Wylie began his studies by working in Roger Gullemin's lab at Baylor in 1968, where he earned his doctorate in physiology and biochemistry. He followed Guillemin to the Salk Institute in 1970 where they continued to work together isolating the first two brain peptides and other research that led to Guillemin's 1977 Nobel Prize. In 1978, Wylie set up his own lab at Salk to pursue his quest for the elusive spark plug that initiated hormonal and neuroendocrine responses to acute stress. Following his triumphant success three years later, and subsequent discoveries, he was the recipient of numerous honors and accolades, and served as President of the Endocrine Society as well as the International Endocrine Society.

I found his *New York Times* obituary by Nicholas Wade disturbing, since it was largely devoted to the 20-year bitter rivalry between Guilleman and Andrew Schally, who shared the Nobel Prize with Guillemin. Like Vale, Schally had also worked under Guillemin at Baylor before establishing his own laboratory and staff, and it was insinuated this was because Guillemin was "loath to share credit for his lab's achievements with his younger colleagues." It went on to describe Guillemin's quotation of Freud's analysis of the Oedipus myth: "Part of any son worth his salt is planning the killing of the father he loves and taking his kingdom". I found this offensive and inappropriate, since Roger Guillemin and I have been friends since 1951, when we were both Fellows at Selye's Institute of Experimental Medicine and Surgery at the University of Montreal. I have always found him to be generous and amiable, and in his Nobel acceptance speech, he paid homage to and acknowledged the contributions of Wiley Vale and others who had

worked with him, including Schally. Since I did not know whether he had seen this obituary, I e-mailed it to him along with a note wishing him and his family a Happy New Year, and received this response a few hours later.

> Paul, Wonderful to hear from you, unfortunately on a sad occasion... we are still under the shock of that untimely passing of Wylie . Let me send you here the text of my opening remarks at the celebration we organized here at Salk for Wylie's 65th bday... 5 years ago. I think it's a good summary of RG-WV relationships over many years and it was all constructive. That obituary in the NYT by that fellow Nicholas Wade is pretty badly done / I did not like it, Betty -Wylie's wife did not like it, and I got similar words from several colleagues all over the country including Cy Bowers who, you may recall, was a member of Schally's group! ! I just finished 10 minutes ago, a 10-15 minutes phone-interview with the BBC, at their request, to be broadcasted next Friday... So there will be another point of view expressed and available to the public thru the website of the BBC. By all means, do include a text of your own re Wylie in your writings about Bob Ader - I think I met him some years ago- Psychoneuroimmunology is a fact and a field...
> Well, Happy New Year to you, too... Please keep in touch... Best regards / RG

The Times obituary was clearly an inaccurate and biased portrayal of Guillemin-Vale personal relationships, which reminded me of Mark Twain's comment, " If you don't read the newspaper, you are uninformed. If you do read the newspaper, you are misinformed." (This is particularly true for media reports on new and exciting "breakthroughs" for treating cancer and other deadly diseases.) Roger later sent me a book recently written by his 25-year-old grandson that he thought I might enjoy, since it covered topics frequently discussed in these Newsletters. As an old saying goes, "The apple never falls far from the tree". It was so authoritative and well written, I was tempted to include parts of it as an attachment along with Nick's elegant obituary, but decided a book review would be preferable — so stay tuned!

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

Health and Stress
The Newsletter of
The American Institute of Stress
124 Park Avenue Yonkers, NY 10703
ANNUAL SUBSCRIPTION RATE:
E-Mail.....$25.00

ISSN#108-148X

PAUL J. ROSCH, M.D., F.A.C.P.
EDITOR-IN-CHIEF
www.stress.org
e-mail: stress124@optonline.net