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Number 9 1994

SEVENTH INTERNATIONAL MONTREUX CONGRESS ON STRESS

February 19 -24, 1995 Grand Hôtel Excelsior, Montreux, Switzerland

Plenary Sessions on Stress and Depression, The Evolution of Global and Coronary Prone Type A Behavior, Clinical Applications of Psychoneuroimmunology, International Labor Organization Survey of Job Stress Around the World, Advances in Occupational Health Promotion and Stress Management. Stress Reduction Workshop Featuring Oriental Approaches, Stress and Subtle Energies (aromatherapy, touch, massage, biomagnetic influences, imagery), Post-Traumatic Stress Disorder. Presentation of Hans Selye Award to Ray H. Rosenman, M.D. Round Table Discussion with other Award Recipients on "Stress and Quality of Life" (Stewart Wolf, Bjorn Folkow, Jim Henry, Yujiro Ikemi, Lennart Levi, Joel Elkes). Registration Limited.

The Session on Depression at our 1995 Congress will emphasize novel therapies that influence specific neurotransmitter activities. Some are also effective in phobic, addictive, eating, and other stress related disorders. Could all these conditions share some common neurohumoral characteristics? This Newsletter will explore the disturbing dimensions of depression, and how new treatment approaches have evolved.

The Hidden Toll of Depression

Depression is a major health problem that is estimated to affect more than 40 million adults in the United States. In a National Center for Health Statistics survey, more than one out of five respondents reported being significantly depressed, bored, lonely, restless, or upset, in the preceding two weeks. The majority had more than one of these symptoms of depression that interfered with their daily activities, and 5% complained of 3 or more. Men were slightly more likely to list being restless, while feeling lonely or upset was more common in females. Depression predisposes to unhealthy lifestyles and behaviors, and there was a clear correlation with drinking and smoking habits. Only 5% of men reporting no symptoms of depression had three or more drinks a day, compared to 10% of those who were often

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lonely, restless, or bored. Depressed women were more than twice as likely to be smokers as their more content counterparts.

In addition to direct effects on quality of life, depression appears to contribute to coronary heart disease, and is associated with a poorer prognosis following a heart

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attack, as reported in prior Newsletters. It also significantly affects health by causing serious disturbances in sleeping and eating patterns, which can impair immune system defenses. An apathetic attitude often prevents depressed patients from recognizing the signs and symptoms of other illnesses, or seeking medical attention in a timely fashion. Although figures were not available for adolescents and children, depression is a growing problem in these age groups, and the major cause of the alarming increase in teenage suicides.

Unfortunately, the diagnosis of depression is often overlooked by primary care physicians, who are frequently the first and sometimes the only health care professionals to treat such patients. As indicated in the 1993 Agency for Health Care Policy and Research report "Depression is under diagnosed and under treated by primary care and other non-psychiatric practitioners, who are, paradoxically, the providers most likely to see these patients". This survey revealed that close to 1 out of 10 of all primary care outpatients suffer from major depression, but that only one-third to one-half were correctly diagnosed by primary care doctors. The incidence may be even higher, since because there may be some stigma attached to mental illness, depressed patients are often coded or listed as having a different diagnosis. In addition, "if a patient is coded as depressed, physicians receive only 50% reimbursement, compared with 80% for other conditions".

There is growing evidence that the majority of depressed patients may suffer from a biochemical disorder over which they have little control, much like abnormalities in insulin production or utilization in diabetics. However, a National Institute of Mental Health study revealed that close to 3 out of 4 Americans believe that mental illness is purely an emotional disorder, and almost half think that the problem is entirely the patient's fault. More than 1 out of 3 actually feel that depression is "sinful", and possibly a punishment for past transgressions, representing a reversion to a notion that was prevalent in the past.

What Causes Depression?

Until very recently, our understanding and attitude about psychiatric disorders, had been largely shaped by the 17th century French philosopher, René Descartes. He viewed the body as an intricate machine, similar in nature to the marvelous multifunctional, complicated clocks that were popular at the time. Physical illness resulted from a malfunction of one of the mechanical parts of this complex contrivance. Therefore, finding and fixing the problem, could best be accomplished by a greater knowledge of the smaller working components of this contraption, and this was the doctor's function. Disorders of the mind, he reasoned, were entirely separate from this, and far beyond man's ability to comprehend or study. In addition, mental illness might represent a punishment from the Almighty, and was therefore more properly under the jurisdiction of the church, to be treated by priests, rather than physicians.

Many of the terms we still utilize to describe mental illness have roots that go back to antiquity. Hysteria was first used by Hippocrates over two thousand years ago to describe abnormal behavior, headache, and vague abdominal complaints in unmarried Greek women. It derives from hysterikos, the Greek work for uterus. Hippocrates believed that such problems were caused by an unnatural state of sexual abstinence, which caused the womb to wander throughout the body in search of satisfaction. The cure for hysteria was to get the uterus to stop its roaming and return to its proper position and alignment in the pelvis. To accomplish this, sweet smelling balms and herbs were placed at the vagina, and noxious, disagreeable potions were positioned at the nostrils, to coax the womb back where it belonged, possibly one of the earliest attempts at aromatherapy. The ancient Greeks also believed that good health depended on the proper amounts and bal-

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ance of the four cardinal body elements or humours: blood, phlegm, yellow bile, and black bile. *Melancholy*, is derived from the Greek words for black bile (*mélas chole*). Galen, believed that an excess of black bile caused depression in females, and made them more prone to malignancy of the breast and uterus.

Lunatics, Werewolves and PMS

The monthly menstrual, moon, or lunar cycle, was also believed to be responsible for many emotional and mental aberrations observed in females, giving rise to the term lunatic. Later, this was applied to both sexes, with folklore accounts of bizarre or violent behaviors associated with the advent of the full moon. The most popular of these was Lycanthropy (Gr. lucus, wolf + anthropos, man), in which an apparently normal person assumed the form and characteristics of a wolf, or lycanthrope (wolfman). In England, these were called werewolves, from the Old English wer, man + wulf, wolf. Lycanthropy also refers to any psychosis where victims believe they can turn into other animals. Such notions were widespread in Medieval times, along with the superstition that affected individuals would crave or require human flesh or blood, when they became transformed into werewolves or vampire bats.

A female predisposition to mental illness, has prevailed in folklore for centuries. Almost 3,000 years ago, in the Khun Papyrus, the ancient Egyptians described "a woman aching in all her limbs, with pain to the sockets of her eyes", a not uncommon hysterical complaint that has been echoed over the centuries. It was generally presumed that only women suffered from hysteria or hypochondria, despite Thomas Sydenham's 1682 dissertation demonstrating that these also occurred in males, although he attributed this to some disturbance in animal spirits. However, women do seem more prone to depression, and there may be several reasons for this.

Hormonal factors may play a role, as suggested by certain symptoms often seen in association with the menstrual cycle, such as premenstrual syndrome (PMS), following childbirth (post partum depression), and the deep depression that often accompanies the menopause (involutional melancholia). Women may also be more sensitive to uncomfortable emotional feelings and somatic symptoms, and more willing to admit their existence then men. More importantly, they are more apt to seek medical attention for them. Macho males who are melancholy are more likely to brood over their misfortunes. Everyone knows that "Big Boys Don't Cry".

Treating Insanity and Exorcism

Some individuals suffering from mental illness were also viewed as having a disturbance in the health, or sanity, of their mind, and were described as having an "insanitie of mind". This subsequently was simply referred to as "insanity". It soon became apparent that this could have important legal repercussions with respect to the validity of wills and other documents executed by mentally disturbed individuals, as well as their legal responsibility for criminal acts. As a result, such individuals increasingly came under the influence of the the judicial system and courts in England. It was felt that in many situations, there was a need to isolate them from society, and hospital facilities or lunatic asylums for the criminally insane were established. As these grew in size and number, they tended to be regulated more by physicians than priests. One of the first of these was The Hospital of St. Mary of Bethlehem in London. Originally founded in 1247 as a priory, it became a hospital for the mentally ill in 1402, and was rebuilt in 1676 near London Wall under government auspices. It was renamed the Bethlehem Royal Hospital, but since this was a mouthful, it was better known by the slurred contraction, Bedlam. Its disturbed inmates were exposed to public view, and some sense of the state of affairs that must have existed may be gained by appreciating that bedlam is the word we still use to refer to an uncontrolled state of generalized uproar, characterized by noise and confusion.

Emotionally disturbed individuals were often presumed to be "possessed" by the devil, or some demon (Gk. daimon, divine power). This was a part of Buddhist beliefs and many other cultures and religions. The only cure lay in the ability to expel or expunge the evil supernatural spirit from the body. The New Testament recounts Christ's ability to drive out such devils, and it was assumed that only a priest, especially trained in exorcism, could accomplish such a feat. This often required the recitation of very specific incantations or adjurations, along with the sprinkling of holy water, burning incense, the prominent display of religious symbols such as a cross or relic from a saint, and various combinations of these, depending on the situation and the experience of the exorcist. Such rites are still practiced all over the world, and are endorsed by many religions, including the Catholic Church, which regulates this practice.

The treatment of mental illness was frequently (Continued on page 4)

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bizarre and cruel. Insane asylum patients were often chained, restrained, abused or even tortured, presumably in an attempt to rid them of evil spirits. This persisted well into the last century, but gradually improved due to the efforts of Phillipe Pinel, a French physician who was in charge of the mentally ill at the Saltpérière Hospital in Paris. He insisted in 1791 that all chains be removed, and classified mental illnesses into four forms, pleading that its inmates were victims of disease, and should be given the same type of humane treatment given to patients with other illnesses. In 1520, the Swiss physician and alchemist, Paracelsus, who rejected Galen's humoral theory of disease, had previously postulated that psychiatric disturbances were not due to demonic possessions, but were natural diseases. However, Robert Burton's popular Anatomy of Melancholy, published 100 years later, still clung to the old beliefs, and in 1773, George Chyne's The English Malady, a term commonly used to refer to depression, attributed this disorder as resulting from sins such as gluttony and intemperance.

Contemporary Concepts of Depression

Our appreciation, classification, and treatment of emotional disorders, continued to be relatively primitive until the present century, and the advent of psychiatry as a medical specialty. Sigmund Freud and others emphasized childhood experiences, sexual, and hereditary influences, as important causes, arguing that depression could best be diagnosed and treated by hypnosis or psychoanalysis. Various attempts at classification were made based on possible causes, symptoms, or clinical course. Kraepelin first observed that many depressed patients followed a clinical course quite similar to others who had initially presented with a manic mood. In 1921, he postulated that mania and depression were components of a single disorder. He termed this manicdepressive insanity, to distinguish it from the depression of dementia praecox, or premature dementia, which Bleuler later termed schizophrenia. The term dementia comes from the Latin demens or madness, and was assumed to be an irreversible deterioration of mental faculties with accompanying emotional disorders. This classification was widely accepted for four decades, until Kendall suggested replacing the term manic-depressive insanity with bipolar disease to minimize the confusion that currently existed. There have been further attempts at subclassifications of bipolar disease,

depression, and mania, but none have significantly improved our understanding of the causes, prognosis, or optimal treatment for these symptoms.

It was not until very recent decades that specific biochemical disturbances were demonstrated to play a major role in depression, and appropriate drugs were developed to address specific abnormalities. Depression may be a manifestation of many different psychiatric and physical disorders, and is really more often a description than a discrete diagnosis. Most depression appears to be associated with disturbances in the limbic system, and particularly the hypothalamus, the site of origin for most neuroendocrine activities and responses to stress. The hypothalamic-pituitary-adrenal cortex axis is primarily activated by stress, and elevated plasma cortisol and ACTH are also commonly observed in depressed patients. Cortisol levels do not show the normal suppression seen following the administration of corticosteroids in many of these individuals, and this forms the basis for the dexamethasone suppression test (DST) for endogenous depression. Many manic and depressed patients also exhibit elevated thyroid hormone levels and abnormal responses to thyrotropinreleasing hormone (TRH). It is likely that other hypothalamic-pituitary-target organ axes may also be involved. As noted previously, depression in women has long been linked to fluctuations in sex hormones in association with the menstrual cycle, giving birth, or the menopause.

Current Treatments for Depression

The modern treatment of depression has evolved through pure serendipity and trial and error, rather than any scientific rationale. The finding that symptoms of depression appeared to improve in epileptics following seizures led to Electroconvulsive Shock Therapy in the thirties, along with the use of metrazol to induce seizures, and insulin to produce coma. A decade later the observation that treatment of tuberculosis with isoniazide often relieved associated symptoms of depression led to the development of imipramine (Tofranil) and other monoamine oxidase inhibitors. Along with Thorazine and other drugs, these proved so successful in treating various mental disorders, that tens of thousands of patients were rapidly released from institutions and returned to society, despite years of poor response to other treatments. This led to a focus on the role of abnormal brain neurotransmitter activities in depression, and attempts to correct these with newer tricyclic

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and tetracyclic drugs that influence concentrations of serotonin, dopamine, norepinephrine, and more recently, selective serotonin reuptake inhibitors. Alterations in melatonin secretion are also associated with depression, particularly in Seasonal Affective Disorder, (SAD). The significant benefits of light therapy in SAD and other types of depression, and improvement of depression following weak cranioelectric stimulation, has increased interest in the therapeutic potential of such subtle energies. The beneficial effects of lithium may be due to its ability to decrease sensitivity to light.

Electroconvulsive therapy is the oldest and probably the most effective treatment for severe depression, further suggesting that disturbances in the brain's electrical activity may play a crucial role in depression. Epileptic seizures were originally treated by stress reducing agents such as barbiturates and bromides until the advent of phenytoin (Dilantin). Although this was the first specific anticonvulsant, it was paradoxically also noted to improve mood and behavior in many depressed patients, and also benefited patients with arrhythmias and other electrical disturbances in the heart. Since then, newer anticonvulsant drugs like Depakote, which promote electrical stabilization in the brain, have been found to be much more effective for the treatment of bipolar disease, and may point the way to superior forms of therapy.

Some Practical Considerations

While mild and non-chronic depression may respond to psychotherapy, medical treatment is indicated for most patients with persistent or disabling depression. The problem is that many patients don't want to take drugs indefinitely, the response to antidepressants is erratic and delayed, side effects occur in at least half the cases, and in 1 out of 5 patients, make it necessary to stop treatment. Government guidelines suggest that "doctors use two trials of drugs, before bringing a mental health professional into a case". Because of the emphasis on cost containment, especially in managed care settings, there is also now a concerted effort to encourage doctors to use less expensive antidepressants first. The newer drugs may cost 20-30 times more, and last year, more than 2 million dollars was spent on Prozac alone, although its use over 8 to 10 months is a lot less expensive than psychotherapy, and often more effective. In addition, most patients tend to show a response to newer drugs within 2 to 3 weeks, with complete remission in 6 to 8 weeks, which is about twice as fast as with previous treatment. This problem is of particular importance in senior citizens, since elderly people are particularly prone to depression and suicide, as well as the side effects of older drugs. However, Medicare pays only half of an already discounted fee for that diagnosis, and as one doctor complained, "physicians who treat Medicare patients for depression are earning less than their overhead".

The situation is even worse when it comes to prepaid plans, and the Communications Director of the National Alliance for the Mentally Ill's concluded that "all HMO's are pretty pathetic when it comes to psychiatric benefits". A Rand Corporation study also confirmed that patients treated for depression in prepaid insurance groups, had worse outcomes than those in fee for service plans. Despite that fact that depression is often chronic, patients in these plans show a sharply reduced use of antidepressants after two years, compared with fee for service patients. While this may result in short term savings, the cost of depression to the health care system is so staggering, that most authorities feel that current practices must be revised to reduce the unavoidable excessive financial burden. A significant percentage of depressed patients fail to recognize that their condition is chronic, and stop medications once their symptoms improve. However, there is a 50% chance of recurrence after one episode, a 70% relapse after two, and in patients who have had 3 episodes, the chances are 9 out of 10 that the condition will recur if treatment is discontinued.

According to the most comprehensive nationwide study ever taken, almost a third of the 8,000 adults surveyed had experienced some psychiatric problem in the preceding year. Major depression was at the top of the list, especially in women, followed by alcohol dependence. Depression is common to all races, ages, and ethnic groups. The average age of onset is in the late twenties, with episodes generally lasting six months or longer if not treated. In addition to the tremendous costs to the health care system, 50% of patients with severe clinical depression eventually take their own lives and at least 60% of all suicides can be attributed to depression.

In 1990, close to 44 billion dollars was spent in direct and indirect costs for the treatment of depression. This is more than was spent for the treatment of coronary heart disease, and this figure is expected to surge sharply over the next five years. Some appreciation of this trend can be gained from noting that sales of antidepressants alone was 610 million dollars in 1989, 900 million dollars in 1992, and is expected to reach 2.2 billion dollars by 1999!

Is Prozac the Antidote to Stress?

In 1932, Aldous Huxley's Brave New World was published. It was a satirical novel portraying life in a utopian 25th century society where everyone was always happy, although they seemed more like robots than people. Each individual was delighted with their occupation and social status, since they had been brainwashed since birth to believe it to be ideal for them. Free love was abundant, and there were none of the problems associated with child rearing or family squabbles, and the population was replenished by the artificial incubation of selected embryos, rather than childbirth. All sorts of innovative and delightful amusements were readily available, such as three dimensional chess and golf. Motion pictures, referred to at the time as "the talkies", because of the advent of sound, had now been replaced by "the feelies". These allowed the audience to grasp two metallic spheres attached to their seats, and not only observe what was taking place on the screen, but instantly experience the sensations and feelings of the characters they were watching. (The Adventures Of The Great White Sperm Whale was a big box office hit.) There were no problems at work, no problems at home, no need to worry or think, and lots of free time to enjoy all sorts of pleasures. However, in the event that something did go wrong, any problem could quickly be alleviated by taking a magical pill called soma. Soma, not to be confused with a muscle relaxant with the same name developed decades later, was a true panacea. It instantly induced a pleasurable state that replaced any unwanted feelings of anxiety, fear, phobia, boredom, sorrow, or stress, without any hangover or side effects.

Many proponents believe that such a pill already exists in the form of Prozac, one of the new generation of antidepressant medications that seems to have spawned a legal drug culture. Prozac users have their own computer bulletin board on Internet, where they compare experiences, and last February, the familiar green and white pill made the cover of Newsweek. Listening to Prozac, quickly made the best seller list and has remained there, as its physician author appeared on top talk shows, touting the miracles that have been attributed to this medication. As a result, doctors are now writing well over 1 million prescriptions a month for Prozac, not only for depression, but a variety of "cosmetic" applications, ranging from phobias, fatigue, insomnia, and difficulty in concentrating, to various mood disturbances, and eating disorders. In one report, it was successful in alleviating such complaints in close to 3 out of 4 patients after only 8 weeks, compared to less than 1 in 5 for placebos. Almost 90% of these had failed to respond to other treatments. Prozac appears to be as effective as psychotherapy in obsessive-compulsive disorders such as excessive hand washing and other ritualized acts, and is approved for this and bulimia in Europe. Sophisticated brain scan studies confirm improved rates of glucose metabolism in specific areas of the cerebral cortex believed to be involved in these disorders. The drug acts by affecting serotonin metabolism, and related medications, such as Zoloft and Paxil, appear to provide similar benefits.

That it is not a placebo is also confirmed by its increasing use by veterinarians, who have given it to depressed puppies and feather-picking parakeets. One five year old dog suffering from "tail chasing mutilation disorder" had failed to respond to conventional treatment, and his distraught owners were advised that the only solution appeared to be amputation of the tail. However, after five days on Prozac, the pooch was a "much more mellow, less restless patient" and after five weeks, was completely cured. As his vet noted, "I had literally saved my patient's tail", and he now also prescribes it for resistant skin disorders. Critics claim that this is a band-aid approach, and that the proper treatment is to find the source of the problem and eliminate it. The Church of Scientology, which is vigorously opposed to Prozac and other mind altering drugs goes much further, warning that Prozac could make pets go "psycho". They describe it as a "killer drug" that has been linked to murder and suicide, although there is little to support this.

Not everyone is on the Prozac bandwagon. A physician who co-authored the book, Talking Back To Prozac, pointed out that the FDA itself does not conduct any of the studies that are used for drug approval. These are financed and supervised by drug companies, who also select the types of patient to be treated, as well as the physicians and statisticians. He claims that only 63 patients were followed for more than 2 years before Prozac was approved, that suicidal and hospitalized patients were excluded, and many in the study were allowed to continue tranquilizers and sedatives to counteract the stimulant effects sometimes seen with Prozac, making it difficult to interpret the data. Although the total number of patients in all the trials was close to five thousand, the actual number who finished the 4 to 6 week period required for approval turned out to be only 286. In addition to this very high drop-out rate, one study

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showed that Prozac proved no better than the placebo. Although the 3 other trials that were used showed it to be somewhat superior to placebos, it was actually less effective than older antidepressants. Because of the high dropout rates, he also claims that the statistics were massaged to make the studies look more positive. For example, in one of these which involved 6 different locations around the country, 5 showed Prozac to be no better than placebo. One of these, which represented 25% of the patients who had finished the trials, was discarded and the data from the remaining sites was then pooled, although this is a scientifically unacceptable practice that the FDA prohibits drug companies from using to support advertising claims. However, the FDA did allow it in this case, otherwise, Prozac would not have been approved.

If the FDA studies showed that Prozac was largely ineffective, why has it become so popular? One explanation is that controlled studies show that placebos can be highly effective in relieving depression. When a drug achieves widespread publicity and numerous testimonials, it becomes a social fad, and its placebo powers are then magnified tremendously. However, the efficacy of the drug in animals, and the observation of relevant objective effects on imaging studies would appear to rule out this suggestion. Another possibly more disturbing reason for Prozac's popularity, which has been suppressed, is that it acts very much like a stimulant, such as the amphetamines and cocaine. Side effects can include nervousness, anxiety, agitation, insomnia, nightmares, sweating, anorexia, weight loss, diminished sexual drive, and occasionally, a manic state. Although the FDA's evaluation confirmed that it acts like a stimulant drug, for some curious reason, this never appeared in its published conclusions.

Stimulant medications have always been popular with the American public, as well as physicians. During the 1960's, amphetamines were prescribed in even greater amounts than Prozac, and for similar symptoms of depression and fatigue. Even Sigmund Freud, who became hooked on cocaine, wrote glowing testimonials about how it markedly improved his personality, without any adverse side effects. For many other individuals, Prozac may be beneficial because it insulates them from the rest of the world, and real life problems. This allows a tolerance for circumstances which would normally be troublesome, because they do not meet their needs or fulfill their goals.

Although he experimented with mind altering drugs like mescaline, Aldous Huxley had no illusions about

these being the answer to society's problems. His final novel, *Island*, published in 1963, the year he died, reflected his growing interest in Eastern philosophies, and his portrait of an ideal society was quite different than *Brave New World*. Healing relied on the powers of the mind, learning came from the power of critical observation and imagination, comfort was furnished by extended families who provided social support, and commercial interests were subservient to ecological concerns. Although Prozac, like its prototype panacea soma, can induce a state of euphoria, could it and its congeners contribute to the appallingly dehumanized culture Huxley originally portrayed.

Celebrated artists, writers, composers and other geniuses seem to suffer from higher rates of depression and mental disorder. While Prozac may improve these symptoms, could it suppress their creative spark. As one worried writer whose depression had been eased by Prozac commented, "Let's talk about Vincent Van Gogh on Prozac. He'd still have both his ears, and he would probably be painting trees and Bambi. Beethoven would have been writing commercial jingles. He would have gone deaf, and he wouldn't have cared."

Additional information on depression can be obtained by calling The National Depressive and Manic-Depressive Association, (800) 826-3632, The Depression Awareness, Recognition and Treatment Program at the National Institute of Mental Health, (800) 421-4211, and The Information Clearing House for The National Institutes of Health, (800) 358-9295. This Newsletter is partially based on articles which appeared in the following publications: Wall St Journal, 11/26/93 American Medical News, 12/6/93, N.Y. Times, 12/13/93, Postgraduate Medicine, February 1994, American Health, May, 1994, Wall Street Journal, June 24, 1994, Psychology Today, July/August 1994, ACP Observer, July/August, 1994, AARP Bulletin, Sept. 1994

All his life he suffered spells of depression, sinking into the brooding depths of melancholia, an emotional state which though little understood, resembles the passing sadness of the normal man, as a malignancy resembles a canker sore.

William Manchester

The Last Lion: Winston Spencer Churchill

When you are down and out, something always turns up - and it's usually the noses of your friends.

Orson Welles

Book Reviews • Meetings and Items of Interest

Book Review

Central Nervous System Peptide Mechanisms In Stress And Depression, Risch, S.C. ed., American Psychiatric Press, Washington, 1991, 128 pgs., \$29.00

Although this volume was published three years ago, it provides a comprehensive glimpse into the neuroendocrine abnormalities associated with depression and other stress related disorders. The central role of Corticotropin Releasing Factor (CRF) in mediating many of these, including anorexia and Alzheimer's disease, is clearly outlined, and suggests the therapeutic potential of novel pharmaceutical agents acting as CRF agonists and antagonists. This is supported by chapters devoted to clinical and experimental animal research, as well as careful measurements of CRF in the brain and cerebrospinal fluid under varying conditions. Of particular interest is the chapter dealing with the effects of stress and depression on immune system function, which suggests that these influences are mediated by CRF and hypothalamic-pituitary activities, as well as endogenous opioids. While the purpose of this volume was admittedly to emphasize the prime role of the limbic hypothalamic-pituitary-adrenal axis, it is regrettable that little discussion was devoted to the important role of serotonin, dopamine, melatonin and other neurotransmitters that contribute to or are at least associated with various forms of depression. The Figures and Graphs are helpful and of fairly good quality. However, a serious defect is the complete absence of any index, which makes cross referencing difficult and time consuming, and is a puzzling departure from the other valuable contributions to this Progress in Psychiatry Series.

Meetings and Items of Interest

Oct. 6-9 7th National Conference on Professional Well-Being, Being Well: Self Care for Health Care Reform, Ritz-Carlton Hotel, Dearborn, MI, call (800) 473-5880 Oct. 6-9 Women's Imaging II: Includes Imaging of the Menopausal Woman, Western Pennsylvania Hospital - U. of Alabama at Birmingham, Ritz-Carlton Hotel, (Tyson's Corner, VA) Washington, D.C., call (404) 641-9773

Oct. 6-9 9th Annual Meeting: Cardiovascular Rehabilitation, Pulmonary Rehabilitation, American Association of Cardiovascular and Pulmonary Rehabilitation, call (608) 831-6989

Oct. 6-9 Addiction Psychiatry Board Review Course, Osler Institute, Chicago, IL, call (800) 356-7537 ext. 200

Oct. 7-8 Coronary Heart Disease Update, Medical Education Resources, Sheraton Desert Inn, Las Vegas, NV, call (303) 798-9682

Oct. 15-16 Update in Cardiovascular Diseases, Mayo Foundation, Mayo Clinic Campus, Rochester, MN, call (800) 323-2688

Oct. 20-25 Clinical Training in Behavioral Medicine, Harvard Medical School Dept. of Continuing Education, Children's Inn, Boston, MA, call (617) 432-1525 Oct. 27-30 First International Conference on Prevention, World Health Organization and Others, Charleston, WV, call (304) 342-1200

Oct. 29 Geriatric Healthcare: Clinical Perspectives in Natural Medicine, Delta Orlando Resort, Orlando, FL, call Elaine Zouzas at Uniglobe of info, (800) 229-8076 or (508) 250-1771

ISSN # 1047-2517



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