The Residents' JOURNAL

a publication of
The American Journal of Psychiatry

March 2012 Volume 7 Issue 3

Inside

In This Issue

This issue of the *Residents' Journal* features articles on the topic of memory disorders. Sarah Jane De Asis, M.D., provides a comprehensive review of pharmacotherapy in treating cognitive decline in patients with Alzheimer's disease, and Taral R. Sharma, M.D., M.B.A. discusses the etiology, clinical presentation, and treatment management of coprophagia in elderly patients with cognitive impairment.

Pharmacotherapy for Preventing Cognitive Decline in Alzheimer's Dementia: A Review

Sarah Jane De Asis, M.D.
Department of Psychiatry, Yale University School of Medicine, New Haven, Connecticut

Alzheimer's disease is the most common form of dementia. More than 35 million people worldwide and 5.5 million in the United States have Alzheimer's (1). It is a fatal neurodegenerative disease that leads to death within 3–9 years after diagnosis. The principal risk factor is age, and the incidence of the disease doubles every 5 years after 65 years of age (1). It is important to be able to diagnose Alzheimer's disease and to initiate treatment to prevent cognitive decline.

There are two main types of medications used to treat the cognitive decline in Alzheimer's: cholinesterase inhibitors and *N*-methyl-D-aspartic acid antagonists. These medications produce moderate symptomatic benefit but do not entirely stop the disease progression (2). The purpose of this article is to provide a brief review of some of the published studies of pharmacotherapy for cognition in Alzheimer's disease and the effectiveness and side-effect profiles of these interventions.

Cholinesterase inhibitors inhibit the breakdown of acetylcholine and therefore improve cholinergic transmission in the brain. Available cholinesterase inhibitors include rivastigmine, galantamine, donepezil, and tacrine, which are all Food and Drug Administration (FDA)-approved for treatment of mild to moderate dementia. However, tacrine has been rarely used due to its hepatoxicity.

Rivastigmine inhibits both acetylcholinesterase and butyrylcholinesterase. It has a half-life of 2 hours and is initiated at a dose of 1.5 mg, taken twice daily; this is increased by 1.5 mg every 2 weeks to a daily maximum dose of 6–12 mg divided into two doses (3). A skin patch is available to minimize gastrointestinal side effects associated with oral dosing.

Galantamine has a half-life of 6–8 hours and is unique in that it modulates neuronal nicotinic receptors (3). It is initiated at a dose of 4 mg twice daily and titrated by 4 mg per dose every 4 weeks up to a dose of 24 mg daily (in total). An extended-release form is available, with a once-daily dose.

Donepezil is approved for all stages of dementia. It has a half-life of 70 hours, with once-daily doses ranging from 5 mg to 23 mg.

Cholinesterase inhibitors generally require dosage adjustments with regard to renal (rivastigmine and galantamine) and hepatic (rivastigmine, galantamine, and donepezil) impairments. Common side effects are nausea, vomiting, diarrhea, headache, dizziness, and anorexia nervosa.

Memantine is the only *N*-methyl-D-aspartic acid (NMDA) antagonist available with FDA-approval for treatment of moderate-to-severe dementia. This treatment may prevent neurotoxicity due to its antagonism of glutamate that has been linked to neurodegeneration and excitotoxicity (3). It has a half-life of 60–80 hours and is initiated at a dose of 5 mg daily, increasing weekly by 5 mg up to a maximum dose of 20 mg daily. It is available in twice-daily doses, and adjustment

continued on page 3

continued from page 2

is needed with regard to renal impairment (3). Side effects are dizziness, headache, constipation, and confusion.

There are studies describing the effectiveness of cholinesterase inhibitors and NMDA antagonists in treating cognitive decline in patients with Alzheimer's disease. Meta-analyses conducted by Ritchie et al. (4), Lanctôt et al. (5), and Takeda et al. (6) reported significant benefits of the use of cholinesterase inhibitors over placebo as indicated by cognitive measures (the Alzheimer's Disease Assessment Scale–Cognitive subscale [ADAS-Cog] and Mini-Mental State Examination [MMSE]) (6). Patients who received cholinesterase inhibitors also showed global improvement over individuals who received placebo as measured by the Clinical Global Impressions Scale (CGI) and Clinician Interview Based Impression of Change incorporating caregiver information (CIBIC-Plus). The side-effect profile was higher in the treatment groups. Additionally, the dropout rates due to Alzheimer's were higher among those receiving cholinesterase inhibitors than among those receiving placebo, with drop out occurring more often in galantamine groups and less often in donepezil groups (5, 6). Herrmann et al. (7) reported that there is continuous use of cholinesterase inhibitors for lengthy periods until death in the community and in long-term facilities. Hogan et al. (8) compared three pharmaceutical-sponsored studies of cholinesterase inhibitors, although there were several limitations in these studies and thus concerns about interpretation of the results.

Several randomized placebo-controlled studies (9–11) have demonstrated that patients receiving donepezil treatment show improvement in scores on the MMSE (9, 11), Severe Impairment Battery (10), and Clinical Dementia Rating Scale (11). These studies also demonstrated benefits of donepezil over placebo as indicated by scores on the following global measures: the Gottfries-Bråne-Steen Scale (9), CIBIC-Plus, and CGI-Improvement (10). There was also a reported advantage of donepezil treatment with regard to activities of daily living (9, 10). Functional decline was reported as being delayed and stabilized in patients receiving donepezil, as measured by scores on the Alzheimer's Disease Functional Assessment and Change Scale (11). Contrarily, in a trial conducted by the AD2000 Collaborative Group (12), the drug showed little benefit, as measured by scores on the MMSE and Bristol Activities of Daily Living Scale.

Memantine is indicated for treatment of moderate-to-severe dementia and usually used off-label, with or without cholinesterase inhibitors for mild dementia (13). Schneider et al. (13) and Herrmann and Lancôt (14) reported that there was no significant difference in mild-to-moderate dementia symptoms with use of memantine over placebo, as measured by scores on the ADAS-Cog, CIBIC-Plus, Alzheimer's Disease Cooperative Study–Activities of Daily Living (ADCS-ADL), and Neuropsychiatric Inventory (NPI). However, for moderate-to-severe dementia (14, 15), it has been consistently demonstrated that memantine, alone or in combination with cholinesterase inhibitors, provides significant improvement over placebo in cognition (ADAS-Cog, SIB), functioning (ADCS-ADL), and global (CIBIC-Plus) measures. In their review, Herrmann and Lancôt (14) reported that adverse events of memantine were similar to those for placebo.

Behavioral and psychological symptoms of dementia, which include depression, anxiety, apathy, delusions, hallucinations, sleep problems, agitation, aggression, and impulsivity, are major concerns for both patients and their caregivers. These symptoms tend to occur in association with substantial cognitive decline, and thus maintaining cognitive ability is vital. In their meta-analysis, Campbell et al. (16) reported that there was a significant reduction in behavioral and psychological symptoms with use of cholinesterase inhibitors, as measured by scores on the NPI. Herrmann and Lancôt (14) and Maidment et al. (17) reported decreased NPI scores among patients with dementia receiving memantine treatment.

Level of cognitive functioning is considered to be one of the strongest predictors for the institutionalization of patients with dementia (16). Overall, results from meta-analyses and clinical trials have shown significant benefits of the use of both cholinesterase inhibitors and memantine for treatment of impairment in cognition and function as well as neuropsychiatric symptoms in patients with Alzheimer's disease.

Dr. De Asis is a Geriatric Psychiatry Fellow in the Department of Psychiatry, Yale University School of Medicine, New Haven, Conn. *The author thanks Rajesh Tampi, M.D., M.S., F.A.P.A., Associate Clinical Professor of Psychiatry, Yale University School of Medicine, for assistance.*

References

1. Querfurth HW, LaFerla FM: Alzheimer's disease. N Engl J Med 2010; 362:329–344
2. Saddichha S, Pandey V: Alzheimer's and non-Alzheimer's dementia: a critical review of pharmacological and nonpharmacological strategies. Am J Alzheimers Dis Other Demen 2008; 23:150–161
3. Brown FW: Cognitive Enhancers. Edited by Schatzberg AF, Nemeroff CB. Washington DC, American Psychiatric Publishing, 2009, pp 811–820
4. Ritchie CW, Ames D, Clayton T: Metaanalysis of randomized trials of the efficacy and safety of donepezil, galantamine, and rivastigmine for the treatment of Alzheimer's disease. Am J Geriatr Psychiatry 2004; 12:358–369
5. Lanctôt KL, Herrmann N, Yau KK, Khan LR, Liu BA, Loulou MM, Einarson TR: Efficacy and safety of cholinesterase inhibitors in Alzheimer's disease: a meta-analysis. CMAJ 2003; 169:557–564
6. Takeda A, Loveman E, Clegg A, Kirby J, Picot J, Payne E, Green C: A systematic review of the clinical effectiveness of donepezil, rivastigmine and galantamine on cognition, quality of life and adverse events in Alzheimer's disease. Int J Geriatr Psychiatry 2006; 21:17–28
7. Herrmann N, Gill SS, Bell CM, Anderson GM, Bronskill SE, Shulman KI, Fischer HD, Sykora K, Shi HS, Rochon PA: A population-based study of cholinesterase inhibitor use for dementia. J Am Geriatri Soc 2007; 55:1517–1523
8. Hogan DB, Goldlist B, Naglie G, Patterson C: Comparison studies of

continued on page 4

continued from page 3

cholinesterase inhibitors for Alzheimer's disease. Lancet Neurol 2004; 3:622–626

9. Winblad B, Engedal K, Soininen H, Verhey F, Waldemar G, Wimo A, Wetterholm A-L, Zhang R, Haglund A, Subbiah P, Donepezil Nordic Study Group: A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. Neurology 2001; 57:489–495
10. Winblad B, Black SE, Homma A, Schwam EM, Moline M, Xu Y, Perdomo CA, Swartz J, Albert K: Donepezil treatment in severe Alzheimer's disease: a pooled analysis of three clinical trials. Curr Med Res Opin 2009; 25:2577–2587
11. Mohs RC, Doody RS, Morris JC, Ieni JR, Rogers SL, Perdomo CA, Pratt RD: A 1-year, placebo-controlled preservation of function survival study of donepezil in AD patients. Neurology 2001; 57:481–488
12. Courtney C, Farrell D, Gray R, Hills R, Lynch L, Sellwood E, Edwards S, Hardyman W, Raftery J, Crome P, Lendon C, Shaw H, Bentham P; AD2000 Collaborative Group: Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomized double-blind trial. Lancet 2004; 363:2105–2115
13. Schneider LS, Dagerman KS, Higgins PT, McShane R: Lack of evidence for the efficacy of memantine in mild Alzheimer disease. Arch Neurol 2011; 68:991–998
14. Herrmann N, Li A, Lancôt K: Memantine in dementia: a review of the current evidence. Expert Opin Pharmacother 2011; 12:787–800
15. Wilkinson D, Andersen HF: Analysis of the effect of memantine in reducing the worsening of clinical symptoms in patients with moderate to severe Alzheimer's disease. Dement Geriatr Cogn Disord 2007; 24:138–145
16. Campbell N, Ayub A, Boustani MA, Fix C, Farlow M, Maidment I, Howard R: Impact of cholinesterase inhibitors on behavioral and psychological symptoms of Alzheimer's disease: a meta-analysis. Clin Interv Aging 2008; 3:719–728
17. Maidment ID, Fox CG, Boustani M, Rodriguez J, Brown RC, Katona CL: Efficacy of memantine on behavioral and psychological symptoms related to dementia: a systematic meta-analysis. Ann Pharmacother 2008; 42:32–38

OCD Management: A Review of Serotonin Reuptake Inhibitor Treatment Options and Pharmacological Augmentation Strategies

Sanaz Kumar, M.D.
Department of Psychiatry and Behavioral Sciences,
George Washington University School of Medicine and Health Sciences, Washington, DC

Obsessive compulsive disorder (OCD), a psychiatric illness characterized by obsessions, which are recurrent, persistent, unwanted thoughts, impulses, images, or compulsions, which are repetitive neutralizing behaviors, affects 2.5% of the population worldwide, across gender and socioeconomic lines (1). OCD is responsible for marked distress and functional impairment. In their study examining the prevalence and effect of OCD, Torres et al. (2) reported that compared with individuals with other neuroses, individuals with OCD were "more likely to be unemployed, of lower occupational social class, of lower income, and less likely to be married."

The present article reviews current literature and guidelines regarding adult OCD treatment with serotonin reuptake inhibitors (SRIs), addressing issues of dosing, tolerability, and efficacy. Augmentation strategies, specifically the use of antipsychotics to improve treatment response, are also explored. Although this article is primarily limited to discussion of the pharmacological management of OCD, it is worthwhile to briefly explore the role of exposure and response prevention, a form of cognitive-behavioral therapy, given established clinical efficacy.

According to APA guidelines (3), exposure and response prevention may be the first strategy in treating patients with OCD who are "not too depressed, anxious, or severely ill to cooperate with this treatment modality" or who would rather not take medication. Overall, these guidelines conclude that exposure and response prevention significantly reduces OCD symptoms.

There are only a small number of randomized trials that have addressed the efficacy of exposure and response prevention in conjunction with SRI therapy, rather than either treatment alone. Although the APA guidelines suggest that these studies are flawed in their design/procedure, it was concluded that combination therapy may be superior in some OCD patients. Specifically, they reported that combination therapy may be advantageous in patients who have co-occurring psychiatric disorders that respond to SRI treatment, who have had only partial success with SRI monotherapy, or who prefer to limit the duration of medication.

SRI Monotherapy

APA guidelines recommend treatment with SRI monotherapy in patients who have responded previously to medication or who prefer SRI monotherapy. Further, beginning with SRI monotherapy may be appropriate in cases in which the patient's severity of illness precludes participation in exposure and response prevention or in cases in which this prevention is not available to the patient. Presently, SRI therapies with Food and Drug Administration approval for OCD treatment include clomipramine, fluoxetine, fluvoxamine, paroxetine, and sertraline. There is, however, some evidence summarized in the APA guidelines suggesting that other SRI agents, such as citalopram or venlafaxine, may also be effective. Although these guidelines make no specific mention of which agent to begin with, authors comment that starting with a selective serotonin reuptake inhibitor (SSRI), rather than clomipramine, may be preferred, given issues of tolerability. Further, the choice for a particular agent within the SSRI class may be driven by other considerations, such as the agent's side effect profile, its potential interaction with other drugs, or its protein binding properties.

Clinicians may start patients on the manufacturer-recommended starting dose of an SRI, and APA guidelines propose that this dose may be titrated rapidly—even on a weekly basis, if tolerated—given data suggesting greater relief of OCD symptoms at higher SRI doses. Unfortunately, higher doses of these agents may contribute to unwanted side effects. Striking a balance between optimal treatment of OCD symptoms and minimal side-effect burden may present a challenge for clinicians and patients.

In a recent meta-analysis, Bloch et al. (4) examined the relationship between SSRI dosage, efficacy, and tolerability with respect to OCD treatment. With respect to dosage and efficacy, the authors demonstrated that for every 13–15 OCD patients treated with high SSRI doses, one patient will respond to treatment who would not have otherwise responded at lower doses. Moreover, patients treated with high doses will experience, on average, a 9% or 7% greater decline in OCD symptoms compared with patients treated with low and medium doses, respectively.

At the same time, given data on dosage and tolerability, Bloch et al. reported that for every 17 OCD patients who were treated with high-dose SSRI therapy, one discontinued medication due to a side effect who would not have done so at lower doses. Ultimately, the authors concluded that the increased treatment efficacy of higher-dose SSRIs may counterbalance the increased side-effect burden at these doses.

Even with the use of higher doses, the current literature summarized in the APA guidelines suggests that patients

continued on page 6

continued from page 5

with OCD are unlikely to experience substantial improvement until 4–6 weeks after starting an SRI, and in fact, some patients will experience little improvement until 10–12 weeks after beginning treatment. If after a trial of 8–12 weeks (with at least 4–6 weeks at the highest comfortably tolerated dose) response remains inadequate, expert opinion, as summarized in the APA guidelines, favors a medication change. This change may be a switch to another SRI or augmenting current treatment with another agent, typically an antipsychotic.

Unfortunately, the reality is that an inadequate response with an SRI monotherapy trial is almost just as common as an adequate response. Studies suggest that with an initial SRI trial, 40%–60% of OCD patients do not demonstrate adequate treatment response, and 25% of patients demonstrate no improvement at all (5).

If patients demonstrate little or no response, clinicians' next step may be to switch to another SRI agent altogether; clinical experience suggests that response rates to a second SRI trial may be close to 50%, but the likelihood of response decreases with the number of medication trials, according to APA guidelines. Alternatively, if patients demonstrate moderate responses, then augmentation strategies, for example adding a low-dose antipsychotic to the SRI, may be the next step.

Augmentation of SRI Treatment With Antipsychotics

In a systematic review conducted in 2006, Bloch et al. (5) examined the efficacy of antipsychotic augmentation in the treatment of refractory OCD. The authors reported several findings. First, patients demonstrated high treatment response even 2–3 months after SRI monotherapy was initiated, leading to the conclusion that patients should be treated with at least 3 months of maximally-tolerated SRI therapy before consideration of antipsychotic augmentation. Second, among OCD patients whose symptoms were treatment refractory, nearly one-third demonstrated a treatment response (defined as a reduction in Yale-Brown Obsessive Compulsive Scale score >35%) when antipsychotic augmentation was initiated. Third, patients with comorbid tics were more likely to respond to antipsychotic augmentation than others. Fourth, patients who did not demonstrate improvement within 1 month of initiating antipsychotic treatment were unlikely to continue treatment with this agent. Further, Bloch et al. concluded that there was sufficient evidence to support the efficacy of haloperidol and risperidone as augmenting agents in OCD treatment, although evidence for the efficacy of quetiapine and olanzapine was inconclusive.

Since this review, further data have emerged supporting augmentation with antipsychotic agents. In fact, with respect to risperidone in particular, Dold et al. (6) recently performed a meta-analysis to examine antipsychotic augmentation for treatment-refractory OCD symptoms and found that only patients receiving augmentation therapy with risperidone demonstrated "significant efficacy." Patients treated with antipsychotic augmentation overall were more likely to respond than those receiving only SSRI monotherapy.

For other atypical antipsychotics, the evidence may be less compelling. Several randomized placebo-controlled trials and open-label trials are suggestive of quetiapine as an effective augmenting agent (7). In a comparative study, ziprasidone was not as effective as quetiapine (8). To date, one might conclude that data regarding olanzapine augmentation remain inconclusive, although it may be used in clinical practice (7). Within the past few months, at least one randomized placebo-controlled trial supporting the use of aripiprazole augmentation has been published (9). Evidence beyond this has been limited. Further, little to no literature is available regarding the efficacy of newer atypical antipsychotics, such as asenapine, paliperidone, iloperidone, or lurasidone, as augmenting agents in OCD treatment. Efficacy aside, clinicians should be mindful that antipsychotics carry many unwanted side effects, and it is prudent for clinicians to monitor patients treated with these agents, both for movement and metabolic side effects.

Augmentation and Monotherapy With Other Agents

If antipsychotic augmentation is not effective, augmentation with other agents may be considered. Currently, literature on the role of glutamate modulating agents in OCD treatment is growing. APA guidelines reference that there are studies supporting the use of glutamate antagonists, such as riluzole and topiramate. A study of patients in the McLean/Massachusetts General Hospital Intensive Residential Treatment program concluded that there was preliminary support for the effectiveness of memantine, an N-methyl-d-aspartic receptor antagonist, as an augmenting agent in treating severe OCD symptoms (10).

Finally, it is important to note that the APA guidelines also summarized that data supporting augmentation with a range of medications, including clomipramine, buspirone, pindolol, weekly-dosed morphine sulphate, and inositol, are weak and that data supporting the use of tramadol and d-amphetamine as monotherapy agents are limited.

Conclusions

Management of adult OCD may begin with SRI and or exposure and response prevention therapy. For partial responders, augmentation with an antipsychotic agent is supported by the literature. Given newer developments in the study of OCD, providers and patients should remain optimistic about achieving greater remission of symptoms.

Dr. Kumar is a third-year resident in the Department of Psychiatry and Behavioral Sciences, George Washington University School of Medicine and Health Sciences, Washington, DC.

References

1. American Psychiatric Association: Diagnostic and Statistical Manual of

continued on page 7

continued from page 6

Mental Disorders, 4th ed–Text Revision. Washington, DC, American Psychiatric Publishing, 2000

2. Torres AR, Prince MJ, Bebbington PE, Bhugra D, Brugha TS, Farrell M, Jenkins R, Lewis G, Meltzer H, Singleton N: Obsessive-compulsive disorder: prevalence, comorbidity, impact, and help-seeking in the British National Psychiatric Comorbidity Survey of 2000. Am J Psychiatry 2006; 163:1978–1985
3. American Psychiatric Association: Practice Guideline for the Treatment of Patients With Obsessive-Compulsive Disorder. Washington, DC, American Psychiatric Publishing, 2007
4. Bloch MH, McGuire J, Landeros-Weisenberger A, Leckman JF, Pittenger C: Meta-analysis of the dose-response relationship of SSRI in obsessive-compulsive disorder. Mol Psychiatry 2010; 15:850–855
5. Bloch MH, Landeros-Weisenberger A, Kelmendi B, Coric V, Bracken MB, Leckman JF: A systematic review: antipsychotic augmentation with treatment-refractory obsessive compulsive disorder. Mol Psychiatry 2006; 11:622–632
6. Dold M, Aigner M, Lanzenberger R, Kasper S: Efficacy of antipsychotic augmentation therapy in treatment-resistant obsessive-compulsive disorder: a meta-analysis of double-blind, randomised, placebo-controlled trials. Fortschr Neurol Psychiatry 2011; 79:453–466
7. Komossa K, Depping AM, Meyer M, Kissling W, Leucht S: Second-generation antipsychotics for obsessive compulsive disorder. Cochrane Database Syst Rev 2010; 8:CD008141
8. Savas HA, Yumru M, Ozen ME: Quetiapine and ziprasidone as adjuncts in treatment-resistant obsessive-compulsive disorder: a retrospective comparative study. Clin Drug Investig 2008; 28:439–442
9. Selvi Y, Atli A, Aydin A, Besiroglu L, Ozdemir P, Ozdemir O: The comparison of aripiprazole and risperidone augmentation in selective serotonin reuptake inhibitor-refractory obsessive-compulsive disorder: a single-blind, randomised study. Hum Psychopharmacol 2011; 26:51–57
10. Stewart SE, Jenike EA, Hezel DM, Stack DE, Dodman NH, Shuster L, Jenike MA: A single-blinded case-control study of memantine in severe obsessive-compulsive disorder. J Clin Psychopharmacology 2010; 30:34–39

Case Report

Navigating Ethical Dilemmas in Psychiatry: An Approach to Teaching Trainees

Jan Schuetz-Mueller, M.D.; Emily Steinberg, M.D.; Kelly Morton, M.D.; Jacob Appel, M.D.
Department of Psychiatry, Mount Sinai School of Medicine, New York

Psychiatrists are often called upon in the hospital setting and in the community to aid in the resolution of ethically challenging issues. While psychiatric residents are inevitably confronted with ethical dilemmas, there are no clear guidelines specifying the amount of teaching that residents should receive regarding ethical issues. As part of the core competency of professionalism, the Accreditation Council for Graduate Medical Education (ACGME) currently expects psychiatric residents to demonstrate "high standards of ethical behavior" (1) and requires psychiatric residency programs to "distribute to residents and operate in accordance with the AMA [American Medical Association] Principles of Ethics with 'Special Annotations for Psychiatry,'… to ensure that the application and teaching of these principles are an integral part of the educational process" (1). In a multisite study that included 151 psychiatry residents, Jain et al. (2) reported that overall, residents expressed a need for greater educational attention to principles of ethics and professionalism. While learning principles of ethics and professionalism may be helpful to trainees, true competency comes from understanding how to systematically approach an ethical or professional dilemma and from being able to apply the necessary principles.

Most ethical dilemmas involving patients can be viewed from three distinct perspectives: legal, ethical, and clinical. By being aware of all three frameworks, clinicians are forced to analyze a case thoroughly and understand the implications of their decisions.

All actions by physicians, whether ethical or not, must fall within the rules outlined by the law. Therefore, the legal aspect of any case must be considered first. The psychiatrist should pose the following question: Does the law dictate what I must do in this particular case? If so, then the ethical and clinical frameworks of the case may play less of a role in the decision making process. Often times, however, there are no state, federal, or institutional regulations that dictate how the psychiatrist should proceed. While some states have adopted the AMA guidelines for ethical conduct into law, many states have not defined physicians' ethical behavior in legal terms (3).

Next, the ethical implications of a case can be examined by applying the commonly accepted principles of medical ethics: autonomy, beneficence, nonmaleficence, and justice. The psychiatrist should determine whether all principles are upheld and, if not, understand wherein any conflict may lie. At times, a physician may be asked to determine what principle should take priority. In addition, the aforementioned AMA guidelines can help steer the decision making process. Of major significance is the guideline in section 8 of that document, noting that a physician should "regard responsibility to the patient as paramount" (4).

Lastly, but of no less importance, the clinical framework should always be considered. The psychiatrist might ask themselves the following questions: How does my decision affect my patient and the treatment? What is the meaning of my actions for the patient? How do my actions affect the therapeutic relationship? The ethical and clinical considerations may often overlap, but it should be understood that clarifying the ethical qualities of an intervention is distinct from appreciating its clinical value.

The following three case scenarios are examples of ethically challenging situations. The aforementioned approaches should be applied to highlight the different aspects of each case and how a psychiatrist might proceed in determining the best plan of action.

Case 1

A female psychiatry resident working in the outpatient clinic has been seeing a 38-year-old female immigrant in weekly psychotherapy for the past 9 months. The patient has a history of rape and post-traumatic stress disorder. She has shown significant improvement, but during a session reveals that she is living illegally in the country and has been receiving therapy under her cousin's name and insurance (Table 1).

Analysis

In this particular case, it is not only helpful to parse out the legal, ethical, and clinical aspects, but it is necessary in order to identify the dilemma. The therapist should consider whether the law dictates an intervention. The patient has essentially revealed that she has been committing insurance fraud. The psychiatrist is instantly forced into a position in which she either reports the patient to the insurance company (or the hospital's risk management team) or breaks the law by failing to report the patient, thus becoming an accomplice (5).

The ethical dilemma arises from being forced to break the principle of nonmaleficence. Reporting the patient will likely result in some negative consequence, causing her legal difficulties, possibly even deportation. How then can the psychiatrist act ethically given the situation? The answer lies in upholding as many ethical principles as possible. Autonomy is not an issue in this scenario, but beneficence is. Despite having to "harm" the patient, it is the psychiatrist's duty to ensure that she receives some form of care.

continued on page 9

continued from page 8

The principle of social justice is another driving force that supports the psychiatrist stopping further insurance fraud.

Finally, one must consider the clinical implications in this scenario. The patient revealing her true identity has meaning in the therapy, which can and should be understood. In addition, the psychiatrist must consider that the patient was lying to her for 9 months. Countertransferential aspects can and may influence further treatment, of which the psychiatrist should be mindful, provided that there is an opportunity to continue treatment.

Case 2

A 50-year-old single, Caucasian female is seeing a psychiatrist in twice-weekly psychotherapy for anxiety and depression. After 2 months of treatment, the patient reveals that she has started dating her previous psychiatrist. The patient had been in analysis with this therapist 12 years ago for a period of 2 years. She recently saw him at a party for the first time since terminating with him. They have been on one date since the party but have not been sexually intimate. She reports that she has never felt happier (Table 1).

Analysis

Instinctively, one might feel that there is a boundary violation on the side of the former therapist. From a legal perspective, is the treating psychiatrist required to take any particular action? Since the patient and her former therapist have not been physically intimate, technically, no illegal activity has taken place. If the patient had reported having sexual relations with her former psychiatrist, then the treating physician may be legally bound to report the former psychiatrist. This would depend on state legislature, which varies in the degree to which a physician must report the unethical behavior of a fellow physician. However, there is no legal obligation to act in this particular case. From an ethical viewpoint, should the treating psychiatrist intervene? While the principle of beneficence reflects the obligation to help a patient, it does not give a physician the right to prevent the patient from making potentially harmful decisions. Telling the patient what to do would, in fact, represent a violation of patient autonomy. The true dilemma in this case stems from a duty to "strive to report physicians deficient in character or competence" while wanting to uphold the principle of nonmaleficence (4). Reporting the former psychiatrist might emotionally harm the patient as well as severely interfere in the therapeutic process. Since there are no clear legal or ethical guidelines that dictate further action in this case, the psychiatrist must rely on the clinical framework to inform his or her decision.

Case 3

A senior psychiatry resident has been treating a 10-year-old girl in weekly psychodynamic therapy for 2 years, since the death of the child's father. The resident also meets with the patient's mother regularly to discuss scheduling and any other concerns that arise. Recently, the patient revealed to the resident that her father abused her and forced her to hide this from her mother. At the next meeting with the mother, she asks whether her daughter has ever said anything about being beaten by her now deceased father. The mother denies having witnessed any abuse but suspects it may have happened (Table 1).

Analysis

From a legal standpoint, the resident's course of action is clearly defined: the pa-

continued on page 10

Table 1: Perspectives to Consider in Cases Involving Ethics and Professionalism

Case	Legal	Ethical	Clinical
Illegal immigrant	Duty to report insurance fraud and avoid becoming an accomplice (5).	Reporting the patient violates nonmaleficence. Beneficence dictates that the physician refers the patient for ongoing care.	Reporting the patient interferes with the therapeutic relationship. The scenario greatly affects transference and counter-transference.
Patient-doctor romance	Sexual relations between the physician and patient are illegal in certain states and should be reported by fellow physicians. No illegal activity was reported in this case.	APA ethics encourage reporting "physicians deficient in character" (4). Reporting the ex-therapist may violate nonmaleficence. Interfering with the relationship may violate patient autonomy.	Reporting the ex-therapist interferes with the therapeutic relationship. It affects transference and counter-transference. How would the patient be most helped?
Child with history of abuse	The child's mother has the right to be informed. Children are deemed unable to make informed decisions. Consider it a duty to report child abuse.	Sharing information with the mother may violate nonmaleficence. Withholding information may be considered beneficent toward the patient.	Consider the effect of revealing information to the mother. This may negatively affect the therapeutic relationship What would be most therapeutic for patient?

continued from page 9

tient is a minor, which gives the parent access to the treatment material. Mandated reporting of abuse may come into play, depending on the level of suspicion, but it is not considered to be central in this dilemma. From an ethical perspective, the resident is forced to consider beneficence and nonmaleficence. Patient autonomy is generally less implicit in work with minors, since they are deemed unable to make informed decisions. From a clinical perspective, the resident's choice of action will have a significant effect on the treatment. In such a scenario, disclosing the information to the parent could result in distrust and, ultimately, the end of treatment. Although legally the resident is required to disclose information to the parent, it may be ethically and clinically unjustifiable. Such a scenario requires careful and sensitive consideration. Ultimately, refusing to disclose information on the basis of acting on the patient's best interest may be legally justifiable (6).

Conclusions

As with all physicians, psychiatrists are required to uphold the highest standards of ethical and professional conduct. Boundaries and appropriate relationships are perhaps more salient in psychiatry than in other medical specialties, as highly personal information is shared between the doctor and the patient. Therefore, it is imperative that psychiatrists not only show empathy and sensitivity toward their patients but that they feel confident in understanding how to navigate the complex seas of ethics and professionalism.

At the time this manuscript was accepted for publication, Drs. Schuetz-Mueller, Steinberg, and Morton were fourth-year residents in the Department of Psychiatry, Mount Sinai School of Medicine, New York. Dr. Appel is currently a third-year resident at Mount Sinai.

References

1. Accreditation Council for Graduate Medical Education: ACGME Program Requirements for Graduate Medical Education in Psychiatry. http://www.acgme.org/acWebsite/downloads/RRC_progReq/400_psychiatry_07012007_u04122008.pdf (Accessed May 29, 2011)
2. Jain S, Lapid MI, Dunn LB, Roberts LW: Psychiatric residents' needs for education about informed consent, principles of ethics and professionalism, and caring for vulnerable populations: results of a multisite survey. Acad Psychiatry 2011; 35:184–190
3. Dobash T: Physician-patient sexual contact: the battle between the state and the medical profession. Wash Lee Law Rev 1993; 50:1725–1758
4. American Psychiatric Association: The Principles of Medical Ethics With Annotations Especially Applicable to Psychiatry, 2009 Edition. Arlington, Va, American Psychiatric Association, 2009
5. United States Code (2011), Title 18, Part I, Chapter 63, § 1347, Health care fraud
6. Behnke S, Warner E: Confidentiality in the treatment of adolescents. Monitor Psychol 2002; 33:44

Coprophagia in Geriatric Patients With Cognitive Impairment

Taral R. Sharma, M.D., M.B.A.
Department of Psychiatry, Carillion Clinic Virginia Tech-Carillion School of Medicine, Roanoke, Va.

Coprophagia is the uncommon symptom of eating feces, often observed in patients with dementia. Despite its presence in the published literature, dating as far back as 1897, the exact prevalence of coprophagia is not known, and the topic is largely neglected (1). However, coprophagia appears to be more prevalent than expected, especially among geriatric patients with cognitive impairment. It has been reported that patients with advanced cognitive impairment often grasp, chew, and eat their feces with great pleasure and satisfaction (2). In the recent literature, coprophagia is considered to be an unusual variant of pica (3, 4). The present study provides a review of available literature detailing the possible etiology, clinical presentation, management, and complications of coprophagia among geriatric patients with cognitive impairment.

Etiology

The etiology of coprophagia among geriatric patients with cognitive impairment remains unknown. Read and Harrington (5) were among the first to study experimental thiamine deficiency in the Beagle, and they observed symptoms of coprophagia at the intermediate stage of thiamine deficiency in this breed of dog. Agleton and Passingham (6) described a syndrome produced by total amygdaloid lesions in monkeys, who showed excessive oral behavior, hyperemotionality, and coprophagia. However, a case series failed to prove any relationship between thiamine deficiency and coprophagia and found the model of dementia affecting the amygdaloid nucleus and accounting for coprophagia to be inadequate (5). Some researchers believe that coprophagia is a result of severe cognitive dysfunction and behavioral disinhibition (8). In line with this, one study found cognitive impairment to be an important factor in the etiology of pica and coprophagia and that both disorders are fairly common in geriatric patients with dementia, but the prevalence of coprophagia and its relationship to other disturbances of eating are unknown (9).

Some reviews have attempted to describe possible psychological explanations of coprophagia (10, 11). Freud (12) reported that some libidinal pleasure exists in the anal stage of human development, which involves components of retaining and expelling feces and pleasure in feces itself. The process of toilet training is believed to result in certain character traits (12). McDonald and Behl (11) stated that disinhibition due to dementia may induce the high-drive personality to dispose of feces by eating it, rather than smearing it or being encopretic.

Clinical Presentation

Clinical presentation of coprophagia in the geriatric population with cognitive impairment is typically of insidious onset among institutionalized individuals, which includes residents of nursing homes and assisted living facilities (7). However, onset could be abrupt in individuals with coexisting medical or psychiatric illness (2, 3). Onset can be associated with disorientation, confusion, physical aggression, or occasional agitation (10). Simultaneously, some geriatric patients are found to be incontinent of urine and feces (7). Coprophagia has also been found to be associated with smearing of feces, also called scatolia (14).

Management

The initial goal of symptom management is often focused on treating possible reversible causes. In a study of scatolia patients who were also incontinent (of urine and feces) and for whom constipation was a common factor, bowel frequencies returned to normal and smearing of feces ceased with use of laxatives (14). Supplementing for existing nutritional deficiencies, especially thiamine, was also recommended. Treatment of coexisting psychiatric illness, relief from constipation and pruritis ani, and ensuring the maintenance of good oral hygiene have all been reported to be effective. Behavioral interventions are considered to be part of first-line management, especially in geriatric patients with limited cognitive abilities. In some studies, recommended intervention targeting behavioral changes included antecedent manipulation, discrimination training regarding edible and inedible items, use of self-protection devices prohibiting placement of objects in the mouth, sensory reinforcement, differential reinforcement of incompatible behaviors, and overcorrection (correcting the environment or practicing appropriate alternative responses) (15, 16). Most of the patients with cognitive impairment in

continued on page 12

continued from page 11

these studies were not taking any psychotropic medications. However, there are reported cases of improved outcome with selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, antipsychotics, donepezil, perospirone, and treatment of nutritional deficiencies (16).

Complications

Coprophagia has been found to be associated with multiple complications, including sialadenitis (17), infestation with intestinal parasites (10), airway obstruction, and possible death due to café coronary (8). Other complications are poor oral hygiene, chronic gingival infection, and chronic lesions on the mucosa of the vestibule secondary to the retention of feces (18). Additionally, coprophagia evokes intense emotional reactions in those who are exposed to the behavior, particularly caregivers, ancillary staff of nursing homes and assisted living facilities, and other residents of care facilities (10).

Future Directions

Although the possible etiology of coprophagia in geriatric patients with cognitive impairment is not consistently explained in the literature, symptoms can be associated with scatolia and include disorientation, confusion, physical aggression, and agitation. Initially, treatment should be focused on managing reversible causes and resolving concurrent medical and psychiatric illnesses, followed by behavioral interventions. The use of psychotropic agents, including SSRIs, mood stabilizers, and antipsychotics, should be targeted at controlling behavioral dysregulation. If untreated, coprophagia could lead to severe complications for geriatric patients and their caregivers. Future prospective investigations should examine factors associated with etiology, evaluation methods, clinical course, and guidelines for management.

Dr. Sharma is a third-year resident in the Department of Psychiatry, Carillion Clinic Virginia Tech-Carillion School of Medicine, Roanoke, Va. The author thanks Azziza Bankole, M.D., for assistance with this manuscript.

References

1. Kellogg TH: A Textbook of Mental Diseases. London, J & A Churchill, 1897
2. Arieti S: The placing-into-mouth and coprophagic habits, in On Schizophrenia, Phobias, Depression, Psychotherapy and the Farther Shores of Psychiatry. Edited by Arieti S. New York, Brunner/Mazel, 1978
3. Zeitlin SB, Polivy J: Coprophagia as a manifestation of obsessive-compulsive disorder: a case report. J Behav Ther Exp Psychiatry 1995; 26:57–63
4. Donnellan CA, Playfer JR: A case of coprophagia presenting with sialadenitis. Age Ageing 1999; 28:233–234
5. Read DH, Harrington DD: Experimentally induced thiamine deficiency in Beagle dogs: clinical observations. Am J Vet Res 1981; 42:984–991
6. Aggleton JP, Passingham RE: Syndrome produced by lesions of the amygdala in monkeys (macaca mulatta). J Compar Physiol Psychology 1981; 95:961–977
7. Ghaziuddin N, McDonald C: A clinical study of adult coprophagics. Br J Psychiatry 1985; 147:312–313
8. Byard RW: Coprophagic café coronary. Am J Forensic Med Pathol 2001; 22:96–99
9. Fairburn CG, Hope RA: Changes in eating in dementia. Neurobiol Aging 1988; 9:28–29
10. Beck DA, Frohberg NR: Coprophagia in an elderly man: a case report and review of the literature. Int J Psychiatry Med 2005; 35:417–427
11. McDonald C, Behl N, Sudhakar P: Recalcitrant behaviour problems, in Rehabilitation in Psychiatric Practice. Edited by Mccreadie RG. London, Pitman, 1982, pp 55–67
12. Freud S: Beyond the pleasure principle, in The Complete Psychological Works of Sigmund Freud, vol 18. Edited by Strachey J. London, Hogarth Press, 1955 (1920)
13. Mason T: Scatolia: psychosis to protest. J Psychiatr Ment Health Nurs 1996; 3:303–311
14. Begg AH, McDonald C: Scatolia in elderly people with dementia. Int J Geriatr Psychiatry 1989; 4: 53–54
15. Donnellan CA, Playfer JR: A case of coprophagia presenting with sialadenitis. Age Ageing 1999; 28:233–234
16. Karpman B: Coprophagia: collective review. Psychoanal Rev 1948; 35:253–272
17. Rose EA, Porcerelli JH, Neale AV: Pica: common but commonly missed. J Am Board Fam Pract 2000; 13:353–358
18. Sharma TR, Aly M, Kavuru B: Coprophagia and pica in individuals with mild to moderate dementia and mixed (iron deficiency and macrocytic) anemia. J Am Geriatr Soc 2011; 59:2375–2377

"Bath Salts": Emergence of an Epidemic

George Loeffler, M.D.
Department of Mental Health, Naval Medical Center, San Diego

"Bath salts" are a collection of structurally related, synthetic sympathomimetic designer drugs, which recently emerged in the United States with alarming results. Mark Ryan, Director of the Louisiana Poison Control, stated that bath salts represent the worst attributes of cocaine, phencyclidine, lysergide, 3,4-methylenedioxy-*N*-methylamphetamine (MDMA or ecstasy), and methamphetamine taken together (1). Legal in the United States until only recently, these drugs are sold online, in retail outlets (such as head shops and gas stations), and via dealers. To circumvent oversight laws, they are marketed as bath salts or plant food and frequently include the disclaimer "not for human consumption." Most of these substances have never been tested in humans, and we are only now beginning to learn of their basic pharmacology.

Bath salts became popular in Europe in about 2009 (1). In the United States, the National Forensic Laboratory Information Systems, a branch of the Drug Enforcement Agency, which monitors reports from poison control centers nationwide, first received reports of the use of bath salts in July 2010. The number of contacts increased from three in July 2010 to 182 in December 2010 and then to 749 in June 2011, the last date for which data are available (2).

Class Pharmacology

Bath salts are a structurally related class of compounds known as cathinones, or beta-keto phenethylamines (3). The progenitor molecule, cathinone, is isolated from the khat plant, which is chewed for its stimulant properties. Cathinone is structurally identical to amphetamine except for a single carbonyl bond. The resultant increased molecular polarity lessens blood-brain barrier penetration (4).

Cathinones bind to monoamine transporters for dopamine, serotonin, and norepinephrine, although individual synthetic cathinones vary in relative potency (4). Cathinones are strong inhibitors of the norepinephrine transporter, which accounts for the sympathomimetic properties (4). Cathinones have been described as more potent inhibitors of monoamine oxidase (MAO), particularly MAO-B, than their amphetamine analogs (5).

Mephedrone: Pharmacology and Clinical Presentation

Mephedrone, or 4-methylmethcathinone, recently became popular in Europe, particularly in the club scene. The purity and availability of MDMA decreased because of prevention by European Union countries of the importation of precursor compounds, and mephedrone emerged to take its place (6). More recently, mephedrone arrived in the United States as one of the two principle synthetic cathinones of abuse (the other being methylenedioxypyrovalerone [MDPV], also discussed in this article) (2).

Little is known of the pharmacology of mephedrone. Kehr et al. (7) compared the effects of mephedrone with that of amphetamine and MDMA on dopamine and serotonin levels in the nucleus accumbens in rats. Following mephedrone ingestion, dopamine levels increased 496% from baseline, whereas they increased 412% with amphetamine and only 235% with MDMA. Serotonin levels were increased 941% from baseline with mephedrone, 165% with amphetamine, and 911% with MDMA (most results were statistically significant, $p<0.001$) (7).

MDMA is an entactogen, a substance that causes one to emotionally identify with or feel connected to another, due to its ability to increase serotonin concentrations. With mephedrone resulting in even greater levels of serotonin, it is understandable that it usurped MDMA (6). Mephedrone also possesses the stimulant and euphoric properties associated with amphetamine. Thus, although it initially became popular in the European club scene principally for its entactogenic properties, in the United States, it appears to have translated into broader arenas of abuse traditionally occupied by cocaine and methamphetamine users.

Mephedrone is a white crystal powder with a light yellow hue and distinctive unpleasant odor described as "vanilla and bleach," "stale urine," or "electric circuit boards." The most common modes of ingestion are insufflation (nasally) and oral. Less commonly, it is administered rectally, via smoking, or intravenously (8).

The "come-up" occurs within 10 to 20 minutes after ingestion, with the peak effect occurring between 45 minutes and an hour, followed by the "come-down," which takes place between 60 and 120 minutes after ingestion. A strong compulsion to redose has been observed, and tolerance is noted to develop quickly (8).

The desired effects of mephedrone include intense stimulation, alertness, and euphoria as well as increased empathy, feelings of closeness, sociability, and talkativeness. Moderate sexual arousal has been described as well as perceptual distortions and intensification of sensory experiences. Numerous untoward effects, including anxiety, agitation, hallucinations, paranoid delusions, insomnia, poor concentration, memory impairment, tremors, seizures, and headaches, have also been described. Case reports of hyponatremia with encephalopathy (9), acute myocarditis (10), and multiple deaths (11), including fatal excited delirium (12), are increasingly reported.

Standard urine drug screens do not detect synthetic cathinones, including mephedrone or MDPV. Gas chromatography and mass spectroscopy can be performed; however, these tests are expensive and often take time. Some hospitals mail tests for mephedrone and MDPV, and results take approximately 2 weeks to return. Recommendations for treatment of patients presenting with an acute toxidrome are limited to benzodiazepines and supportive measures (13).

continued on page 14

continued from page 13

MDPV: Pharmacology and Clinical Presentation

MDPV is a synthetic cathinone that, while less prevalent in Europe than mephedrone, has quickly become popular in the United States (2). There are no pharmacological studies of MDPV, and thus we are limited to inferring similarities with structurally related compounds, in particular another cathinone, pyrovalerone. Pyrovalerone inhibits norepinephrine and dopamine reuptake, while having minimal effect on serotonin (14). This is consistent with reports of MDPV describing marked sympathomimetic stimulation and euphoria, with minimal entactogenic effect.

Response to use of MDPV appears to last approximately twice as long as that of mephedrone, with the come-up occurring at about 1 hour postingestion, the peak occurring at 90 minutes and lasting an hour, and the come-down occurring between 2½ and 3½ hours postingestion. Similar to mephedrone, there appears to be significant compulsion to redose and quick development of tolerance (15).

In the United States, emergency department visits for sympathomimetic toxidromes related to MDPV as well as frank paranoid psychosis are becoming increasingly reported.

Penders and Gestring (16) described three cases of MDPV-induced hallucinatory delirium. The patients in these cases endorsed dream-like audio-visual hallucinations of threatening intruders and a tremendous sense of fearfulness. Prominent deficits with attention and memory encoding warranted the diagnosis of hallucinatory delirium. All three patients received low-dose antipsychotics (either risperidone [0.5 mg p.o. b.i.d.] or haloperidol [1 mg p.o. b.i.d.]) during their brief inpatient psychiatric hospital admission (16).

In a case series conducted by poison control centers in Kentucky and Louisiana, it was observed that "aggressive violent behavior, hallucinations, and paranoia in higher percentages than previously reported" occurred following the use of bath salts (3). The following behaviors were reported in case patients who used bath salts: jumping out of a window to flee from nonexistent pursuers; demonstrating out-of-control behavior that required electric shock to subdue as well as physical restraint from others; repeatedly firing guns out of house windows at strangers who were not there; walking into a river in January to look for a friend who was not there; leaving a 2-year-old child in the middle of a highway because the child had demons; climbing into the attic of a home with a gun to kill demons that were hiding there; and breaking all the windows in a house and wandering barefoot through the broken glass. Although the samples of bath salts that were purchased, which were analyzed, contained MDPV, mephedrone, and methylone, urine samples collected from symptomatic patients were positive only for MDPV (3).

A recent article regarding acute treatment of MDPV toxidrome, published in the *New England Journal of Medicine*, recommended intravenous benzodiazepines, for both sedation and control of seizures, and intravenous fluids, specifically for possible rhabdomyolysis (14).

Table 1: Comparison of Mephedrone and MDPV

Characteristic	Mephedrone	MDPV
Common names	Meow meow; MMCat; Meph	Ivory wave; vanilla sky; energy-1
Pharmacological class	Synethetic cathinone	Synthetic cathinone
CNS effects	Increased dopamine Increased norepinephrine Increased serotonin	Increased dopamine Increased norepinephrine no serotonin
Route of administration	Snorting (insufflation); swallowing capsules; "bombing" (wrapping in cigarette paper and swallowing); smoking; intravenous injection; rectal (plugging or enema)	Snorting (insufflation); swallowing capsules; "bombing" (wrapping in cigarette paper and swallowing); smoking; intravenous injection; rectal (plugging or enema)
Duration of response: "come-up," peak, "come-down," respectively	10–20 minutes; 45–60 minutes; 60 minutes–2 hours	60 minutes; 1.5–2.5 hours; 2.5–3 hours
Desired psychoactive effects	Euphoria; empathy; stimulation ("speediness"); intensification of sensory experience	Euphoria; stimulation
Untoward effects	Anxiety; hallucinations; insomnia; dysphoria; increased heart rate; chest pain; muscle twitches/tension; lack of appetite/thirst	Severe, prolonged panic attacks; hallucinations; paranoia; suicidal ideation; insomnia; dysphoria; irregular, increased heart rate; chest pain; muscle twitches/tension; lack of appetite/thirst
Tolerance and desire to redose, respectively	High; high	High; very High
U.S. legal status	Class 1 controlled substance	Class 1 controlled substance

Response to the Rise of Mephedrone and MDPV in the United States

The Drug Enforcement Agency recently classified three synthetic cathinones as

continued on page 15

continued from page 14

schedule-1 controlled substances: mephedrone, MDPV, and methylone (17). Numerous states have also banned either individual substances or the entire cathinone structural class.

How this government regulation will affect distribution or usage remains uncertain. After the ban of synthetic cathinones in Europe, a number of other substances became popular, such as flephedrone and pyrovalerone (18).

In England, following the ban of mephedrone, new substances emerged, including naphyrone. Marketed as "NRG-1," naphyrone has excellent brain penetration, with approximately 1,000 times the lipophilicity of mephedrone. This increased lipophilicity theoretically allows much greater penetration of the blood-brain barrier, and hence CNS effect. With a half-life suspected to be 34 hours and with 10 times the potency of cocaine for blockade of the three monoamine transporters, naphyrone is extremely concerning (19). Additionally, an analysis of 24 products purchased in England after the mephedrone ban were shown to contain nine different compounds, 70% of which were banned cathinones (20).

Future Considerations

While the acute clinical presentation of mephedrone use has been well described in the European literature and there is a small, but growing, body of literature concerning pharmacology, the most effective methods of treatment as well as long-term effects remain unknown. For MDPV, we are only at the beginning stages of describing the acute clinical presentation. Laboratory results often require 2 weeks for return, far exceeding the clinical usefulness in most situations.

The Drug Enforcement Agency ban of mephedrone and MDPV is a step in the right direction. However, by outlawing the individual compound rather than the structural class, we invite a "whack-a-mole" type of scenario in which chemists stay one step ahead by churning out new and unknown compounds. As a medical community, we should be vocal in warning the public of the dangers of these substances.

Dr. Loeffler is a third-year resident in the Department of Psychiatry at the Naval Medical Center, San Diego. *The author reports no financial relationships with commercial interests. The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, the Department of Defense, or the United States Government.*

References

1. Goodnough A, Zezima K: An alarming new stimulant, legal in many states. New York Times, July 16, 2011. http://www.nytimes.com
2. National Forensic Laboratory System: Synthetic cannabinoids and synthetic cathinones reported in NFLIS, 2009–2010. https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/SynCannabSynCath.pdf (accessed November 19, 2011)
3. Spiller HA, Ryan ML, Weston RG, Jansen J: Clinical experience with and analytical confirmation of bath salts and legal highs (synthetic cathinones) in the United States. Clin Toxicol 2011; 49:499–505
4. Advisory Council on the Misuse of Drugs: Consideration of cathinones. http://www.namsdl.org/documents/ACMDCathinonesReport.pdf (accessed November 19, 2011)
5. Kelly JP: Cathinone derivatives: a review of their chemistry, pharmacology and toxicology. Drug Test Anal 2011; 3:439–453
6. Brunt TM, Poortman A, Niesink RJ, van den Brink W: Instability of the ecstasy market and a new kid on the block: mephedrone. J Psychopharmacol 2011; 25:1543–1547
7. Kehr J, Ichinose F, Yoshitake S, Goiny M, Sievertsson T, Nyberg F, Yoshitake T: Mephedrone, compared to MDMA (ecstasy) and amphetamine, rapidly increases both dopamine and 5-HT levels in nucleus accumbens of awake rats. Br J Pharmacol 2011; 164:1949–1958
8. Psychonaut Web Mapping Research Project: Mephedrone report. http://www.psychonautproject.eu/documents/reports/Mephedrone.pdf (accessed November 19, 2011)
9. Sammler EM, Foley PL, Lauder GD, Wilson SJ, Goudie AR, O'Riordan JI: A harmless high? Lancet 2010; 376:742
10. Nicholson PJ, Quinn MJ, Dodd JD: Head shop heartache: acute mephedrone meow myocarditis. Heart 2010; 96:2051–2052
11. Maskell PD, De Paoli G, Seneviratne C, Pounder DJ: Mephedrone (4-methylmethcathinone)-related deaths. J Anal Toxicol 2011; 35:188–191
12. Lusthof KJ, Oosting R, Maes A, Verschraagen M, Dijkhuizen A, Sprong AG: A case of extreme agitation and death after the use of mephedrone in the Netherlands. Forensic Sci Int 2011; 206:e93–e95
13. Schifano F, Albanese A, Fergus S, Stair JL, Deluca P, Corazza O, Davey Z, Corkery J, Siemann H, Scherbaum N, Farre' M, Torrens M, Demetrovics Z, Ghodse AH; Psychonaut Web Mapping; ReDNet Research Groups: Mephedrone (4-methylmethcathinone; meow meow): chemical, pharmacological and clinical issues. Psychopharmacology 2011; 214:593–602
14. Ross EA, Watson M, Goldberger B: Bath salts intoxication. N Engl J Med 2011; 365:967–968
15. Psychonaut Web Mapping Research Project: MDPV report. http://www.psychonautproject.eu/documents/reports/MDPV.pdf (accessed November 19, 2011)
16. Penders TM, Gestring R: Hallucinatory delirium following use of MDPV: bath salts. Gen Hosp Psychiatry 2011; 33:525–526
17. United States Drug Enforcement Agency: Chemicals used in bath salts now under federal control and regulation. http://www.justice.gov/dea/pubs/pressrel/pr102111.html (accessed November 19, 2011)
18. Morris K: UK places generic ban on mephedrone drug family. Lancet 2010; 375:1333–1334
19. Derungs A, Schietzel S, Meyer MR, Maurer HH, Krähenbühl S, Liechti ME: Sympathomimetic toxicity in a case of analytically confirmed recreational use of naphyrone (naphthylpyrovalerone). Clin Toxicol 2011; 49:691–693
20. Davies S, Wood DM, Smith G, Button J, Ramsey J, Archer R, Holt DW, Dargan PI: Purchasing legal highs on the Internet: is there consistency in what you get? QJM 2010; 103:489–493

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)

This month's questions are courtesy of Sanaz Kumar, M.D., from the Department of Psychiatry and Behavioral Sciences, George Washington University School of Medicine and Health Sciences, Washington, DC. Please also see the accompanying treatment-in-psychiatry article in this issue.

Question #1

A 25-year-old woman presents to your psychiatric outpatient office reporting that she spends more than 1 hour each morning engaging in complex hand-washing rituals before going to work. If she accidentally touches the sink during her ritual, she says that she must start the process over again to avoid contamination. Because of this morning ritual, the patient reports that she has been late for work many times and is "on thin ice" with her employer. Which of the following diagnosis applies?

A. Delusional disorder
B. Obsessive-compulsive disorder
C. Specific phobia
D. Major depressive disorder

Question #2

You decide to begin monotherapy treatment for the aforementioned patient with hand-washing rituals. Which agent would be preferred in initiating treatment?

A. Risperidone
B. Clomipramine
C. Sertraline
D. Lorazepam

ANSWERS TO FEBRUARY QUESTIONS

Question #1

Answer: E. Psychosis

Psychiatric complications following a traumatic brain injury in descending order of frequency: depression, anxiety, substance abuse, personality disorders, and psychosis (1).

Reference

1. Hibbard MR, Uysal S, Kepler K, Silver J: Axis I pathophysiology in individuals with traumatic brain injury. J Head Trauma Rehabil 1998; 13:24–39

Question #2

Answer: B. A second head injury resulting in severe brain swelling

A second head injury can result from allowing an athlete to return to play sooner than what is recommended. A subsequent second head injury can result in catastrophic brain swelling and likely death (1).

*R*eference

1. Wetjen NM, Pichelmann MA, Atkinson J: Second impact syndrome: concussion and second injury brain complications. J Am Coll Surg 2010; 211:553–557

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.

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.
ginory@ufl.edu

June 2012
Section Theme: Advocacy in Psychiatry
Guest Section Editor: John Lusins, M.D.
drjlusins@gmail.com

July 2012
Section Theme: ADHD
Guest Section Editor: Justine Wittenauer, M.D.
jwittenauer@emory.edu

August 2012
Section Theme: International Health
Guest Section Editor: Nicole Zuber, M.D.
nicajean@gmail.com