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Bipolar Disorder and Pregnant Women

ABSTRACT & COMMENTARY

Source: Viguera AC, et al. Risk of recurrence of bipolar disorder in pregnant and nonpregnant women after discontinuing lithium maintenance. *Am J Psychiatry* 2000;157(2):179-184.

Bipolar disorder (manic-depression) affects 1-3% of the population. It is a life-long condition with an age of onset that frequently overlaps with the reproductive years. First trimester exposure to all of the established mood stabilizers (lithium, valproate, and carbamazepine) is associated with an increased risk of fetal malformations. As such, many women with bipolar disorder choose to discontinue these and all other medications during pregnancy and while trying to conceive.

However, recurrent acute illness (mania or depression) may pose an even greater threat to the fetus, and is certainly detrimental to the patient. Many patients and clinicians believe that pregnancy is protective. To address this important issue, Viguera and colleagues retrospectively compared recurrence rates for 101 women with bipolar disorder during pregnancy and postpartum or during equivalent time period for age-matched nonpregnant women, following discontinuation of lithium maintenance treatment. Rates of recurrence during the first 40 weeks after lithium discontinuation were similar for pregnant (52%) and nonpregnant women (58%). Recurrence rates were much lower for both groups in the year before lithium discontinuation (21%). Among women who remained stable during the first 40 weeks after lithium discontinuation, postpartum recurrences were 2.9 times more frequent in the nonpregnant women over the same time period (weeks 41-64), 70% vs. 24%. Recurrence rates were greater after rapid than gradual discontinuation.

COMMENT BY LAUREN B. MARANGELL, MD

Viguera and colleagues provide extremely important information that should be used to guide treatment decisions in collaboration with women with bipolar disorder who are planning to become pregnant. There is a common misperception that pregnancy is protective,

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which is clearly not the case in the current cohort. Although this was a retrospective review, an appropriate control group was included. Over the 64-week period following lithium discontinuation, recurrences occurred in 85.71% of the pregnant/postpartum women, and 67.80% of the nonpregnant women. The markedly high recurrence rate in the postpartum period is noteworthy. Many patients and clinicians understandably prefer to avoid fetal exposure to medications. However, the current data indicate that a careful risk-benefit analysis is imperative. For women with more severe episodes, the adverse consequences of recurrence may outweigh the risk of ongoing medication. Consistent with previous data, the recurrence rate with a gradual taper (15-30 days) was less than with abrupt discontinuation, but still 37.14%. When planning pregnancy, if the woman decides to discontinue medication, a gradual taper is recommended. Unplanned pregnancy is more of a challenge, and the decision regarding discontinuing medication, and if so how rapidly, should be made with consideration of gestational age. A nonteratogenic mood stabilizer is urgently needed. ❖

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VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.

EDITORIAL GROUP HEAD: Glen Harris.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

ASSOCIATE MANAGING EDITOR: Robin Mason.

ASSISTANT MANAGING EDITOR: Neill Larmore.

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Customer Service E-Mail Address: customerservice@ahcpub.com

Editorial E-Mail Address: neill.larmore@medec.com

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Psychiatric Drug Combinations and the Serotonin Syndrome

ABSTRACTS & COMMENTARY

Sources: Hamilton S, Malone K. Serotonin syndrome during treatment with paroxetine and risperidone. *J Clin Psychopharm* 2000;20(1):103; Smith DL, Wenegrat BG. A case report of serotonin syndrome associated with combined nefazodone and fluoxetine. *J Clin Psychiatry* 2000;61(2):146.

Serotonin syndrome characterizes a constellation of symptoms that occur in the presence of excess central serotonergic activity. Prominent symptoms include mental status changes, restlessness, myoclonus, hyper-reflexia, agitation, diaphoresis, shivering, tremor, diarrhea, and autonomic instability. Hamilton and Malone report the first case of serotonin syndrome associated with the selective serotonin reuptake inhibitor (SSRI) paroxetine (Paxil) and the atypical antipsychotic risperidone (Risperdal).

The patient was a 53-year-old Hispanic man with psychotic depression. After failing treatment with nortriptyline and haloperidol, he was switched to risperidone 3 mg/d and paroxetine 20 mg/d 10 weeks prior to presentation. After the medication was increased to paroxetine 40 mg/d and risperidone 6 mg/d, the patient experienced ataxia, tremor, shivering and bilateral jerking movements, and a change in mental status, which was characterized as confusion and subsequently lethargy, followed by autonomic instability. Laboratory tests were unremarkable and no other etiology was found. Symptoms resolved within two days of medication discontinuation.

Smith and Wenegrat report the case of a 50-year-old man with major depression who developed serotonin syndrome on a combination of nefazodone (Serzone), a 5HT2 antagonist, and fluoxetine (Prozac), an SSRI. The patient had been taking fluoxetine, 60 mg/d. He was to be switched to nefazodone due to sexual dysfunction. Nefazodone was taken concurrently with fluoxetine 40 mg/d for six days, at which time he was admitted to the hospital with symptoms of lethargy, inattention, ataxia, disorientation, vomiting, myoclonus, and visual hallucinations. Concomitant medication included alpha interferon for multiple myeloma. Other etiologies were ruled out and the patient was given a presumptive diagnosis of serotonin syndrome. Smith and Wenegrat note a prior report of serotonin syndrome associated with nefazodone and fluoxetine.

COMMENT BY LAUREN B. MARANGELL, MD

Life-threatening serotonin syndrome is fortunately a rare event and most often occurring with medication combinations involving monoamine oxidase inhibitors. As with most syndromes, there is a spectrum of severity. Mild serotonin syndrome has been reported to occur even with SSRI monotherapy. However, the syndrome is more likely to occur in the presence of multiple serotonergic agents. This is of critical importance because combination treatment is becoming more commonly used. Treatment for serotonin syndrome is generally limited to supportive care and most symptoms tend to improve following medication discontinuation. As Hamilton and colleagues note, paroxetine (and fluoxetine) inhibit cytochrome P450 2D6, which may result in increased plasma risperidone levels. ❖

Does Prior Use of a Benzodiazepine Predict a Negative Response to Buspirone?

ABSTRACT & COMMENTARY

Source: DeMartinis N, et al. Prior benzodiazepine use and buspirone response in the treatment of generalized anxiety disorder. *J Clin Psychiatry* 2000;61:91-94.

Very little is known about predictors of positive or negative outcomes for anxiolytic treatments. It has been hypothesized that significant psychic anxiety predicts a response to serotonergic drugs and somatic anxiety predicts a response to benzodiazepines.[1-2] In addition, a preliminary report suggested that prior treatment with a benzodiazepine might predict a reduced response to buspirone[3] for several reasons: 1) patient perception that buspirone is ineffective (i.e., the former works fast, may induce a mild euphoria, and causes a potentially welcome sedation); 2) buspirone is initiated in the midst of withdrawal from the benzodiazepine; and 3) a selection bias (i.e., a patient who fails the benzodiazepine may be more likely to fail a subsequent treatment because of being treatment-resistant or -refractive).

DeMartinis and associates examined a large data set that consists of pooled results from all placebo-controlled studies for buspirone's application for general anxiety disorder (GAD), including data on prior benzodiazepine use. They hypothesized that remote benzodiazepine use would have significantly less effect on the anxiolytic response of buspirone than recent benzodiazepine use, and that patients with no prior use would achieve the highest overall response to buspirone.

The data set included eight double-blind, placebo-controlled studies for patients diagnosed with GAD by semi-structured interviews. Each study used a one-week, single-blind placebo washout period before randomizing patients to four weeks of buspirone (< 30 mg/d), diazepam (< 30 mg/d), or placebo; the average dose of the drugs was 20 mg/d. Evaluations were done at weeks 1, 2, and 4 with the Hamilton Rating Scale for Anxiety. For the purposes of the analysis, patients were placed into one of three groups: 1) no prior benzodiazepine use within five years; 2) remote benzodiazepine use, defined as use discontinued more than one month prior to the study; and 3) recent benzodiazepine use, defined as within a month of the study. No baseline differences were found in terms of age, gender, and age of onset and severity of GAD for the buspirone, diazepam, or placebo groups. Buspirone patients in the recent benzodiazepine group dropped out of the study significantly more than those with remote benzodiazepine or no prior benzodiazepine groups (42% vs 21% vs 27%). No differences in attrition occurred between the recent, remote, and no prior benzodiazepine use for those randomized to the benzodiazepine or placebo groups. Buspirone patients in the recent benzodiazepine group also reported significantly more adverse events than those with remote benzodiazepine or no prior benzodiazepine use. Once again, the same was not true for those randomized to the benzodiazepine or placebo groups. Finally, buspirone patients in the recent benzodiazepine group had insignificant efficacy in terms of anxiety and overall clinical global improvement vs. placebo compared to those with remote benzodiazepine or no prior benzodiazepine use. Patients randomized to benzodiazepine did significantly better than placebo regardless of recent, remote, or no prior use of a benzodiazepine. Patients randomized to placebo did significantly poorer than the treatment groups (except for those on buspirone who had had recent benzodiazepine use). DeMartinis et al concluded that this study confirmed the hypothesis that recent benzodiazepine use negatively predicts outcome with buspirone for GAD. This retrospective study cannot rule out benzodiazepine withdrawal as a mediator of these results, but it can rule out the potential effect of initial treatment failure with a benzodiazepine as an indicator of a treatment-resistant or -refractive population, since they responded as well or better upon being randomized to a benzodiazepine in this study.

COMMENT BY DONALD M. HILTY, MD

There is no clear explanation for why recent benzodiazepine use negatively predicts outcome with buspirone for GAD. The drug's mechanisms are distinct. It is possible that clinically obvious benzodiazepine withdrawal and/or subclinical withdrawal (if it exists, not discussed in the literature) increases anxiety and adverse events that are subsequently attributed to buspirone. The initiation of buspirone, or other nonbenzodiazepine anxiolytics following benzodiazepine use should be accompanied by patient education, and close clinical monitoring. ❖

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Hepatitis Associated With Venlafaxine

ABSTRACT & COMMENTARY

Source: Cardona X, et al. Venlafaxine-associated hepatitis. *Ann Intern Med* 2000;355:547-548.

Venlafaxine (effexor) is an antidepressant that exerts its effect via selective inhibition of serotonin reuptake (in doses of 75-375 mg/d) as well as norepinephrine (in doses 225 mg/d). Venlafaxine has been shown to be effective in hospitalized, depressed patients as well as patients with melancholic depression, making it a useful alternative to selective serotonin reuptake inhibitors (SSRIs).

The side effect profile of venlafaxine is relatively benign and quite similar to that of the SSRIs, including gastrointestinal disturbances, insomnia, and sexual dysfunction. In addition, venlafaxine is associated with dose-dependent increases in supine diastolic blood pressure (probably related to its effects on norepinephrine uptake). Regarding liver function, venlafaxine is not typically categorized as hepatotoxic; the product information lists "hepatitis" as rare. Cardona and colleagues describe a case of acute hepatic injury with a prominent element of cholestasis in a patient taking venlafaxine.

A 78-year-old man with a history of Parkinson's disease that was being treated with levodopa and pergolide was started on venlafaxine 37.5 mg/d. After approximately one month of therapy, the dose was increased to 150 mg/d. Six days after the dosage increase, the patient was admitted to the hospital with icteric acute hepatitis. Abdominal ultrasound revealed no abnormalities. His liver enzymes had increased from normal baseline values to approximately four times the upper limit for alanine transaminase (ALT) and approximately six times the upper limit for aspartate aminotransferase. In addition, GGT, ALT, direct and total bilirubin were all significantly elevated. Lab panels for hepatitis A, B, and C were negative.

The patient's health gradually improved after venlafaxine was discontinued. Liver function tests returned to normal within five weeks. The authors concluded that venlafaxine was the cause in the patient's acute liver toxic insult, since all other possible causes of toxic hepatic injury were excluded and liver function returned to normal after discontinuation of venlafaxine therapy.

COMMENT BY MICHAEL F. BARBER, PharmD

The current report is consistent with another report within the past year in which a 44-year-old woman was seen for acute hepatitis approximately six months after the initiation of venlafaxine 150 mg/d.[1] Findings included an alanine aminotransferase level of 1082 U/L (normal, < 56 U/L) and an aspartate aminotransferase level of 661 U/L (normal, < 40 U/L). Lab panels for viral etiology were negative. Further, a percutaneous liver biopsy specimen revealed well-demarcated zone three confluent necrosis, with some inflammation and clumps of perivenular Kupffer cells containing lipid-rich ceroid pigment. The portal tracts were unaffected. Liver function test results progressively improved and returned to normal four months after venlafaxine therapy was discontinued.

While two published cases of hepatitis associated with venlafaxine certainly do not constitute a clinical dilemma of epidemic proportions, the reports do bring some attention to the possibility for venlafaxine-induced hepatotoxicity. Most psychotropic medications (except lithium and gabapentin) are metabolized by the liver. Some, like valproic acid and pemoline, have metabolites that can cause damage to hepatocytes. These medications require frequent laboratory monitoring of the transaminases to ensure that little if any hepatic damage is taking place. In the two cases mentioned, venlafaxine was being given at a total daily dose of 150 mg/d. Apparently, in one case, the dose was initiated at 150 mg/d while the other dose started at only 37.5 mg/d and was escalated directly to 150 mg/d after one month. Thus, it is possible that either 1) doses of 150 mg/d and

above, or 2) a large increase in dose, such as jumping from 37.5 mg/d to 150 mg/d or starting at 150 mg/d, may increase the risk of hepatitis with venlafaxine. In the first scenario, it may be reasonable to monitor liver enzymes slightly more frequently in patients receiving 150 mg/d or more. In the second scenario, it would be reasonable to increase venlafaxine doses in increments no greater than 75 mg/d.

In summary, the incidence of venlafaxine-induced hepatitis is probably low, given the limited number of published reports. As such, extensive monitoring of liver transaminases is probably not warranted at this time. However, clinicians should be aware of any potential venlafaxine may have for causing hepatotoxicity and use caution when escalating venlafaxine doses to and above 150 mg/d. ❖

Reference

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Nortriptyline vs. Fluoxetine in Post-Stroke Depression

ABSTRACT & COMMENTARY

Source: Robinson RG, et al. Nortriptyline versus fluoxetine in the treatment of depression and in short-term recovery after stroke: A placebo-controlled, double-blind study. *Am J Psychiatry* 2000;157:351-359.

Depression is common among patients who have suffered an acute stroke, with slightly more than 40% of patients meeting criteria for a major depressive episode. While clinicians are aware of this problem, there are limited data on the effectiveness of antidepressants in treating post-stroke depression.

The present study evaluated 104 patients with acute stroke who were randomized in double-blind fashion to receive nortriptyline, fluoxetine, and placebo for 12 weeks. In order to determine whether improved recovery could be mediated by mechanisms unrelated to depression, both depressed and nondepressed patients were enrolled. Patients assigned to nortriptyline were started on 25 mg/d and gradually increased to 100 mg/d. The fluoxetine patients were initiated at 10 mg/d and gradually increased to 40 mg/d. Response to treatment of depression for individual patients was defined as a greater than 50% reduction in scores on the Hamilton Rating Scale for Depression and no longer fulfilling diagnostic criteria for major or minor depression. Improved recovery for a treatment group was defined as a significantly higher mean score from baseline to end of the treatment trial, compared with patients treated with placebo, on measures of impairment in activities of daily living and levels of cognitive and social functioning.

Among the 104 patients enrolled in the study, 66 were diagnosed with depression. Of the 23 patients assigned to fluoxetine, 14 completed the 12-week trial. Of the 16 and 17 patients assigned to nortriptyline and placebo, respectively, there were 13 completers in each group. Although fluoxetine had a significantly higher dropout rate, it appeared equally tolerated compared to nortriptyline and placebo; several patients who had dropped out simply refused treatment. Among completers, the successful treatment rate was 10 of 13 (77%) for nortriptyline, two of 14 (14%) for fluoxetine, and four of 13 (31%) for placebo. Although there were no differences between fluoxetine and placebo at any time point, nortriptyline was superior to placebo and fluoxetine at 12 weeks of treatment and to placebo at nine weeks of treatment ($P < 0.05$). Nortriptyline was also significantly superior to fluoxetine and placebo in improving anxiety symptoms as well as in improving recovery of daily activities. There was no effect of nortriptyline or fluoxetine on recovery of cognitive or social functioning among depressed or nondepressed patients.

COMMENT BY MICHAEL F. BARBER, PharmD

Clearly, in terms of efficacy, the results of this study favor nortriptyline over fluoxetine in post-stroke depression. Typically, fluoxetine is considered more tolerable than nortriptyline in elderly patients. Nortriptyline, a secondary amine tricyclic antidepressant (TCA), causes sedation, orthostasis, and anticholinergic effects; however, these effects are usually less pronounced than tertiary amines such as imipramine and amitriptyline. Usually, this difference in tolerability, as well as the potential for arrhythmias, seizures, and fatality in overdoses results in the selection of selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, rather than a TCA for depressed patients. However, the results of this trial do not support this practice. Perhaps the initial dose of 25 mg/d and careful titration to a total daily dose of 100 mg enhanced the tolerability of nortriptyline. Moreover, fluoxetine tended to worsen rather than improve anxiety and depression scores in this trial. It is unclear whether this striking difference in efficacy would extrapolate to the other SSRIs. Although fluoxetine has recently been given approval for the treatment of geriatric depression, at this time it cannot be recommended for post-stroke depression.

In summary, more data are needed to be able to derive clear recommendations on the first-line therapy of post-stroke depression. Based on the available data, nortriptyline should be initially considered for post-stroke depression; if it is found to be inappropriate (i.e., patient with cardiovascular disease or suicidal intent), SSRIs other than fluoxetine may be considered. ❖

The Effect of Testosterone on Sexual Arousal in Women

ABSTRACT & COMMENTARY

Source: Tuiten A, et al. Time course of effects of testosterone administration on sexual arousal in women. *Arch Gen Psychiatry* 2000;57:149-157.

Female sex steroids are necessary for the expression of sexual behavior in many mammals. Copulation is typically limited to the period of ovulation, except in higher primates (i.e., humans) who have sex outside the periovulatory period; testosterone is believed to be involved in this. A lack of testosterone (e.g., ovariectomy) is associated with a loss of libido, which is reversed upon replenishment.[1-2] Physiological responses to sexual stimuli are an important aspect of sexual functioning, marked by vaginal vasocongestion. In females with hypothalamic amenorrhea, testosterone substitution enhanced vaginal responsiveness, but not in a parallel group with panhypopituitarism.[3]

Tuiten and colleagues investigated the effect of a single, sublingual dose of testosterone in eight sexually functional women on physiological and subjective sexual arousal, using a double-masked, randomized, placebo-controlled, crossover design. Participants were tested within 10 days of the end of their period of menstruation, with five days separating the two periods of treatment. Subjects were exposed to pornographic or neutral videotape at six time intervals: immediately before, 15 minutes after, and every one-and-a-half hours for six hours after testosterone administration. Blood levels of testosterone were measured at all six intervals. Within 15 minutes of testosterone intake, there was a 10-fold+ increase in total testosterone levels and a return to baseline within 90 minutes. Compared to placebo, testosterone significantly increased genital responsiveness four-and-one-half hours after peak levels and was associated with increased genital arousal, as well as subjective reports of genital sensations and sexual lust. Tuiten et al concluded there is a lag in the effect of sublingually administered testosterone, perhaps due to the time it takes for neurophysiologic alterations in the brain.

COMMENT BY DONALD M. HILTY, MD

Testosterone may have an important clinical role in terms of sexual functioning. In aging men, testosterone levels decline with age and are correlated with symptoms of depression. Testosterone replacement is being evaluated at the present time. In HIV-positive men who often have hypogonadal symptoms, testosterone is well-tolerated and appears to restore libido and energy.[4] A recent study estimated that 43% of women suffer from sexual dysfunction, mainly low sexual desire (22%), sexual arousal problems (14%), and sexual pain (7%).[5] Intermittent testosterone may be helpful, though the four-hour delay in response may be an impediment to use. The "correct" dose is yet unclear and its use has potential adverse events. At doses 4-8 times normal levels, 4% of patients may become hypomanic; at 8+ times normal levels, over 18% of patients demonstrated psychosis or euphoria.[6] ❖

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Exercise and the Brain

ABSTRACT & COMMENTARY

Source: Russo-Neustadt A, et al. Exercise, antidepressant medications, and enhanced brain derived neurotrophic factor expression. *Neuropsychopharmacology* 1999;21(5):679-682.

Brain-derived neurotrophic factor (bdnf) is a widely distributed growth factor in the brain with profound influence on neural activity. Both antidepres-

sants and physical exercise have been shown to increase BDNF mRNA levels in that hippocampus. Russo-Neustadt and colleagues note that BDNF expression is diminished in the hippocampus of patients with Alzheimer's disease, and that antidepressants are helpful in attenuating problematic behavioral symptoms common in patients with dementia.

In the current study, rats were treated with either a monoamino oxidase inhibitor or a tricyclic antidepressant for a 20-day period with and without concomitant physical activity. Differences in BDNF mRNA levels between groups were determined by two-way analysis of variance. The combination of antidepressant and physical activity led to a potentiation of BNDF mRNA density in the hippocampus, above levels seen with either intervention alone.

COMMENT BY LAUREN B. MARANGELL, MD

Arguably, the area of scientific development most likely to lead to promising breakthroughs for neuropsychiatric disorders involves elucidation of the mechanism and therapeutic effects beyond simple receptor pharmacology. Recent evidence that antidepressant and exercise, and now the combination of both, increase the neurotrophic factor BDNF is a prime example. These data are particularly interesting in light of the relatively recent finding that the adult human brain is capable of neurogenesis, at least in the hippocampus. For the time being, clinicians have another reason to recommend physical activity in their patients. ❖

CNS Whipple's Disease with Insomnia

ABSTRACT & COMMENTARY

Source: Lieb K, et al. Insomnia for 5 years. *Lancet* 1999; 354:1966.

This one-page report underscores the protean symptoms, difficult diagnosis, and treatment of CNS Whipple's disease. A 45-year-old man had been accurately identified and treated for the intestinal form of the disease from 1989 to 1996. Gradually increasing insomnia began in 1994, at which time polysomnographic records showed a sleep duration of 265 minutes. Physical examination, EEG, and CT scan were normal. Hypnotics had little effect. Memory and mood deteriorated by 1999 and examination identified an isolated supranuclear defect in upward gaze. Monitoring showed nocturnal sleep activity to be less than 60 minutes per 24 hours. Only sleep patterns 1 and 2 appeared, leaving absent sleep patterns 3, 4, and REM. Brain MRI disclosed nonspecific white matter patches, EEG patterns slowed to 7-8 seconds, and PCR testing of CSF identified Whipple's disease. Among several drug trials, only carbamazepine brought sleep behavior back to approximately four hours per day.

COMMENT BY FRED PLUM, MD

Whipple's disease is rare and its brain involvement even more so. Thus, the long comment over the short index report. Early systemic symptoms consist of migratory polyarthralgia, chronic diarrhea, and unexplained fever. Progress may be slow in the non-neurologic portion of the illness but accumulates rapidly once central nervous system abnormalities express clinical symptoms. Whipple, a Johns Hopkins surgeon, identified the disease as the result of microorganisms in the gut.[1] The illness is uncommon, and clinically expressed central nervous system invasion is even less frequent (about 5%). Neither transmission nor independent development of the illness is as yet understood. The organism has resisted culturing, but can be identified by electron microscopy or PCR testing of tissue. Using PAS stain, Sieracki and colleagues[2] first identified the bacillus within a single macrophage in CSF. Mistaken diagnoses since 1963 often have identified the disease as "chronic encephalitis." According to Louis and associates, important clues to brain intrusion of the organism include gradual functional evidence of supranuclear ophthalmoplegia, dementia, somnolence, insomnia, cranial-facial myoclonus, and hypothalamic dysfunction.[3] Myorhythmia and masticatory movements that synchronize with pendular vergent oscillations were considered pathognomonic by Louis et al. About half of affected persons suffer from gradually advancing impaired cognitive functions. Brain imaging to date has shown only nonspecific changes. Treatment has limited success; tetracycline appears best but nothing has yet been effective in the late stage of the illness.

Of interest is the severe insomnia suffered by this unfortunate man and others described in Louis et al's survey, cited above. One can also note similar examples of pathological insomnia associated with other brainstem illness. Aldrich and associates[4] described 10 patients with progressive supranuclear palsy (PSP) whose nocturnal sleep ranged from 163-352 minutes (mean, 234 min). Patients with brain trauma, acute ischemia, or hemorrhage affecting the pontine midline tegmental structures often undergo severe reductions of sleep of less than two-and-a-half hours. Some suffer

from no sleep at all and many of the others have reduced or absent REM. Many such persons retain their awareness but may become confused or severely delirious. Markand and Dyken,[5] for example, described two such "locked-in" examples of this stroke syndrome. Both displayed no sleep at all when twice monitored for 24 hours. Both died, and postmortem examination confirmed the pontine tegmental abnormalities. Other examples in the pre-1990s literature demonstrate similar structural damage to the medial pontine tegmentum. Most famous of present conditions causing malignant sleeplessness, of course, is the prion disease of fatal familial insomnia in which widespread spongiform changes are found diffusely in the cerebrum. *(Dr. Plum is University Professor, Weill Medical College, Attending Neurologist, New York Presbyterian Hospital, Cornell Campus, New York, NY.)* ❖

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CME Questions

10. Which of the following is *not* characteristic of the serotonin syndrome?
a. Mental status changes, restlessness, agitation
b. Myoclonus, hyper-reflexia, tremor
c. Diaphoresis, shivering, autonomic instability
d. Diarrhea
e. Muscular rigidity and increased CPK

11. Which of the following classes of medication is most often associated with lethal serotonin syndrome?
a. SSRIs
b. TCAs
c. MAOIs
d. Antipsychotics

12. Which of the following is true about testosterone and sexual functioning?
a. Testosterone is believed to be involved with sex outside the periovulatory period.
b. In females with hypothalamic amenorrhea, testosterone substitution enhanced vaginal responsiveness.
c. A lack of testosterone (e.g., ovariectomy) is associated with a loss of libido, which is reversed upon replenishment.
d. In HIV-positive men who often have hypogonadal symptoms, testosterone is well tolerated and appears to restore libido and energy.
e. All of the above

13. Recent benzodiazepine use is a negative predictor for outcome for GAD patients subsequently given buspirone in terms of:
a. anxiety scores.
b. adverse events.
c. overall clinical global improvement.
d. All of the above
e. None of the above

14. Since 1963, Whipple's disease has often been misdiagnosed as chronic encephalitis.
a. True
b. False

In Future Issues:

Antidepressant Treatment of Fibromyalgia