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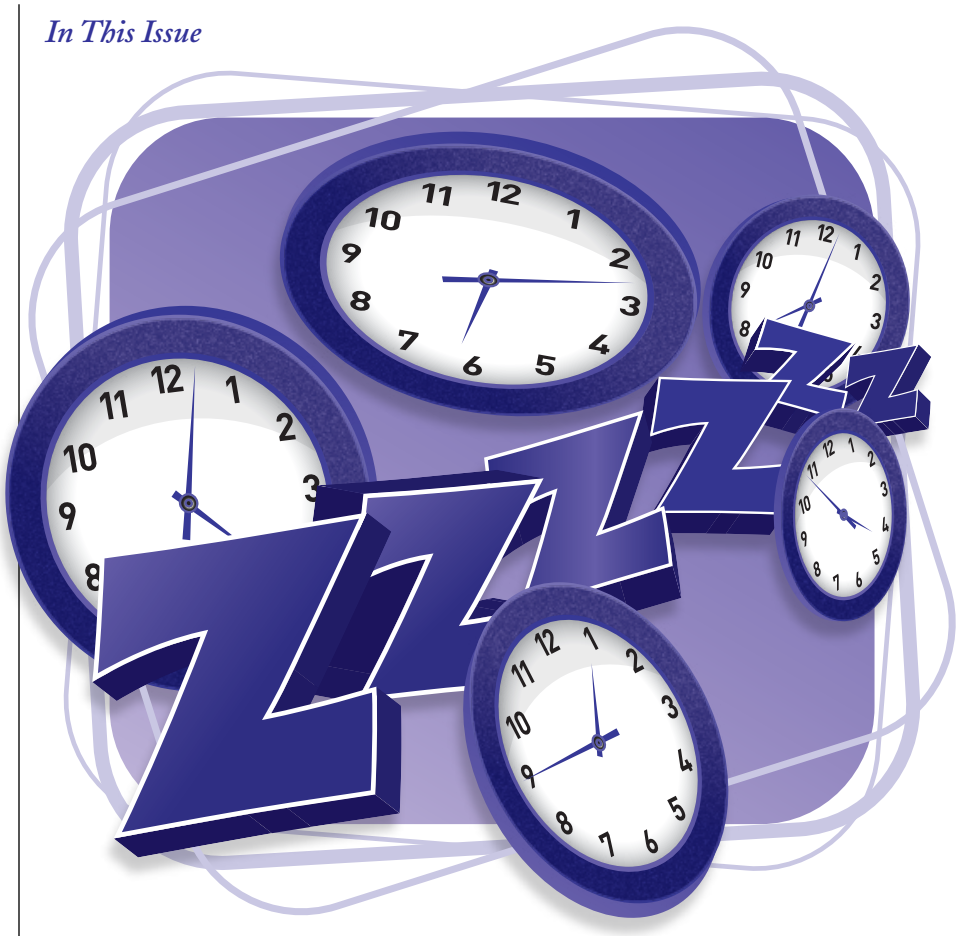

This issue of the *Residents' Journal* features two articles on the topic of sleep, which is an area of research encompassing a variety of different disorders. Harita Raja, M.D., discusses the effects of substance use on sleep, providing useful information on clinical effects, specific substances, and treatment. Addressing issues specific to the resident physician, Dawn L. Flosnik, M.D., outlines the effects of sleep deprivation and inertia on resident performance, along with official guidelines, implemented by the Accreditation Council for Graduate Medical Education, regarding work-hour restrictions designed to improve patient safety, which may be compromised when residents are fatigued.

Editorial

Women's Mental Health and the *Residents' Journal*

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Editor-in-Chief

The World Health Organization (WHO) has indicated that unipolar depression is twice as common in women than in men and is predicted to be the second leading cause of global disability by the year 2020 (1). Women tend to balance numerous roles in their life cycle while undergoing complex hormonal changes. Wise et al. (2) identified the woman's life cycle according to her reproductive status and described these stages as adolescence, the childbearing years, pregnancy, breastfeeding and the postpartum period, and perimenopause and menopause. Some of the more commonly seen mood disturbances associated with the reproductive life cycle in women are premenstrual dysphoric disorder, postpartum depression, and perimenopausal depression. These disturbances are thought to be due in part to fluctuations in estrogen, which influences neurotransmitters, such as serotonin, norepinephrine, and dopamine (2).

As residents, we will frequently encounter women who come to us seeking help at various points in their reproductive life cycle. Perhaps it is the patient who is experiencing depression during pregnancy or the woman suffering from postpartum psychosis. It may also be a woman who is perimenopausal. It is important to be aware of the hormonal changes occurring in these patients as well as appropriate treatment options during the specific phase of life the patient is in. Correct treatment options could vary from psychotherapy to pharmacotherapy to more interventional methods, such as ECT.

A relatively newer area of focus is that of infertility, its treatment, and its effect on the mental health of the couple involved. An article published in the Harvard Mental Health Letter discussed a study indicating that women who were faced with infertility felt as depressed and anxious as those diagnosed with cancer or who were recovering from a myocardial infarction (3). Men are affected as well, although this has not been studied in as much detail.

In an upcoming issue, the *Residents' Journal* would like to publish manuscripts on women's mental health as well as the effects of infertility on the mental health of couples. We look forward to receiving your submissions.

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REMEMBER TO VOTE

APA's annual election is fast approaching, with online voting beginning on January 3, 2012 (http://www.psych.org/Resources/Governance/Elections.aspx). This election is of significant importance, as many of those elected will be serving APA members during a pivotal time in the Association's history: the anticipated publication of DSM-5.

Sleep Disorders and Substance Abuse

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Sleep disorders are among the most common clinical problems encountered in psychiatry. Although patients rarely present primarily for a sleep problem, it is a frequent comorbidity at presentation. This is especially true with substance use. Different substances may affect an individual's sleep in unique ways. This article focuses on insomnia and the effects of substance abuse on sleep.

Approximately 10% of Americans will experience insomnia in their lifetime (1). Insomnia can be defined as "difficulty initiating sleep, difficulty maintaining sleep, or having nonrestorative sleep longer than 1 month," which causes some form of daytime impairment (2). The risk factors for insomnia (3) include older age, female sex, Caucasian ethnicity, and the presence of medical or mental disorders (1). Insomnia is an important aspect of health to address because inadequate or nonrestorative sleep can lead to a markedly impaired quality of life (4). Moreover, chronic insomnia is associated with increased risk of multiple medical and psychiatric consequences, including cognitive dysfunction, depression, and anxiety. In fact, one study found that 33.6% of individuals who had unresolved insomnia at the 1-year follow-up analysis also had psychiatric disorders. This prevalence dramatically decreased to 12.7% when the insomnia was treated and essentially resolved (2).

Briefly, sleep disorders can be divided into two categories: primary and secondary (5). Primary sleep disorders result from disturbances in circadian rhythm and homeostatic mechanisms not related to physical or mental conditions. Secondary sleep disorders, on the other hand, result from underlying physical or mental conditions. In particular, there are many primary DSM-IV axis I psychiatric conditions that lead to secondary sleep disorders, including, but not limited to, depression, posttraumatic stress disorder, anxiety, and substance abuse. Antidepressant use can also lead to secondary sleep disorders (2).

In order to understand the ways in which different substances can affect sleep, it is helpful to have a basic knowledge of the sleep cycle. Sleep can be divided into periods of relative slow-wave sleep and active sleep (6). The former, non-REM sleep, comprises the first four stages of sleep, which is roughly 75% of an individual's total sleep time, while the latter, REM sleep, is the fifth stage.

Clinical Issues

Patients who use substances often find themselves in a particularly vicious cycle regarding sleep (7). The euphoric effects of substances are both pleasurable and addictive, causing an individual to maintain intoxication regardless of sleep loss. Therefore, initial use of substances may potentially lead to secondary sleep disorders. To counterbalance this effect, patients often self-medicate through further illicit substance use, with either their initial drug of choice or a different substance. This further alters the sleep pattern and exacerbates the sleep cycle. One may wonder, how common is this phenomenon? In a cross-sectional study conducted at the Alcohol and Drug Recovery Center at the Cleveland Clinic (8), individuals who were actively using substances were recruited to complete a comprehensive sleep disorder questionnaire. Of these patients, 96% reported sleep impairment, and 46% used substances as a means of self-medication for their sleep impairment. Thus, sleep disturbances can be a considerable problem in patients with substance use disorders and should be addressed in this population.

Specific Substances

Alcohol is a CNS depressant. It has been shown that intoxication increases slow-wave (stage 3) sleep and suppresses REM (stage 5) sleep (9). Withdrawal, on the other hand, increases sleep latency, or the time it takes to fall asleep, and decreases total sleep time. Brower and Perron (10) investigated the prevalence of withdrawal-related insomnia in adults with alcohol dependence. Through data from a 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions, the authors were able to retrospectively assess 43,093 patients, of whom 31.7% had alcohol withdrawal-related insomnia. Further bivariate analysis showed that insomnia was associated with a family history of alcohol use disorders, comorbid psychiatric conditions (such as depression and anxiety), middle-age, female gender, and more than 7 years of heavy drinking. As discussed previously, it is the insomnia that leads to a higher rate of relapse as a result of the unfortunate cycle that often occurs in patients who suffer from substance use disorders. Of note, slow-wave and REM sleep generally return to baseline patterns after the withdrawal process (9).

Conversely, opiates increase wakefulness and decrease total sleep time, including slow-wave and REM sleep (1). One double-blind study investigated the effects of opioid medications on sleep architecture (11). The authors assessed 42 healthy patients using polysomnography after a dose of placebo, morphine-sulfate, or methadone was administered before bedtime. Each patient group had significantly decreased REM sleep and increased stage 2 sleep. However, neither opiate had effects on total sleep time or sleep efficiency. The authors concluded that even single doses of opioids have an effect on sleep architecture in adults.

Cocaine and amphetamines work similarly, since they also lead to decreased total sleep time with decreased REM sleep (12). In cocaine withdrawal, non-REM sleep specifically is markedly decreased, while REM sleep is increased (13). Over-

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all, however, individuals in withdrawal exhibit hypersomnia, or increased sleep and an increase in the number of sleep-wake cycles.

Finally, marijuana is a complex substance that contains two active constituents: [9]-tetrahydrocannabinol and cannabidiol. Smoked marijuana has been shown to reduce REM sleep, while acute administration leads to reduced sleep latency and increased stage 4 sleep (12). Feinberg et al. (14) examined the effects of marijuana on sleep and found that it led to reduced eye-movement activity and less REM sleep, with increased REM activity in the withdrawal process. Withdrawal also has been shown to lead to difficulty sleeping as well as bizarre dreams, with increased sleep latency and reduced slow-wave sleep (12).

Treatment

Despite the deleterious sleep changes caused by substance abuse, treatment can help to manage or alleviate these effects. For example, Lukas et al. (15) studied the reversal of sleep architecture with buprenorphine in men with cocaine and heroin dependence. Treatment with low-dose buprenorphine was associated with improvement in sleep latency, total sleep time, REM latency, and overall sleep architecture. Interestingly, this was not observed for high doses of buprenorphine.

First and foremost, physicians must encourage abstinence from substances that affect sleep. Sleep hygiene and education are first-line treatments for patients with sleep disturbances (6), especially since patients may overlook hygiene-related reasons for insomnia. The following guidelines are important for sleep hygiene and should be addressed when caring for patients with sleep disorders:

- Use the bed for sleep/sex only (no television, no reading);
- Do not exercise right before bedtime;
- Monitor caffeine intake, especially late at night (including coffee and soda);
- Avoid struggling to fall asleep in bed; instead, get up and go back to bed only when tired; and
- Avoid naps during the day

Cognitive-behavioral therapy may also be helpful. The ability to discuss sleep in a psychotherapeutic setting has been shown to be effective. In addition to psychotherapy, pharmacological treatment options are particularly common and can be effective (2). Medications can be categorized into those that are Food and Drug Administration-approved for treating sleep disorders (e.g., zolpidem, ramelteon, and diphenhydramine) and those that are not approved for the treatment of sleep problems (e.g. clonazepam, doxepin, risperidone) but in which sedation is a major side effect. Antidepressants with sedation as a side effect, such as trazodone and mirtazapine, are useful options in patients who are also diagnosed with depression. Finally, in cases of intractable insomnia or to obtain objective findings about a patient's sleeping pattern, one may consider a polysomnography.

Conclusions

Patients with substance use disorders are often afflicted with sleep disturbances as a direct result of their substance use. Sleep quality is an important, often neglected aspect of their health that should be treated appropriately. Treating sleep disorders in these patients can make a significant difference in their quality of life and ability to progress through the recovery process.

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Sleep and Residency: A Brief Review

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Although the exact function of sleep is not completely known, it plays a role in restoring physiological and psychological functioning. However, the medical profession is open 24-hours a day year-round, and resident physicians often must stay awake for extended periods of time in order to care for patients. In response to growing research indicating that resident physicians suffer fatigue and sleep deprivation, which may negatively affect patient and physician safety, physiology, and neurobehavioral performance (1), the Accreditation Council for Graduate Medical Education (ACGME) implemented updated resident duty-hour rules as of July 1, 2011 (2). In light of these recent stricter changes implemented nationwide, a brief review of the literature is warranted to elucidate the effects of sleep deprivation and fatigue on residents.

Recent 2011 ACGME Guidelines

The new ACGME guidelines preserve the original 2003 guidelines of an 80-hour work-week limit averaged over 4 weeks, with 10 hours off between duty periods. However, interns are now prohibited from working more than 16 hours continuously. The ACGME based this decision on recommendations from the Institute of Medicine's 2008 report, which concluded that 5-hour uninterrupted naps for every 16 hours worked reduces medical errors (3). However, senior residents may work in the hospital up to 24 hours continuously, with an additional 4 hours permitted for continuity of patient care and handoffs. For these residents, strategic napping is strongly suggested, but not required, between the hours of 10:00 p.m. and 8:00 a.m.

In addition, the new ACGME requirements have updated the section on "Alertness Management/Fatigue Mitigation" from the 2003 standards (2, 4). The new version continues to necessitate the education of faculty and residents on the signs of fatigue and sleep deprivation but additionally calls for instruction on alertness management and fatigue mitigation. Moreover, the 2011 guidelines suggest adding back-up call schedules, in addition to naps, in order to counteract negative consequences on patient care. Each program is now required to ensure that patient care will not be compromised if a resident is unable to perform his or her duties secondary to fatigue. Lastly, residency programs are now mandated to provide sleep facilities and/or alternate transportation options for residents who are too fatigued to travel home safely.

History of ACGME Guidelines

One of the earliest examinations of the effects of sleep loss, particularly in resident physicians, was a 1971 study conducted by Friedman et al. (5) in which interns who were deprived of sleep were found to be significantly more likely to make errors when reading ECGs, compared with their rested counterparts (5). In addition, these sleep-deprived interns reported feeling "increased sadness" and subjectively reported "abnormalities in cognitive, perceptual and physiologic functioning" (5). It was not until 2003 that the first nationwide ACGME work-hour rules were implemented, partly as a response to the case of Libby Zion, the 18-year-old woman who died in a New York hospital in 1984 as the result of serotonin syndrome caused by medications prescribed by sleep deprived, undersupervised, and overworked resident physicians (6).

Sleep Deprivation and Sleep Inertia

Sleep deprivation can be classified as either acute continuous or chronic partial (1). Taking overnight call shifts exposes resident physicians to acute continuous sleep deprivation, which is defined as staying awake for a continuous period of time. It has been shown that just 24 hours of complete wakefulness may impair psychomotor coordination similarly to a blood alcohol level of 0.1% (7), which is above the nationwide legal limit of 0.08%. In contrast, chronic partial sleep deprivation occurs when an individual does maintain a consistent sleep schedule, but less than the optimal amount of sleep is attained. One study, conducted by van Dongen et al (8), demonstrated that restricting sleep in otherwise healthy adults to less than 6 hours nightly for 2 weeks may produce significant deficits in cognition. The authors concluded that "even relatively moderate sleep restriction can seriously impair waking neurobehavioral functions in healthy adults" (8).

In addition to sleep deprivation, several other factors increase fatigue and decrease alertness in residents on call, including fragmented sleep and poor sleep quality (9). Particularly, residents who are suddenly awakened by the beeping of a pager are likely familiar with the term sleep inertia, which refers to the reduced cognitive performance experienced upon suddenly and immediately awakening (10). The circadian rhythm also influences cognition and alertness, which are impaired most significantly between the hours of 3:00 a.m. and 5:00 a.m. (11), suggesting that tasks performed during this window of time may be suboptimal (1).

Sleep Deprivation and Resident Performance

With regard to the effects of resident sleepiness on clinical performance, the literature reveals mixed results. A 1991 review conducted by Samkoff and Jacques (12) found that residents who were sleep-deprived and fatigued committed more errors on tasks requiring "prolonged

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vigilance" and had worse moods and attitudes overall. However, psychomotor tests measuring manual dexterity, reaction times, and short-term memory were not adversely affected. Philibert (13) conducted a meta-analysis confirming that physicians' cognitive performance is negatively affected by sleep deprivation; however, the studies analyzed were heterogeneous, making the results tentative. Barger et al. (14) reported that "extended-duration work shifts were associated with an increased risk of significant medical errors, adverse events, and attentional failures." A recent systemic review (15) conducted by Baldwin et al. revealed that since the introduction of statewide work-hour rules in New York following the Libby Zion case and nationwide work-hour regulations implemented by the ACGME in 2003, there has been a decrease in mortality across specialties, although no studies specifically examined psychiatry. It should be noted that there were no significant differences found between teaching and nonteaching hospitals, suggesting that the findings may not be related to work-hour restrictions. The authors proposed that the decrease in mortality may be a function of advancements in technology or improved hospital-based safeguards and staff education.

Although data reviewing the effects of sleep deprivation on clinical performance are inconclusive, the effect of fatigue on resident safety and quality of life is more straightforward. One study reported that following a shift of 24 hours or more, interns were found to have a doubled risk of being involved in a motor vehicle collision (16). In this same study, interns who worked at least five shifts of 24 hours or more within a given month, compared with those working shifts that were not extended in duration, were significantly more likely to fall asleep while driving or stopped at a traffic light, particularly when commuting home from work, exemplifying the dangers of frequent overnight shifts. The risk of needle-stick injury was also found to be increased in this population of interns during nighttime hours and following a shift of at least 24 hours (17). Additionally, it has been reported that sleep deprivation in residents negatively affects family life and personal/professional relationships (18).

Conclusions

Sleep deprivation and fatigue have been shown to have negative effects on the physician-in-training, from both a physiologic and quality-of-life standpoint. It is intuitive to assume that clinical performance would be affected in a similar way. However, conclusions remain uncertain as to whether or not patient safety has improved as a result of work-hour regulations. In an effort to continue the practice of evidence-based medicine when instituting policy change, further research must clarify the effect of sleepiness and fatigue on residents' clinical performance.

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Case Report

Psychosis and Pregnancy

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Case

"Ms. J" was a 32-year-old woman with schizoaffective disorder depressed type. She presented to the training clinic for an annual assessment. Her psychiatric history revealed two suicide attempts during psychotic episodes, which led to inpatient treatment. At the time of evaluation, the patient denied any symptoms. The rest of the psychiatric examination, including laboratory work up, yielded normal results, with the exception of a routine urine pregnancy screen, which was positive. A confirmatory test revealed a 4- to 6-week gestation period.

A family meeting was subsequently held, during which an exhaustive discussion of the risks of psychotropic treatment during pregnancy took place. Ms. J wanted to discontinue all psychotropic medications (fluphenazine and bupropion). She agreed to close weekly monitoring. Within 3 weeks, she was hospitalized for suicidal ideation and emerging psychotic symptoms. She was stabilized at an outside institution and discharged while receiving treatment with aripiprazole (10 mg daily) and sertraline (100 mg daily). Upon her return to the outpatient setting, another series of family meetings took place to address her complicated clinical situation. Given her positive clinical response and exposure to the medications, it was recommended that she continue treatment throughout her pregnancy, and her family concurred. The patient received regular obstetric care, and the remainder of her pregnancy was uneventful both psychiatrically and obstetrically. She had a spontaneous, although premature, vaginal delivery at the 36th week of gestation, yielding an otherwise healthy 5 lb, 6oz infant. Both the child and mother were discharged home within 48 hours and remained well at the 1-month follow-up evaluation.

Discussion

This case represents a rarely reported but not uncommonly encountered clinical situation (i.e., the treatment of psychosis during pregnancy with a selective serotonin reuptake inhibitor [SSRI]) and an atypical antipsychotic). Studies directed at exploring the effects of psychotropic treatment during pregnancy have yielded variable and controversial findings. Calderon-Margalit et al. (1) concluded that there is a statistically significant risk of preterm delivery positively correlated with the number of psychotropic medications used. They found an increased risk of preterm labor and low birth weight associated with the use of SSRIs during the second and third trimesters. However, a review of the literature between 1966 and 2008, conducted by Einarson and Boskovic (2), cited no definitive association between antipsychotic medications and adverse fetal outcomes, including persistent pulmonary hypertension. Presently, the available data lack sufficient statistical power to draw consistent correlations.

Use of Aripiprazole During Pregnancy

Mendhekar et al. (3) described the case of a 27-year-old woman who was diagnosed with schizoaffective disorder and began receiving treatment with aripiprazole (10 mg daily) in the second trimester. No adverse outcomes were observed at the full-term delivery or the 6-month follow-up evaluation. The authors also reported the case of a 22-year-old woman with schizoaffective disorder who was treated with aripiprazole (15 mg daily) during the third trimester. The patient bore a healthy child, and the 6-month follow-up evaluation revealed no abnormalities (4). Mervak et al. (5) outlined the case of a 24-year-old woman with schizoaffective disorder who began treatment with aripiprazole (20 mg daily) at the eighth week of pregnancy. At the 39th week of gestation, she developed hypertension but went on to have an uncomplicated delivery at 40 weeks. Her child remained in good health at the 12-month follow-up evaluation. It is notable that in these instances, the psychotropic agent was not started during the critical first semester of pregnancy. Thus, these results may not reflect the full burden of comorbidity of the effect of aripiprazole on the developing fetus.

Use of Other Atypical Antipsychotics During Pregnancy

Case reports of the use of atypical antipsychotic medications other than aripiprazole show wide-ranging outcomes. Dickson and Hogg (6) reported the case of a woman with treatment-resistant schizophrenia who became pregnant during transition from treatment with a typical antipsychotic to clozapine treatment. The pregnancy was complicated by gestational diabetes; however, the patient and her child returned home after an unremarkable full-term delivery. Yeshayahu (7) described the case of a 25-year-old woman who received treatment with olanzapine (10 mg daily) during the course of pregnancy. Significant anomalies were present upon the delivery and included unilateral clubfoot and atrioventricular canal defect, which required surgical repair 6 months following delivery (7). In a multicenter, comparative prospective study, McKenna et al. (8) addressed these variable findings. The authors examined a sample of 151 pregnancies in which the fetus was exposed to olanzapine (N=60), risperidone (N=49), quetiapine (N=36), or clozapine (N=6), relative to a comparison group. The only significant difference observed between the groups was higher rates of low birth-

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weight babies in the active group.

In 2008, the American College of Obstetricians and Gynecologists detailed treatment guidelines with respect to the use of antipsychotics during pregnancy (9). The guidelines emphasized the risk of untreated maternal mental illness carrying unfavorable pregnancy and infant outcomes. These guidelines, summarized by Howland (10), pointed to the limited evidence suggesting that antipsychotic medications pose a significant risk during pregnancy or breastfeeding. However, there is a small but significant risk of congenital anomalies occurring in the context of maternal obesity exacerbated by the use of atypical antipsychotic agents. With the exception of clozapine and lurasidone, which belong to pregnancy category B agents (defined as a lack of controlled studies of the drug in humans implicating adverse effects on the fetus), the remaining antipsychotic agents fall under pregnancy category C (defined as the drug having adverse fetal effects in animals but no data are available for humans). The use of these category C medications can be appropriate in the context of psychotic illness. It is noteworthy that the classification of lurasidone may change given that it is a newer drug and lacks dissemination into clinical samples.

The American College of Obstetricians and Gynecologists recommendations also emphasize that untreated or undertreated maternal psychiatric illness may result in poor compliance with prenatal care, inadequate nutrition, exposure to additional medication or herbal remedies, increased alcohol and tobacco use, and deficits in mother-infant bonding. As such, associations between untreated illness have been made with congenital malformations, increased incidence of preterm delivery, low birth weight, placental abnormalities, antenatal hemorrhage, and increased rates of post-natal death (9, 10).

Finally, in February 2011, the Food and Drug Administration updated its pregnancy warning for all antipsychotic agents with regard to the development of extrapyramidal symptoms in newborns (11). The agency reviewed its adverse event reporting system database and identified 69 cases of neonatal extrapyramidal symptoms or withdrawal associated with the use of antipsychotics in the third trimester. However, the majority of these cases were confounded by the presence of multiple medications in addition to the finding that psychotic illness may in and of itself manifest with movement disorders (11).

In conclusion, there is a lack of prospective data about the safety profiles of psychotropic medications during pregnancy. This underscores the need for future case reports to provide meaningful points of reference for further and more statistically sophisticated investigation. Furthermore, clinicians would benefit from long-term follow-up studies emphasizing the neurodevelopment consequences of in utero exposure to psychotropic medications.

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Case Report

Metoclopramide-Induced Delirium

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Delirium is an acute disorder of attention and cognition resulting in a decreased awareness of one's environment (1). The management of this disorder is particularly tricky because of the multifactorial causation and the need to address predisposing, precipitating, and iatrogenic factors that may contribute to the presentation of symptoms. Approximately 40% of delirium cases in the geriatric population are caused by medications (2). The present case is of a patient with gastritis and chronic renal failure who developed delirium and abnormal movements after receiving treatment with metoclopramide.

Case

"Mr. X" was a 74-year-old retired factory worker who was admitted to the hospital after 3 days of confusion. He lived with his wife, who was his primary caregiver and helped him with activities of daily living. She also provided most of his psychiatric and medical history. The patient had a history of new-onset auditory hallucinations. He said, "I heard Jesus; he is asking us to come to Heaven." He had been "euphoric, sleeping poorly, and dancing and jumping around the house at night." The night previous to his admission, he had become excited and pulled his wife out of bed, inviting her to travel to heaven. He was an active preacher at his church but had been more religiously preoccupied, as well as intrusive and argumentative with family and neighbors, for the last several days.

The patient had no history of head trauma, loss of consciousness, seizures, fever, chills, or chest pain. He had no past neurological or psychiatric disorder, and no substance abuse history was noted. He did have a medical history of hypertension, diabetes, and end-stage renal disease for which he had been receiving hemodialysis three times per week. His home medications were atorvastatin (40 mg daily), losartan (50 mg daily), amlodipine (10 mg daily), esomeprazole (40 mg daily), metoclopramide (5 mg thrice daily), insulin aspart (19 units), sevelamer (800 mg thrice daily), water-soluble vitamins, pregabalin (75 mg daily), and aspirin (325 mg daily).

Prior to the patient's current admission, he had been admitted twice in the last 5 weeks for gastritis, nausea, and vomiting. Pantoprazole (150 mg daily) and metoclopramide (5 mg twice daily) were started, and treatment with alendronate was discontinued. An upper gastrointestinal endoscopy revealed inflammation of the esophagus and stomach. Ten days after discharge, the patient's symptoms persisted, and he had lost nearly 10 pounds. The metoclopramide dose was raised to 5 mg thrice daily.

On his present admission, Mr. X was well-groomed and appeared to be his stated age. He was alert and oriented to person but not to time or place. He was restless and easily agitated when questioned. He showed a normal motor tone with small bulk. His strength was full in both his bilateral upper and lower extremities. There was increased psychomotor activity with dyskinetic finger tremors and sudden nonrythmic tremors in both his hands. He showed no rigidity of limbs or mask facies. His mood was "frustrated," with mood-congruent labile affect, changing from tearful to euphoric rapidly. The patient's speech was spontaneous and coherent, with his tone of voice changing rapidly, from tearful to agitated and excited. His thought process was illogical at times and nongoal directed. He did not cooperate with memory and cognition testing and showed limited insight and poor judgment.

His medications were reevaluated, and metoclopramide was discontinued. Laboratory data revealed a normal electrolyte panel and urine drug screen. was placed on hemodialysis. He had been receiving metoclopramide for approximately 3 weeks at a dose of 15 mg per day, which is high for an elderly patient. He was prescribed olanzapine (2.5 mg at bedtime) on 3 inpatient days because of agitation, hallucinations, and excessive excitement. He tolerated the dose well, and his symptoms were resolved. Mr. X showed rapid improvement following discontinuation of metoclopramide; he was more alert and oriented and less delusional within 2 days, and his dyskinetic movements were less severe.

Discussion

Metoclopramide is a peripheral and central D_2 receptor antagonist. It is commonly used in treating nausea, vomiting, and gastroparesis associated with chemotherapy and diabetes (3, 4). This agent acts like a neuroleptic on the brain. It produces movement disorder side effects in 20% of patients as a result of D_2 blockade. In the elderly it produces extrapyramidal side effects at lower doses because of greater CNS penetration at equivalent serum levels (5). D_2 blockade also leads to impaired executive function, as a result of decreased mesocorticolimbic output to the frontal lobes, distractibility, poor attention, and impaired working memory (5). This effect of D_2 blockade was manifested as change in the level of cognition, mood symptoms, hyperreligiosity, agitation, and insomnia in Mr. X (also see reference 6). The baseline religiosity of this patient made it difficult to differentiate between delusional and normal thought content. Metoclopramide is commonly known to cause symptoms of depression and anxiety but rarely delirium. High doses in a patient with baseline renal impairment, such as Mr. X, lead to a high blood level, particularly because the drug is nondialyzable. This may lead to side effects of akithesia, restlessness, insomnia, mood changes,

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and extrapyramidal symptoms. Fishbain and Rogers (4) described a case of delirium secondary to metoclopramide, with the patient presenting with "non-delirious toxic psychosis" with visual hallucinations, excitation, and hyperactivity without disorientation.

In the present case, careful review of the patient's medications and discontinuation of metoclopramide helped to resolve symptoms. Metoclopramide can cause delirium and neurological symptoms in the elderly, especially when there is prexisting cognitive decline. In the present case, special attention was given to the patient' cognitive baseline as well as psychosocial factors, medications, and drug/alcohol use in order to differentiate the symptoms.

Dr. Mishra is a third-year resident in the Department of Psychiatry, Detroit Medical Center/Wayne State University, Detroit.

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Introspection

My Other Psychopharmacology Professor

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As he stood up and walked toward the door, I prepared myself for "Stevie's" inevitable doorknob zinger. He turned around and smiled at me for a moment before staring at the ground and asking me if I knew that armodafinil had been shown to mitigate negativistic symptoms in psychotic patients. And though I was not aware of the specific study to which he was referring, I was a veteran in navigating the treacherous waters where this conversation was heading.

Our sessions always ended with a therapeutic waltz to some variation of this theme. First, Stevie would request a prescription—most recently, he had asked exclusively for stimulants—and then cite a study he had found, which may or may not be clinically relevant. I would follow his lead and discuss the psychopharmacology with him, the neurobiological correlates of his illness, and how the intervention—stimulants in this case—might be contraindicated given his history. This time there was an absolute contraindication. Stevie's severe psychotic pathology (i.e., paranoid delusions that his brother was providing information about him to the Drug Enforcement Administration) had worsened in the context of stimulant abuse. In line with our previous dances, he smiled and presented me with an angry jab of sarcastic humor before telling me he looked forward to seeing me the following week.

Stevie was a young man who was being treated in our community psychiatry clinic for schizophrenia. Prior to our initial interview, my supervisor stated, "You'll learn a lot from working with him." Having heard the same phrase applied to most cases I had seen in residency, I may have been jaded, but Stevie actually did teach me a lot.

A treasured mentor wrote the following in the dedication of his psychopharmacology textbook: "to our young patients… who have taught us so much over the years" (1). Certainly, as training physicians, we expect to learn much from managing our patients, perhaps even to discover novel treatments or rare adverse reactions through our clinical practice. Working with Stevie was different. It was not just his complex psychopathology and diagnostic dilemmas that made his case a fascinating one, but it was also that his psychotic preoccupation happened to be the underlying mechanisms of psychopharmacology. In an ironically grandiose fashion, he considered himself "a veritable professor of psychopharmacology." And sometimes he was.

Many of our sessions began with him handing me an article that he had printed from pubmed.org. It did not strike me as abnormal one day when he greeted me with, "I know that you think that long-acting injectable antipsychotics are more efficacious because of that Finnish study from the *American Journal of Psychiatry*." I admitted that I was unfamiliar with the study at the time, and he advised me to read it. I did. At our next meeting he asked me what I thought, and I told him that I was impressed with the study's thorough methodology. He grinned and then stared at the coat rack before looking at me again, "Well shots hurt like getting stabbed with a pitchfork so you'd better be sure I have schizophrenia…okay?"

Beyond the psychopharmacology journal club that Stevie had established during our appointments, I learned other more obscure "clinical pearls" from being his psychiatrist. According to Stevie, crack is cheaper on the streets than dextroamphetamine/amphetamine, and obtaining a prescription for tadalafil is very easy and that at least three different psychiatrists

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in our town were willing to prescribe it to a healthy young man in his twenties without referring him for further work-up or asking "more than two questions before reaching for their prescription pad." This was certainly new information.

One day at the end of a particularly turbulent session, Stevie warned me, "If you don't prescribe me what I want, I'll just order it online!" He went on to inform me that a few years ago, he had been using selegiline patches that he had ordered online while receiving prescriptions for escitalopram from his previous psychiatrist. When I looked at him quizzically, he told me, "I think I know enough psychopharmacology to recognize a hypertensive crisis when I see one, and I would have stopped before that happened—I'm not suicidal you know." He then offered to show me the various websites that a person can use to obtain medications from Europe and Canada without a prescription or medical license. I thanked him for showing me this novel method of obtaining potentially dangerous prescription medications.

And then Stevie taught me to always remember that alliance is paramount, both in achieving treatment goals and maintaining patient safety. After one long, frustrating session, I was told, "You don't know half of what they know at Massachusetts General Hospital. You'd never get hired at McLean because you only play by the rules. I'll just start taking the [dextroamphetamine] I bought off the streets if you won't prescribe it to me." Stevie had lost his cool. In an angry moment, he yelled, "Why don't you just get senile and sign all my prescriptions so I can get better already!" When I asked him to clarify, he said, "You know what I mean, old geezers don't ask questions; they just sign prescriptions for whatever you want."

I asked him if he was willing to wait 60 years for me to get old enough to stop asking questions and to blindly sign my pad. He told me that he was not. He said, "I want to get better before either of us hits 80. That's why I guess it's okay when you think twice before giving me methamphetamine just because I ask for it. Maybe you think I'll get better if you talk things out with me instead so I understand why I need these medications instead of the other ones?"

"Not maybe," I told him, "Absolutely. But first give me the dextroamphetamine you bought off the streets."

He did.

Dr. Freedman is a third-year resident in the Department of Psychiatry, Beth Israel Deaconess Medical Center, Boston. *The author thanks Suzanna Zimmet, M.D., Matcheri Keshavan, M.D., and Michael Kahn, M.D., of the Beth Israel Deaconess Medical Center, Boston.*

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TEST YOUR KNOWLEDGE

In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions.
(answers will appear in the next issue)

In preparation for the PRITE and ABPN Board examinations, test your knowledge with the following questions (answers will appear in the next issue).

This month's questions are courtesy of Krzysztof Mlak, M.D. Dr. Mlak is a fifth-year resident in the Department of Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit. Please see the case report in this issue (pp. 7–9) accompanying this month's questions.

Question #1

When used near the time of birth, tricyclic antidepressants are associated with perinatal withdrawal symptoms, such as constipation, urinary retention, and tachycardia, in neonates. Which one of the following tricyclic medications is least likely to cause these symptoms when used during the peripartum period?:

A. Amitryptiline
B. Imipramine
C. Desipramine
D. Trimipramine
E. Doxepin

Question #2

A 20-year-old young woman with a diagnosis of bipolar disorder is being treated with lithium. A routine pregnancy test reveals a positive result. Upon careful consideration of risks and benefits, lithium treatment is continued. At what gestational age are cardiac malformations detected earliest?:

A. 6 weeks
B. 12 weeks
C. 18 weeks
D. 24 weeks

ANSWERS TO NOVEMBER QUESTIONS

Question #1

Answer: D

Autistic disorder is characterized by impairments in three core symptom groups. Impairment in social interaction, including eye-eye gaze and lack of social reciprocity, is the most commonly encountered group. Qualitative impairments in communication, such as delayed speech or lack of appropriate social imitative play, may also be noted. The final symptom group consists of a restricted pattern of behavior and interests as demonstrated by prominence of routines and repetitive motor mannerisms, such as hand flapping. Symptoms occur before age 3 (1).

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Question #2

Answer: C

The term autism spectrum disorder is widely used among clinicians, researchers, and caregivers. While it is not specifically coded in DSM-IV, the Centers for Disease Control and Prevention as well as prominent research groups define autism spectrum disorders as encompassing three key conditions: Asperger's syndrome, autistic disorder, and pervasive developmental disorder not otherwise specified (1, 2). Tourette's syndrome is not conceptualized as falling under the umbrella term autism spectrum disorder. Tourette's syndrome presents with vocal and motor tics and does not require impairment of social interaction or in communication or a restricted range of interests (3).

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We are currently seeking residents who are interested in submitting Board-style questions to appear in the Test Your Knowledge feature. Selected residents will receive acknowledgment in the issue in which their questions are featured.
Submissions should include the following:
1. Two to three Board review-style questions with four to five answer choices.
2. Answers should be complete and include detailed explanations with references from pertinent peer-reviewed journals, textbooks, or reference manuals.
***Please direct all inquiries and submissions to Dr. Seawell; mseawell@med.wayne.edu.**

Author Information for *The Residents' Journal* Submissions

The Residents' Journal accepts manuscripts authored by medical students, resident physicians, and fellows; manuscripts authored by members of faculty cannot be accepted.

1. **Commentary:** Generally includes descriptions of recent events, opinion pieces, or narratives. Limited to 500 words and five references.
2. **Treatment in Psychiatry:** This article type begins with a brief, common clinical vignette and involves a description of the evaluation and management of a clinical scenario that house officers frequently encounter. This article type should also include 2-4 multiple choice questions based on the article's content. Limited to 1,500 words, 15 references, and one figure.
3. **Clinical Case Conference:** A presentation and discussion of an unusual clinical event. Limited to 1,250 words, 10 references, and one figure.
4. **Original Research:** Reports of novel observations and research. Limited to 1,250 words, 10 references, and two figures.
5. **Review Article:** A clinically relevant review focused on educating the resident physician. Limited to 1,500 words, 20 references, and one figure.
6. **Letters to the Editor:** Limited to 250 words (including 3 references) and three authors. Comments on articles published in *The Residents' Journal* will be considered for publication if received within 1 month of publication of the original article.
7. **Book Review:** Limited to 500 words and 3 references.

Abstracts: Articles should not include an abstract.

Upcoming Issue Themes

Please note that we will consider articles outside of the theme.

January 2012
Section Theme: PTSD and Traumatic Brain Injuries
Guest Section Editor: Brandon Cornejo, M.D., Ph.D.
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February 2012
Contact Sarah M. Fayad: fayad@ufl.edu

March 2012
Section Theme: Memory Disorders
Guest Section Editor: Sarah Jane De Asis, M.D.
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April 2012
Section Theme: Family Psychiatry
Guest Section Editor: Michael Ascher, M.D.
michaelaschermd@gmail.com

May 2012
Section Theme: Sexual Disorders
Guest Section Editors: Almari Ginory, D.O., Laura Mayol-Sabatier, M.D., and Nicole Edmond, M.D.
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June 2012
Section Theme: Advocacy in Psychiatry
Guest Section Editor: John Lusins, M.D.
drjlusins@gmail.com