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Inside

In This Issue

This issue of *The Residents' Journal* features articles on psychosomatic medicine. In a case report, Rupinder Kaur Legha, M.D., discusses how both cognitive- and dialectical-behavioral therapy can be efficacious in the treatment of anorexia nervosa, and Amit Pradhan, M.D., demonstrates how psychotherapeutic intervention can be used to manage symptoms of demoralization in hospitalized patients.

Editorial

Ethics and *The Residents' Journal*

Joseph M. Cerimele, M.D.

Psychiatry residents encounter ethical problems in day-to-day clinical practice on the wards (e.g., whether to provide treatment without obtaining a patient's informed consent), in the emergency room (e.g., whether to admit a patient against his or her will), and in ambulatory care settings (e.g., whether to notify a third party about a patient's reported threat to harm others).

Psychiatrist-researchers also face ethical problems, for example, in enrolling patients with dementia or schizophrenia in research studies. One recent study conducted by Kim et al. (1) assessed the preservation of the capacity to appoint a research proxy in patients with Alzheimer's disease. The investigators recruited 138 patients with Alzheimer's disease to determine if these patients could appoint a proxy to provide consent for hypothetical lower-risk (new drug randomized, controlled trials) and higher-risk (cell implants via neurosurgery) clinical trials. The authors concluded that patients in their study were better able to appoint a research proxy than to provide consent to participate in a research study and that few patients were able to consent to participate in higher-risk clinical trials. These results are interesting and will lead to further discussion and research among ethicists and physicians.

Residents can manage clinical ethical problems by reading articles or book chapters, discussing the problem with colleagues or senior physicians, or, for complex matters, through consultation with an ethics team. Often, however, residents from other disciplines will consult a psychiatrist for help in managing an ethical problem in a patient with a psychiatric disorder. While we are experts in diagnosing and treating psychiatric disorders, we are not uniformly experts in managing ethical problems. However, psychiatric publications frequently describe commonly encountered ethical problems.

Psychiatric Times recently announced that the editors, along with ethicist Cynthia M. A. Geppert, M.D., Ph.D., M.P.H., are conducting a 2011 Ethics Survey that "wants to go beyond the ethics lessons and find out how you would handle some hypothetical dilemmas" (2). I took this survey and noted that each page contained a subtitle and that the questions on each page were linked by themes such as Dilemmas With Psychiatric Palliative Care, Dilemmas With Practice Boundaries, Dilemmas With Truth Telling, and Dilemmas With Confidentiality/Duties to Report. Many of the scenarios presented the usual ethical questions discussed in residency training classes but asked specifically what I would do in each situation as well as about my reasoning in uncertain situations. Some of my classmates also completed the survey and talked about how to manage specific scenarios. We are eager to see this survey's results.

The Residents' Journal has published articles addressing ethical problems and situations. For example, Seawell (3) described the history of the Tarasoff cases, the effect these cases had on clinical practice, and the common Tarasoff-related ethical problems encountered in clinical practice. We hope to further examine case-based ethical problems by publishing clinical case conferences or review articles addressing relevant clinical ethics. We will accept these pieces on a rolling basis but hope to publish a substantial number of articles.

References

1. Kim SYH, Karlawish JH, Kim M, Wall IF, Bozoki AC, Appelbaum PS: Preservation of the capacity to appoint a proxy decision maker: implications for dementia research. Arch Gen Psychiatry 2011; 68:214–220
2. Psychiatric Times: http://www.psychiatrictimes.com/home (Accessed February 2011)
3. Seawell M: A Resident's Guide to Tarasoff. Am J Psychiatry Res J 2011; 6:7–9

Early Intervention for Schizophrenia, Part 1: A Review

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The movement toward earlier intervention for schizophrenia has gained increasing traction in recent years. However, this initial enthusiasm has been dampened by mixed results, leaving many clinicians and the lay public confused about the best course of action. The Kraeplinian paradigm of schizophrenia as a necessarily progressive and deteriorating illness has been challenged by emerging evidence that intervention early, or even before the onset of frank psychosis, may be neuroprotective and improve outcomes (1–6). Yet attempts to intervene earlier have been plagued by disappointing results, and concerns about exposing young individuals to neuroleptics have come into increasing focus. This two-part article will provide a brief introduction to the complex subject of prodromal schizophrenia. Part one of this article will review the definition, neurobiologic alterations, risk factors, and rationale for early treatment of prodromal schizophrenia as well as diagnostic challenges and attempts to further refine criteria for diagnosis. Part two, which will be published in the upcoming May issue, will focus on the instruments developed for more accurate diagnosis, the evidence for early intervention, and, finally, ethical considerations and possible future directions for the field.

What Is the Prodromal State of Schizophrenia?

Schizophrenia tends to be dormant in early life, with clinical and social consequences manifesting typically after puberty, during adolescence and early adult life (7). One of the challenges of early intervention in schizophrenia is accurate diagnosis of a *prodromal state*. This term refers to a period of time prior to frank psychosis during which attenuated (subclinical psychotic) symptoms emerge that represent a clear change from an individual's premorbid functioning (8). In 80%–90% of patients, pre-existing deficits can be retrospectively identified, with problems arising in childhood or functional decline occurring during adolescence. A minority of patients (10%–20%) appear to have no significant prodromal period (9, 10).

The term *prodrome* itself is contentious and has been challenged for being misleading (8–10). Yung et al. (9–13) proposed the term *at-risk mental state* as a preferable alternative. They also suggested criteria to more accurately identify this group. First, patients may experience brief, limited symptoms, and although frank psychotic symptoms may intermittently appear, they are too brief to meet criteria for a full psychotic disorder. Patients may also demonstrate attenuated symptoms, such as pseudohallucinations or other perceptual abnormalities, subtle thought disorder, peculiar ideation, ideas of reference, or somatic preoccupations, which may even occur for months but are not severe enough to represent a full psychotic disorder. Finally, the authors included trait-related definitions as an identifier; namely, recent functional decline in the context of a first-degree family history or schizotypal personality disorder.

Certain symptoms and risk factors are more predictive of future conversion, such as changes in perceptual quality and cognition, poor psychosocial functioning, recent and rapid onset of severe and disabling symptoms, and comorbid depression and disorganization (14). Patterns in the order of presentation of symptoms have also been identified, with mood and sleep disturbances occurring earliest, followed by negative symptoms, attenuated positive symptoms, and, finally, frank psychosis (15). Social deficits appear as early as 2–4 years before the first hospital admission (15).

Neurobiologic Alterations of Prodromal Schizophrenia

Neurobiologic alterations have also been identified. First-degree relatives of patients with schizophrenia have shown relative volume reductions and membrane abnormalities in the temporal and frontal lobes, amygdala, and hippocampus (16–18). Structural alterations in the prefrontal, temporal, and anterior cingulate cortex occur before illness onset, suggesting a possible future role for magnetic resonance imaging as a diagnostic modality (6). Delayed motor development and psychiatric and neuropsychological dysfunction are also more common in schizophrenia patients (18–20). Interestingly, olfactory impairment suggests orbitofrontal cortex involvement (15), which may partially explain schizophrenia patients' common suspicion of food and drinks.

Risk Factors for Schizophrenia

A number of risk factors are implicated in schizophrenia, such as heavy cannabis use, urban upbringing, and genetic risk (21). Viral, nutritional, and neurodegenerative etiologies have been associated with schizophrenia, but the evidence remains inconclusive. Of note, all of these risk factors lack specificity or positive predictive value, which limits their utility. Evidence continues to emerge regarding neurobiologic alterations and risk factors, and a more complete discussion is outside the scope of this article.

Rationale for Early Treatment of the Prodromal State

The rationale for early treatment is supported by emerging evidence, such as outcome studies, finding an association between the duration of untreated psychosis and poor functional outcome (1, 2, 22). Furthermore, psychosis has been shown to exert a detrimental effect on brain tissue, analogous to tissue damage in myocardial infarction or stroke (3).

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Other potential benefits of early intervention have been proposed (5). Early engagement may promote trust for future therapy and provide an avenue for help, irrespective of whether or not transition ultimately occurs. If the individual does develop schizophrenia, early treatment may also blunt other consequences of the illness, such as social withdrawal and poor functioning that may become entrenched over time. Early intervention may allow for identification and treatment of other comorbidities that may otherwise remain unnoticed. Finally, patients are more likely to be fully competent and able to provide informed consent for research early in their disease course.

Diagnostic Challenges of Prodromal Schizophrenia

As previously discussed, it may be difficult to define the onset of prodromal schizophrenia, since the earliest symptoms tend to be nonspecific, without a reliable pattern to guide clinicians. Furthermore, the differentiation of normal from abnormal in the earlier stages is especially blurred because the general population may have psychotic-like experiences (5). Delusions or other psychotic symptoms likely exist along a continuum ranging from mild manifestations in otherwise high-functioning adults to the most severely ill schizophrenia patient. Finally, subjective versus objective symptoms differ, with observers typically dating onset after patients (23). For these and perhaps other reasons, attempts have been made to refine the ability to diagnose prodromal states.

New and Improved Criteria for Diagnosis of the Prodromal State

McGorry (24) developed the Personal Assistance and Crisis Evaluation Clinic, the goal of which was to study and treat patients who presented for help out of concern that they were developing symptoms of schizophrenia (11). In an attempt to further refine diagnosis, they developed new criteria to identify ultra-high risk individuals, which increased the conversion rate from between 10% and 20% to between 40% and 60% at 1 year (12, 13, 25). The new criteria combined recent-onset functional decline with genetic risk and included recent-onset subthreshold or brief-threshold psychotic symptoms (8, 9, 11, 24). Although the criteria were found to be reliable (8, 26) and the risk to be high in this population, conversion is not inevitable.

The attempt to diagnose prodromal schizophrenia raises many difficult questions. Even among ultra-high risk individuals, some will never develop schizophrenia (although the 6-month to 1-year follow-up period in most prodromal schizophrenia studies severely limits the ability to predict conversion further down the road). These false positive patients could be exposed to unnecessary treatments and their side effects as well as to stigmatization and labeling. Moreover, some patients prefer not knowing such burdensome information about their future, and those that do not convert may feel misled. On the other hand, if effective treatments for prodromal schizophrenia were found that prevent or significantly delay disease onset, such ultra-high risk patients might choose early intervention despite the aforementioned risks. This is not unlike other fields of medicine, such as oncology, where *BRCA*-positive women sometimes choose a prophylactic mastectomy despite the significant risks and side effects while others choose a more conservative watch-and-wait approach. The difference is whether treatments for early intervention in schizophrenia are effective, which will be explored further in the second part of this article.

Conclusions

To summarize, the field has refined its understanding of the prodromal state, and evidence continues to grow regarding potential neurobiologic disturbances and risk factors. Identification of high-risk and ultra-high risk patients has improved, but questions remain about the utility of such identification in the absence of effective interventions. Part two of this article will expand on the difficulties of accurate diagnosis of the prodromal state, the evidence for and against early intervention, and, finally, ethical considerations and possible future directions for the field.

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Note From the Editor:

For further reading about early intervention and conversion to psychosis among high-risk individuals, see The American Journal of Psychiatry *article by Jean Addington, Ph.D., et al., published in advance of print April 15, 2011.*

The May issue of The American Journal of Psychiatry *will include a commentary by two leaders in the field, William T. Carpenter, Jr., M.D., and Jim van Os, M.D., Ph.D., M.R.C.Psych., who contribute to this discussion in their analysis of attenuated psychosis syndrome as a diagnostic category in DSM-5.*

References

1. Addington J, van Mastrigt S, Addington D: Duration of untreated psychosis: impact on 2-year outcome. Psychol Med 2004; 34:277–284
2. Bottlender R, Sato T, Jäger M, Wegener U, Wittmann J, Strauss A, Möller HJ: The impact of the duration of untreated psychosis prior to first psychiatric admission on the 15-year outcome in schizophrenia. Schizophr Res 2003; 62:37–44
3. Marshall M, Lewis S, Lockwood A, Drake R, Jones P, Croudace T: Systematic review of the association between duration of untreated psychosis and outcome in cohorts of first episode patients. Schizophr Res 2004; 70:27
4. Lieberman JA: Is schizophrenia a neurodegenerative disorder? a clinical and neurobiological perspective. Biol Psychiatry 1999; 46:729–739
5. Philips L, McGorry P, Yung A, McGlashan T, Cornblatt B, Klosterkotter J: Presychotic phase of schizophrenia and related disorders: recent progress and future opportunities. Br J Psychiatry 2005; 187(suppl 48):S33–S44
6. Jun WH, Jang JH, Byun MS, An SK, Kwon JS: Structural alterations in individuals at ultra-high risk for psychosis: a review of magnetic resonance imaging studies and future directions. J Korean

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Med Sci 2010; 25:1700–1709

7. Jones P, Rodgers B, Murray R, Marmot M: Child development risk factors for adult schizophrenia in the British 1946 Birth Cohort. Lancet 1994; 344:1398–1402
8. Addington J: An ounce of prevention: identifying patients with prodromal schizophrenia. Medscape Psychiatr Ment Health 2006. http://www.medscape.org/viewarticle/529848
9. Yung AR, McGorry PD, McFarlane CA, Jackson HJ, Patton GC, Rakkar A: Monitoring and care of young people at incipient risk of psychosis. Schizophr Bull 1996; 22:283–303
10. Yung AR, McGorry PD: The initial prodrome in psychosis: descriptive and qualitative aspects. Aust N Z J Psychiatry 1996; 30:587–599
11. Yung AR, McGorry PD: The prodromal phase of first-episode psychosis: past and current conceptualizations. Schizophr Bull 1996; 22:353–370
12. Yung AR, Phillips LJ, McGorry PD, McFarlane CA, Francey S, Harrigan S, Patton GC, Jackson HJ: Prediction of psychosis: a step towards indicated prevention of schizophrenia. Br J Psychiatry 1998; 172:14–20
13. Yung AR, Phillips LJ, Yuen HP, Francey SM, McFarlane CA, Hallgren M, McGorry PD: Psychosis prediction: 12-month follow-up of a high-risk (prodromal) group. Schizophr Res 2003; 60:21–32
14. Ruhrman S, Schultze-Lutter F, Klosterkötter J: Early detection and intervention in the initial prodromal phase of schizophrenia. Pharmacopsychiatry 2003; 3(suppl 3):S162–S167
15. Hafner H, Loffler W, Maurer K, Hambrecht M, van der Heiden W: Depression, negative symptoms, social stagnation and social decline in the early course of schizophrenia. Acta Psychiatr Scand 1999; 100:105–118
16. Keshavan MS, Dick E, Mankowski I, Harenski K, Montrose DM, Diwadkar V, DeBellis M: Decreased left amygdala and hippocampal volumes in young offspring at risk for schizophrenia. Schizophr Res 2002; 58:173–183
17. Diwadkar VA, Sweeney JA, Montrose DM, et al.: Cognitive impairments and structural MRI abnormalities in schizotypal first-degree relatives of schizophrenia patients. Biol Psychiatry 2003; 53(suppl 8):500
18. Keshavan MS, Diwadkar VA, Montrose DM, Stanley JA, Pettegrew JW: Premorbid characterisation in schizophrenia: the Pittsburgh High Risk Study. World Psychiatry 2004; 3:163–169
19. Cannon M, Tarrant CJ, Huttunen MO, Jones P: Childhood development and later schizophrenia: evidence from genetic high risk and birth cohort studies, in The Epidemiology of Schizophrenia, 1st ed. Edited by Murray RM, Jones PB, Susser E, van Os J, Cannon M. Cambridge, United Kingdom, Cambridge University Press, 2003, pp 100–124
20. Reichenberg A, Weiser M, Rabinowitz J, Caspi A, Schmeidler J, Mark M, Kaplan Z, Davidson M: A population-based cohort study of premorbid intellectual, language, and behavioral functioning in patients with schizophrenia, schizoaffective disorder, and nonpsychotic bipolar disorder. Am J Psychiatry 2002; 159:2027–2035
21. Howes OD, McDonald C, Cannon M, Arseneault L, Boydell J, Murray RM: Pathways to schizophrenia: the impact of environmental factors. Int J Neuropsychopharmacol 2004; 7(suppl 1):S7–S13
22. Peters ER, Joseph SA, Garrety PA: Measurement of delusional ideation in the normal population: introduction to the PDI (Peters et al. Delusions Inventory). Schizophr Bull 1999; 25:553–576
23. Hafner J, Maurer K, Loffler W, Riecher-Rössler A: The influence of age and sex on the onset and early course of schizophrenia. Br J Psychiatry 1993; 162:80–86
24. McGorry PD, Yung A, Phillips L: Ethics in early intervention in psychosis: keeping up the pace and staying in step. Schizophr Res 2001; 51:17–29
25. Miller TJ, McGlashan TH, Rosen JL, Somjee L, Markovich PJ, Stein K, Woods SW: Prospective diagnosis of the initial prodrome for schizophrenia based on the Structured Interview for Prodromal Syndromes: preliminary evidence of interrater reliability and predictive validity. Am J Psychiatry 2002; 159:863–865
26. Schaffner KF, McGorry PD: Preventing severe mental illnesses: new prospects and ethical challenges. Schizophr Res 2001; 51:3–15

Schizophrenia Associated With Prenatal Exposure to Dutch and Chinese Famines

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Early prenatal exposure to nutritional deficiencies could be an important risk factor for developing schizophrenia (1). More importantly, it could provide us with a clue in unearthing at least one etiology of a serious and chronic disease. Growing evidence suggests that neurodevelopmental disruption plays an important role in schizophrenia. The natural experiments created first by the Dutch Hunger Winter of 1944–1945 and later by the Chinese Famine of 1959–1961 have provided researchers with an experimental framework from which to study the association of prenatal nutritional deficiencies with risk for postnatal schizophrenia. The present article is a review of studies published on the topic of schizophrenia specifically associated with the Dutch and Chinese famines and includes a brief discussion of areas for future research.

The Dutch Hunger Winter of 1944–1945

The study that first elucidated the connection between prenatal starvation and postnatal schizophrenia examined data collected during the Dutch Hunger Winter of 1944–1945, which occurred within the course of World War II (2). The height of this famine was brief and clearly defined, and thus associations could be made to health outcomes several decades later. Before an association with schizophrenia was found in relation to the Dutch famine, the major neurodevelopmental finding was an increase in neural tube defects in infants conceived during the height of the famine (3). This observation led investigators to hypothesize that latent effects of prenatal famine could lead to mental disorders in adulthood. This provided the impetus for the analytic design of the Dutch Famine Birth Cohort Study of schizophrenia (4).

The findings of the Dutch Famine Birth Cohort Study, which has become an early model for epidemiologic research on prenatal exposures, have been released piecemeal over the last 30 years (4). An essentially ecological study by design, the central comparison has been between exposed and unexposed monthly birth cohorts from 1944 to 1946 in the six famine-stricken cities (3). The exposed birth cohorts are defined by low food rations during the first trimester of gestation, conception at the height of the famine (as indicated by adverse health effects in the general population), and an excess of congenital neural defects relative to the unexposed cohorts. Ecological studies often possess a number of weaknesses that this study does not. For example, misclassification error for exposed individuals on the basis of birth cohort membership is unlikely because the famine was so well-circumscribed in time and place. Additionally, confounding is minimized because exposed and unexposed individuals were born a few months apart in the same cities. Because of these features, this study has been most often referred to in the literature as a natural experiment.

In a seminal study, Susser et al. (5) examined whether the birth cohort with excess CNS anomalies also had an increased risk of schizophrenia (5). The Dutch psychiatric registry was used to compare psychiatric outcomes in adulthood for this exposed cohort with that of the unexposed cohorts. The primary outcome was a diagnosis of schizophrenia. The authors found a twofold significant increase in the cumulative risk of schizophrenia in the exposed birth cohort (relative risk=2.0, 95% confidence interval [CI]=1.2–3.4, $p<0.01$) in both men (relative risk=1.9, 95% CI=1.0–3.7, $p=0.05$) and women (relative risk=2.2, 95% CI=1.0–4.7, $p=0.04$).

A study published 2 years later, also conducted by Susser et al., showed a twofold increased risk (relative risk=2.01, 95% CI=1.03–3.94, $p=0.04$) of schizoid personality disorder in this same exposed birth cohort (6). These data were obtained from military induction examinations for 18-year-old men. This provided additional evidence of a famine effect on schizophrenia spectrum disorders from an independent data source.

The principal authors of the Dutch Famine Birth Cohort Study have defined the birth cohort of October 16 to December 31, 1945, as severely exposed to famine in early gestation. There is an excess of neural tube defects and other congenital anomalies of the CNS in this birth cohort, which had an increased risk of schizophrenia in adulthood and an excess of schizoid personality disorder diagnoses at age 18 years among male members (7).

Based on these findings, one could interpret that the same exposure could lead to different neurodevelopmental disorders at different points in the life course. Indeed, both neural tube defects and schizophrenia have been associated with a genetic variant in the folate pathway, methylenetetrahydrofolate reductase C677T polymorphisms (8), and there is a growing body of evidence suggesting that schizophrenia and schizophrenia spectrum personality disorders share a genetic diathesis (9).

The Chinese Great Leap Forward Famine of 1959–1961

From 1959–1961, a famine was precipitated in China by the marked economic and social campaign known as the Great Leap Forward, which involved the use of unsuccessful agricultural practices as well as diversion of agricultural labor to other purposes. This famine is estimated to have caused 30–40 million deaths (10).

St. Clair et al. (11) conducted a study of

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a cohort in the Wuhu region of Anhui Province, China. Similar to the studies on the Dutch famine birth cohorts, the authors compared the cumulative risk of schizophrenia among the birth cohorts at the height of the famine with that of cohorts prior to and subsequent to the famine. Outcomes were obtained via records from the only psychiatric hospital in the Wuhu region. The increased twofold risk found was similar to the risk reported for the Dutch famine. The authors compared findings from the years during and after the famine (1959–1962) with those from 3 years before (1956–1958) and 3 years after (1963–1965) the famine to create relative risk ratios. Mortality-adjusted relative risks were 2.3 (95% confidence interval=1.99–2.65) for individuals born in 1960 and 1.93 (95% confidence interval=1.68–2.23) for individuals born in 1961. A weakness of this study was that famine-exposure data were not available by month, and thus periods of famine and their effect on gestational stage could not be estimated as they were in the Dutch studies. A strength of this study was that it had a much larger sample size than those of the Dutch studies. Additionally, the biological causation hypothesis was bolstered by replication of study findings in a different part of the world.

Xu et al. (12) conducted a second study using a similar design to test the same hypothesis in another Chinese population in Liuzhou Prefecture of the Guangxi autonomous region. The authors examined individuals born in 1960 and 1961 under the hypothesis that they would have been exposed to the height of the famine during conception or early gestation. The overall mortality-adjusted relative risk for schizophrenia was 1.5 (1960) and 2.05 (1961). The effect was observed to be from rural areas relative to urban areas, and when set apart the rural relative risks were 1.68 (1960) and 2.25 (1961). In this study, the twofold increased risk of schizophrenia among individuals in early gestation at the height of famine was replicated once again. This second study on the Chinese famine was important, since it explained the different effects of the famine in urban and rural areas. This was needed because in contrast to the Dutch famine, the famine in China primarily affected rural areas, with the rural population suffering starvation on a massive scale. Thus, an increased risk of schizophrenia due to prenatal malnutrition should have been evident in rural and not urban areas, and the authors demonstrated this to be true.

Limitations of the Studies

As in all observational studies, there is the possibility that the results of the aforementioned studies were confounded. The exposed populations were likely to have been under severe stress as a result of the combination of famine and war. Because prenatal stress has been associated with schizophrenia (13), this is an important potential confounder. Other limitations include the use of group data to define exposure and the inability to separate the effects of different types of nutritional deficiencies.

Future Directions for Research

Epidemiology has been important in the case for generating hypotheses for candidate nutritional exposures that lead to schizophrenia risk, but it has been unable to prove any of them. Cross-disciplinary efforts between epidemiology and the basic sciences are more likely to help us understand the potential pathways that lead to schizophrenia.

Although the Dutch and Chinese studies have offered compelling clues, there is still a need to directly advance understanding of how nutrition may perturb prenatal neural development in a manner that influences risk for schizophrenia. Perhaps the most important question from a public health standpoint is whether potential causative nutritional deficiencies represent a global nutritional deficiency or a specific micronutrient deficiency.

A current path being taken by researchers is to better define the role of DNA methylation in producing changes in gene expression and function without disrupting the primary DNA sequence. Diet-triggered DNA methylation may therefore be an environmental agent capable of producing changes in gene activity. Findings from the Dutch Hunger Winter Families Study (of famine-exposed persons from Amsterdam, Rotterdam, and Leiden who were reexamined in 2003–2005) indicate that persistent changes in DNA methylation could result from prenatal famine exposure and that gestational timing plays a key role (14). In studying those persons prenatally exposed to the Dutch famine, scientists are further supporting the hypothesis that very early fetal development is a critical period for establishing and maintaining epigenetic marks that can persist throughout life (15).

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References

1. Butler PD, Susser ES, Brown AS, Kaufmann CA, Gorman JM: Prenatal nutritional deprivation as a risk factor in schizophrenia: preclinical evidence. Neuropsychopharmacology 1994; 11:227–235

2. Susser ES, Lin SP: Schizophrenia after prenatal exposure to the Dutch Hunger Winter of 1944–1945. Arch Gen Psychiatry 1992; 49:983–988

3. Stein Z, Susser M, Saenger G, Marolla F: The Dutch Hunger Winter of 1944–1945. New York, Oxford University Press, 1975

4. Susser E, Hoek HW, Brown A: Neurodevelopmental disorders after prenatal famine: the story of the Dutch Famine Study. Am J Epidemiol 1998; 147:213–216

5. Susser E, Neugebauer R, Hoek HW, Brown AS, Lin S, Labovitz D, Gorman JM: Schizophrenia after prenatal famine: further evidence. Arch Gen Psychiatry 1996; 53:25–31

6 Hoek HW, Susser E, Buck KA, Lumey LH, Lin SP, Gorman JM: Schizoid personality disorder after prenatal exposure to famine. Am J Psychiatry 1996; 153:1637–1639

7. Susser E, St Clair D, He L: Latent effects of prenatal malnutrition on adult health:

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the example of schizophrenia. Ann N Y Acad Sci 2008; 1136:185–192

8. Gilbody S, Lewis S, Lightfoot T: Methylenetetrahydrofolate reductase (MTHFR) genetic polymorphisms and psychiatric disorders: a HuGE review. Am J Epidemiol 2007; 165:1–13
9. Owen MJ, Craddock N, Jablensky A: The genetic deconstruction of psychosis. Schizophr Bull 2007; 33:905–911
10. Smil V: China's great famine: 40 years later. BMJ 1999; 319:1619–1621
11. St Clair D, Xu M, Wang P, Yu Y, Fang Y, Zhang F, Zheng X, Gu N, Feng G, Sham P, He L: Rates of adult schizophrenia following prenatal exposure to the Chinese famine of 1959–1961. JAMA 2005; 294:557–562
12. Xu MQ, Sun WS, Liu BX, Feng GY, Yu L, Yang L, He G, Sham P, Susser E, St Clair D, He L: Prenatal malnutrition and adult schizophrenia: further evidence from the 1959–1961 Chinese famine. Schizophr Bull 2009; 35:568–576
13. van Os J, Selten JP: Prenatal exposure to maternal stress and subsequent schizophrenia: the May 1940 invasion of the Netherlands. Br J Psychiatry 1998; 172:324–326
14. Tobi EW, Lumey LH, Talens RP, Kremer D, Putter H, Stein AD, Slagboom PE, Heijmans BT: DNA methylation differences after exposure to prenatal famine are common and timing- and sex-specific. Hum Mol Genet 2009; 18:4046–4053
15. Heijmans BT, Tobi EW, Stein AD, Putter H, Blauw GJ, Susser ES, Slagboom PE, Lumey LH: Persistent epigenetic differences associated with prenatal exposure to famine in humans. Proc Natl Acad Sci U S A 2008; 105:17046–17049

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Treatment of PTSD With Alpha-Adrenergic Blocking Agents

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A diagnosis of posttraumatic stress disorder (PTSD) indicates that an individual experienced an event that involved a threat to his or her life or physical integrity or to that of another and that the individual responded with intense fear, helplessness, or horror. PTSD is associated with sexual abuse, physical assault, military combat, torture, accidental trauma, natural or man-made disasters, and diagnosis of threatening illness. Several epidemiological studies have found that traumatic events are ubiquitous, with more than one-half the population experiencing a traumatic event during their lifetime by witnessing, rather than directly experiencing, the event (1). Although exposure to trauma is common, only 7%–8% of those exposed develop PTSD (2). Risk factors for developing PTSD after exposure to a traumatic event are history and severity of trauma, female gender, family or personal history of mood or anxiety disorders, and having less than a college education.

In the National Vietnam Veterans Readjustment Study (3), which examined 3,016 individuals, including 1,632 Vietnam theater veterans, 716 veterans from the Vietnam era who did not serve in theater, and a civilian cohort, the lifetime prevalence for PTSD was 31% for male veterans and 27% for female veterans. Exposure to extreme stressors has obtained a lot of attention recently in the United States because of combat operations in Iraq and Afghanistan, which also involve some unintentional attacks on civilians.

The burgeoning field of disaster psychiatry includes both trauma-related and nontrauma-related psychiatry. The treatment of PTSD is challenging, even independent of common comorbid disorders. Remission of PTSD symptoms is important, since this illness leads to numerous psychosocial difficulties, such as work or marital problems, substance abuse, aggression, suicidality, and homelessness.

The present article is a review of the literature on the efficacy of the alpha-adrenergic antagonist prazosin as well as of central alpha-2 agonists (such as clonidine and guanfacine) for the treatment of sleep disturbances (such as insomnia and persistent posttraumatic nightmares), which have been found to be present in up to 70% of combat veterans (4). The hypothesis for the cause of sleep disruption and nightmares in PTSD suggests that there exists overactive noradrenergic activity in the amygdala that escapes normal inhibition from the medial prefrontal cortex. Germain et al. (5) examined 367 individuals with PTSD for a period ranging from 6 months to more than 30 years and found that the severity of PTSD paralleled the severity of the nightmares. Nightmares associated with PTSD cause REM fragmentation, occur earlier in sleep, replicate real events, and may lead to other sleep disruptive behaviors, including a fear of going to sleep (6).

For the present review, an Ovid search was conducted, encompassing the past 36 years, using the search terms "PTSD." "prazosin." and "clonidine," and 39 articles were examined. The articles on PTSD related to treatment with alpha-adrenergic antagonists, such as prazosin and clonidine, provide the main content for this review.

Pagel and Helfter (7) demonstrated that REM-off centers (in the locus coeruleus and dorsal raphe) are more active while REM-on centers (in the tegmentum) are inhibited. This leads to disrupted REM sleep by intrusive alpha-adrenergic signals. Strawn and Geracioti (8) hypothesized that agents blocking central norepinephrine release may normalize REM sleep.

The first double-blind crossover study was conducted by Raskind et al. (4), who examined 10 Vietnam combat veterans with PTSD who were administered prazosin (mean dose=9.6 mg/night) over a period of 9 weeks (3 weeks of titration and 6 weeks of clinical maintenance). Prazosin was superior to placebo in reducing nightmares, based on the recurrent distressing dreams and sleep disturbance items on the Clinician-Administered PTSD Scale, and it also resulted in a change in the total score on all three clusters. A paired-samples t test found significant improvement (decrease in scores [$p<0.0005$]) after 8 weeks of treatment with a stable dose of prazosin. Overall, PTSD severity was reported as "markedly improved" in six patients, "moderately improved" in 11 patients, and "minimally improved" in six patients. The study also showed improvement in ratings on the Clinical Global Impression of Change scale.

Raskind et al. (9) conducted another trial of a group of 40 veterans with chronic PTSD secondary to combat-related trauma. The patients were administered prazosin at a mean dose of 13.3 mg/night during a period of 4 weeks of titration and 8 weeks of clinical maintenance. Nightmares and sleep disturbances improved. In the experimental sample (N=34), primary outcome measures showed that prazosin was significantly superior to placebo for reducing nightmares related to trauma, which improved sleep quality and global clinical status with large effect sizes. Prazosin treatment shifted dream characteristics from those typical of trauma-related nightmares to those typical of normal dreams.

Taylor and Raskind (10) performed a double-blind placebo-controlled cross-over study of 13 civilians with trauma-related PTSD. Prazosin was titrated to 3 mg/night during a 3-week treatment phase. The resulting reductions of nighttime PTSD symptoms in this civilian-trauma PTSD group were accompanied by increased total sleep time, increased REM sleep time, and increased mean REM duration in the absence of a sedative-like effect on sleep-onset latency. Taylor et al.

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(11) demonstrated that when there is a reduction in nightmares, symptoms such as reactivity and hyperarousal as a result of trauma cues can be reduced by adding small doses of prazosin during the day.

Clonidine, a central alpha 2 (2A, 2B, 2C) agonist, and guanfacine, a central alpha 2A agonist, have been shown to improve PTSD symptoms in children and adults (8, 12). However, a controlled study demonstrated that guanfacine was not effective for nightmares related to PTSD (13).

In an uncontrolled study of sleep disturbances, Maher et al. (14) reviewed the empirical evidence for efficacy of pharmacotherapy and of certain cognitive behavior treatments for PTSD and concluded that the recommended first-line treatments do not effectively resolve PTSD-related sleep disruption. The findings that generated this hypothesis as well as the recently reported effects of prazosin on sleep architecture are encouraging, and the convincing controlled data on the effects of prazosin on sleep disturbance are of clinical utility.

Conclusions

These studies indicate noradrenergic overdrive and REM dysregulation as factors contributing to PTSD nightmares. Prazosin is available in doses of 1, 2, and 5 mg. It can be started at 1 mg and increased by 1 mg every 3 nights (up to 15 mg total daily dosing) (10). The most common side effect is postural hypotension, which occurs in 10% of patients and has a first-dose effect. Other side effects include priapism, headache, somnolence, and arthralgia (15, 16). The effect of prazosin on sleep architecture is valuable. Future research on the emotional brain (amygdala) may provide a better understanding of fear conditioning as well as insight into other treatments on the horizon, thereby enhancing current treatments and fostering attainment of remission.

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References

1 Goenjian AK, Steinberg AM, Najarian LM, Fairbanks LA, Tashjian M, Pynoos RS: Prospective study of posttraumatic stress, anxiety, and depressive reactions after earthquake and political violence. Am J Psychiatry 2000; 157:911–916

2. Galea S, Nandi A, Vlahov D: The epidemiology of post-traumatic stress disorder after disasters. Epidemiol Rev 2005; 27:78–91

3. National Vietnam Veterans Readjustment Study (NVVRS): 5-HTTLPR serotonin transporter gene and environmentally 2004.

4. Raskind MA, Thompson C, Petrie EC: Prazosin reduces nightmares in combat veterans with posttraumatic stress disorder. J Clin Psychiatry 2002; 63:565–568

5. Germain A, Buysse DJ, Shear MK, Fayyad R, Austin C: Clinical correlates of poor sleep quality in posttraumatic stress disorder. J Trauma Stress 2004; 17:477–484

6. Zayfert C, DeViva JC: Residual insomnia following cognitive behavioral therapy for PTSD. J Trauma Stress 2004; 17:69–73

7. Pagel JF, Helfter P: Drug induced nightmares: an etiology based review. Hum Psychopharmacol 2003; 18:59–67

8. Strawn JR, Geracioti TD Jr: Noradrenergic dysfunction and the psychopharmacology of posttraumatic stress disorder. Depress Anxiety 2008; 25:260–271

9. Raskind MA, Peskind ER, Hoff DJ, Hart KL, Holmes HA, Warren D, Shofer J, O'Connell J, Taylor F, Gross C, Rohde K, McFall ME: A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. Biol Psychiatry 2007; 15:928–934

10. Taylor F, Raskind MA: The alpha-1 adrenergic antagonist prazosin improves sleep and nightmares in civilian trauma posttraumatic stress disorder. J Clin Psychopharmacol 2002; 22:82–85

11. Taylor FB, Lowe K, Thompson C: Daytime prazosin reduces psychological distress to trauma specific cues in civilian trauma posttraumatic stress disorder. Biol Psychiatry 2006; 59:577–581

12. Boehnlein JK, Kinzie JD: Pharmacologic reduction of CNS noradrenergic activity in PTSD: the case for clonidine and prazosin. J Psychiatr Pract 2007; 2:72–78

13. Neylan TC, Lenoci MA, Samuelson KW: No improvement of posttraumatic stress disorder symptoms with guanfacine treatment. Am J Psychiatry 2006; 163:2186–2188

14. Maher MJ, Rego SA, Asnis GM: Sleep disturbances in patients with post-traumatic stress disorder: epidemiology, impact and approaches to management. CNS Drugs 2006; 20:567–590

15. Raskind MA, Peskind ER, Kanter ED: Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. Am J Psychiatry 2003; 160:371–373

16. Taylor FB, Martin P, Thompson C, Williams J, Mellman TA, Gross C, Peskind ER, Raskind MA: Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma posttraumatic stress disorder: a placebo-controlled study. Biol Psychiatry 2008; 63:629–632

Case Report

A Case of Anorexia

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For many psychiatry residents, anorexia nervosa represents a complicated illness that they may feel unequipped to manage (1, 2). Its ego-syntonic nature and the lack of pharmacologic interventions are particularly challenging (3), and the potential for countertransference is strong (4, 5). However, the persistent prevalence and high mortality rate necessitate an understanding of its development and management (6, 7). The present case traces the emergence of anorexia nervosa as well as the challenges associated with this disorder. It also highlights several therapeutic modalities residents can invoke with patients suffering from this illness.

Case

"Miss A" was a 19-year-old college student who was admitted medically for malnutrition and bradycardia secondary to anorexia nervosa and depression. The patient first felt depressed 10 months prior when her parents' divorced. She stated that she felt "caught in the middle" and guilty about the "burden" she placed on her parents financially. To cope with her distress, she cut back on "junk food" in order to be healthier and began running regularly. Several months later, her food restriction intensified, as she reduced her intake to 600 calories per day. Through her declining weight, she enjoyed a sense of achievement and self-acceptance. Concerned friends who noticed her dramatic weight loss and increased social isolation convinced her to visit the student health center, where her weight was reported to be 40 kg (80% of her ideal body weight). Her heart rate was 35 beats per minute, and she was orthostatic and hypotensive. She had lost 25 pounds in 6 months. The student health physician notified her parents, who flew her home and brought her to the local children's hospital. She was admitted medically for initial weight restoration, observation for refeeding syndrome, and cardiac monitoring. The patient initially expressed significant distress about her weight gain and insisted that she was healthy. Once medically stable, her parents informed her that she would be transferred to the hospital's eating disorders inpatient unit. At the time of transfer, she resisted admission and stated her desire to return to school immediately. However, when the unit's medical director emphasized that the decision to enter treatment was hers to make, she relented and walked onto the unit.

The eating disorders inpatient unit followed a family-based treatment model developed at the Maudsley Hospital in London (8). With the help of a registered dietician, Ms. A's parents assumed complete responsibility for her meal planning, and her weight restoration continued. Through cognitive-behavioral therapy, the patient learned to challenge automatic negative thoughts related to her anorexia. She identified her tendency to "catastrophize," for example, by perceiving a relatively minor mistake, such as a parking ticket, as evidence of her ineptitude. She also began to appreciate her tendency to engage in black and white, or all or nothing, thinking. For instance, she acknowledged how she equated leaving college with being a failure. For several weeks, she recorded her automatic negative thoughts, her associated emotions, and her resultant eating disordered behaviors. This exercise enabled her to grasp the relationship between all three, to challenge her self-defeating thought patterns, and to reduce her food restricting and overexercising behaviors.

Dialectical-behavioral therapy allowed her to accept her intolerable affective states with less judgment and to regulate these states with healthier and more adaptive strategies. Mindfulness exercises were focused on remaining present during moments of distress, and distress tolerance skills emphasized the importance of distraction, self-soothing, and social support during moments when she felt most inclined to engage in eating disordered behaviors (9). Individual and family therapy, respectively, were focused on her distorted self-perception and the effect of her parents' divorce on her illness. Additionally, family therapy sessions centered on how family members could support the patient in her recovery.

To dissect her ambivalence about recovery, Miss A's providers relied on motivational interviewing techniques. This approach helped her to acknowledge how her anorexia was negatively affecting her life and empowered her to normalize her eating habits. She eventually shifted from the precontemplative stage to the action stage of change and became more engaged in her treatment, planning meals with her parents' support. After she reached 90% of her ideal body weight, she transitioned to the day treatment program and was started on an antidepressant for her persistent depressive symptoms and associated anxiety. She continued with the day treatment program for 6 weeks and resumed her university studies several months later.

Discussion

The present case provides insight into how anorexia nervosa often emerges slowly and insidiously before generating momentum rapidly and forcefully, often with significant health consequences. Given the association between the duration of anorexia nervosa and mortality, inpatient admissions should be considered for patients with precipitous weight loss (10). Less severe cases (as determined by the ideal body weight percentage and the presence or absence of medical complications) can be treated on an outpatient basis with therapy, nutritional

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support, and medical oversight (11). In the present case, the patient's preceding mood symptoms and eventual diagnosis of depression were also indicative, since eating disorders often represent maladaptive attempts to regulate mood and are often accompanied by depression, anxiety, and obsessive-compulsive symptoms. Clinicians should screen for the presence of mood and anxiety disorder symptoms prior to onset of an eating disorder and monitor the intensity of these symptoms during treatment of the eating disorder. Pharmacologic interventions are usually considered after patients have attained sufficient weight restoration. Selective serotonin reuptake inhibitors and low-dose antipsychotics are commonly used once patients have achieved 90% of their ideal body weight (12).

The present patient's initial reservations about weight gain highlight the importance of the stages of change model in psychotherapy and in other approaches to treatment. Motivational interviewing techniques can help patients shift from one stage to another without invoking resistance or feelings of judgment. Asking patients to rate the importance of change, as well as readiness and confidence, on a scale of 1–10 represents one specific starting point (13). To help patients progress beyond the precontemplative and contemplative stages, providers must promote a cognitive and affective re-evaluation of the illness, a shift in the balance of the pros and cons of being ill, and self-efficacy. Making a list of the pros and cons in having anorexia and writing two letters to anorexia, one as if it were an enemy and one as if it were a friend, can help patients acknowledge ambivalence. Reflecting on life goals and, more specifically, on life *with* anorexia 5 years later versus life *without* anorexia 5 years later also promotes reappraisal. Regardless of the approach, adopting a directive client-centered counseling style is critical in avoiding resistance and promoting behavior change (14).

The treatment for the patient in the present case demonstrates the dual importance of weight restoration and psychotherapy. Nutritional support facilitates weight gain, normalizes eating patterns, and reconfigures food as "medicine" for healing. Clinicians can reinforce this effort by challenging the notion of "good" and "bad" foods and emphasizing that any food can fit into a meal plan. Separating the eating disorder from the person serves as an additional therapeutic approach. By literally referring to "the eating disorder," clinicians can address its negative consequences without blaming the patient. This approach is consistent with client-centered motivational interviewing methods that empower patients to change as well as with dialectical-behavioral therapy techniques that encourage a tolerance and acceptance of the eating disorder. This approach can also be helpful for practitioners by mitigating frustration and judgment (15).

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References

1. Williams M, Leichner P: More training needed in eating disorders: a time cohort comparison study of Canadian psychiatry residents. Eat Disord 2006; 14:323–334
2. Ghadirian AM, Leichner P: Psychiatric residents' educational experiences and attitudes toward eating disorders. Can J Psychiatry 1990; 35:254–256
3. Crow SJ, Mitchell JE, Roenig JD, Steffen K: What potential role is there for medications in anorexia nervosa? Int J Eat Disord 2009; 42:1–8
4. Satir DA, Thompson-Brenner H, Boisseau CL, Crisafulli MA: Countertransference reactions to adolescents with eating disorders: relationships to clinician and patient factors. Int J Eat Disord 2009; 42:511–521
5. Hamburg P, Herzog D: Supervising the therapy of patients with eating disorders. Am J Psychotherapy 1990; 44:369–380.
6. Berkman ND, Lohr KN, Bulik CM: Outcomes of eating disorders: a systematic review of the literature. Int J Eat Disorders 2007; 40: 293–309
7. Papadopoulos FC, Ekbom A, Brandt L, Ekselius L: Excess mortality, causes of death and prognostic factors in anorexia nervosa. Br J Psychiatry 2009; 194:10–17
8. Lock J, Couturier J, Agras WS: Comparison of long-term outcomes in adolescents with anorexia nervosa treated with family therapy. J Am Acad Child Adolesc Psychiatry 2006; 45:666–672
9. Linehan MY, Chen EY: Dialectical behavior therapy for eating disorders, in: Encyclopedia of Cognitive Behavior Therapy. Edited by Freeman A. Berlin, Heidelberg, Springer, 2005, pp 168–171
10. Huas C, Caille A, Godart N, Foulon C, Pham-Scottez A, Divac S, Lavoisy G, Guelfi JD, Rouillon F, Falissard B: Factors predictive of ten-year mortality in severe anorexia nervosa patients. Acta Psychiatr Scand 2011; 123:62–70
11. Gowers SG, Clark AF, Roberts C, Byford S, Barrett B, Griffiths A, Edwards V, Bryan C, Smethurst N, Rowlands L, Roots P: A randomized controlled multicentre trial of treatments for adolescent anorexia nervosa including assessment of cost-effectiveness and patient acceptability: the TOuCAN trial. Health Techn Assess 2010; 14: 1–98.
12. Sansone RA, Sansone LA: Eating disorders and psychiatric comorbidity, in Clinical Manual of Eating Disorders. Edited by Yager J, Powers PS. Washington, DC, American Psychiatric Publishing, 2007, pp 79–111
13. Treasure J, Schmidt U: Ready, willing, and able to change: motivational aspects of the assessment and treatment of eating disorders. Europ Eat Disord Rev 2001; 9:4–18
14. Treasure J, Ward A: A practical guide to the use of motivational interviewing in anorexia nervosa. Europ Eat Disord Rev 1997; 5:102–114
15. Lock J, Le Grange D, Agras SQ, Dare C: Treatment Manual for Anorexia Nervosa: A Family-Based Approach. New York, Guildford Press, 2001

Case Report

Wernicke-Korsakoff Syndrome Developing After Bariatric Surgery

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Obesity is a serious public health concern and one of the leading preventable causes of death in the world. Bariatric surgery is becoming increasingly utilized in the obese patient population, and therefore postoperative complications from nutritional deficiencies are becoming more common. Wernicke's encephalopathy, characterized by the clinical triad of mental status changes, ophthalmoplegia, and ataxia, is the result of thiamine (vitamin B1) deficiency. If left untreated, it can result in irreversible cognitive deficits, with the inability to recall past events (retrograde amnesia) or to form new memories (antegrade amnesia), which is seen in Wernicke-Korsakoff syndrome. We present a case of Wernicke-Korsakoff syndrome that developed after bariatric surgery.

Case

A 49-year-old African American woman with a medical history significant for hypertension, asthma, and morbid obesity presented with a 4-month history of mental status changes (consisting of short-term memory loss, confabulation, emotional lability, episodic visual hallucinations, and confusion), which started approximately 1 month after Roux-en-Y gastric bypass surgery was performed. The patient's postoperation recovery was complicated by prolonged nausea and vomiting. Per her family members' observations, she had been high-functioning prior to the surgery and had maintained a full-time job. She had no history of alcohol abuse.

The patients' neuropsychiatric evaluation was consistent with Wernicke's encephalopathy, with confusion, confabulation, and short-term memory impairment evident during the assessment. Significant findings on physical examination included mild weakness and hypoactive deep tendon reflexes in the lower extremities. Extraocular movement examination revealed saccadic pursuit movements. Mini-Mental Status Examination revealed a score of 16/30 (orientation, 3/10; registration, 3/3; attention and calculation, 2/5; recall, 1/3; and language, 7/9). The patient refused gait examination due to pain, describing a "pins and needles" sensation in her lower extremities. Routine laboratory tests and a lumbar puncture were performed, and results were within normal limits. A magnetic resonance imaging (MRI) scan of the brain demonstrated scattered nonspecific subcortical and periventricular white matter changes within the cerebral hemispheres that were bilaterally consistent with small vessel ischemic changes.

Discussion

The classic clinical triad of altered mental status, ophthalmoplegia, and ataxia is rarely seen simultaneously in the majority of patients with Wernicke's encephalopathy. When present, however, these symptoms can take a variety of forms. Altered mental status can range from drowsiness, confusion, agitation, hallucinations, cognitive impairment, or, in the most extreme cases, a comatose state (1, 2). Ophthalmic findings may include nystagmus, a sixth cranial nerve palsy, or a total ophthalmoplegia. Ataxia may be difficult to assess as a result of the patient's altered mental status and has multiple proposed etiologies, one of which is related to a peripheral polyneuropathy (1). A series investigation of the clinical presentation in Wernicke's encephalopathy found that the simultaneous presence of the full triad was present in less than 29% of patients (2).

The diagnosis of Wernicke's encephalopathy is typically clinically-based. However, ancillary testing may help to aide in the diagnosis. Low serum thiamine levels can help confirm the diagnosis and should be measured prior to treatment in all patients (3). A MRI of the brain has a sensitivity of 53% and a specificity of 93% in patients with the disease. A brain MRI may show hyperintense signals in the area of the mammillary bodies, periventricular thalamus, and periaquaductal midbrain as well as the area surrounding the third and fourth ventricles (4).

For preventive purposes, all bariatric surgery patients should receive parenteral thiamine supplementation and regular follow-up assessment of thiamine levels for at least 6 months postoperatively (3). In patients with suspected or evident Wernicke's encephalopathy, immediate parenteral administration (200 mg/three times daily) should be given in order to arrest the progression of the disease (3). Ophthalmic findings are typically the first symptoms to improve while gait abnormalities typically persist longer (1). The importance of thiamine administration prior to the administration of any dextrose solutions must be emphasized. Dextrose consumes thiamine as a cofactor through two enzymatic pathways, and irreversible damage may occur if glucose is administered prior to thiamine (1).

Singh and Kumar (5) conducted a systematic review of 32 published case reports of Wernicke's encephalopathy occurring after bariatric surgery. Patient's were between the ages of 23 and 55 years. The majority of patients (27/32 [84%]) were women. The onset of symptoms typically occurred within 4–12 weeks postsurgery. Vomiting was a predisposing factor in the

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majority of patients (25/32 [78%]), and rapid weight loss ranging from 0.11 kg/day to 0.54 kg/day was also noted to be a risk factor (5, 6).

Conclusions

The overall prognosis of Wernicke's encephalopathy varies but may be completely reversible with early detection and treatment. Delay in treatment may result in chronic sequela or possibly even death. Preventive steps should be implemented, including educating bariatric surgery patients regarding vitamin supplementation, reviewing the warning signs of deficiency, and instructing patients and their families to seek early evaluation if symptoms occur. Patients with prolonged postsurgical emesis appear to have an elevated risk of developing Wernicke's encephalopathy and require immediate treatment upon presentation.

Dr. Thomas is a third-year resident and Dr. Caringi is a first-year Child Psychiatry Fellow in the Department of Psychiatry, University Hospitals Case Medical Center, Cleveland.

The authors thank Joseph Locala, M.D., attending in the Department of Psychiatry, University Hospitals Case Medical Center, Cleveland, for assistance.

References

1. Yamamoto T: Alcoholic and non-alcoholic Wernicke's encephalopathy: be alert to the preventable and treatable disease. Int Med 1996; 35:754–755
2. Jiang W, Gagliardi JP, Raj YP, Silvertooth EJ, Christopher EJ, Krishnan KR: Acute psychotic disorder after gastric bypass surgery: differential diagnosis and treatment. Am J Psychiatry 2006; 163:15–19
3. Galvin R, Bråthen G, Ivashynka A, Hillbom M, Tanasescu R, Leone MA; EFNS: EFNS guidelines for diagnosis, therapy and prevention of Wernicke encephalopathy. Eur J Neurol 2010;17:1408–1418
4. Bhardwaj A, Watanabe M, Shah J: A 46-yr-old woman with ataxia and blurred vision 3 months after bariatric surgery. Am J Gastroenterol 2008; 103:1575–1576
5. Singh S, Kumar A: Wernicke encephalopathy after obesity surgery: a systematic review. Neurology 2007; 68:807–811
6. Cirignotta F, Manconi M, Mondini S, Buzzi G, Ambrosetto P: Wernicke-Korsakoff encephalopathy and polyneuropathy after gastroplasty for morbid obesity: report of a case. Arch Neurol 2000; 57:1356–1359

Case Report

Demoralization

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Demoralization is characterized by the following five components: 1) helplessness and hopelessness, 2) subjective incompetence, 3) less perceived social support or gratification from others, 4) broken sense of connectedness between the past and the future, and 5) re-experiencing of earlier failures. The goal of treatment is the restoration of morale. One important step toward achieving this goal is to allow the patient to describe his or her illness experience in a historical manner (1). The present report demonstrates a prototypical case of demoralization resulting in psychiatric consultation.

Case

"Mr. Z" was a 54-year-old Caucasian male executive who was admitted for a planned duodenal switch procedure as part of management of chronic bile gastritis. The patient's hospital course was complicated by emesis, and on hospital day 3, he stated, "I don't feel like living anymore, I just want this to end." The primary team subsequently consulted psychiatry service.

Prior to having the surgical procedure, the patient had expected complete relief of chronic nausea and vomiting. He recounted his frustrations since being admitted into the hospital and reported ongoing anxiety about the possibility of recurrence of chronic emesis.

Furthermore, he reported feeling increasingly frustrated with his situation and feared having a bad outcome. He related that he felt as though his voice was not being heard and that the "medical system and professionals operated on a basis [that] seemed to lack consistency and logic." As president of a company, he was able to "make people jump." He felt as though he had no control over his current situation. Although he had no personal history of psychiatric disorders, his father and mother had used substantial amounts of alcohol. He had been happily married for 25 years and had two children.

The consulting psychiatrist empathized with the patient about the disorganizing effect of being in a hospital and recognized that "being powerless" was contrary to his general day-to-day experiences. Normalizing his experience reduced his anxiety. His medical history and examination were inconsistent with an acute or chronic psychiatric disorder but were in line with demoralization (1). The consultant recommended clonazepam (0.25 mg by mouth at bedtime as needed) for short-term relief of anxiety but made sure to allow the patient to request one additional dose if symptoms persisted. The next day, Mr. Z was noted to be "in better spirits," presumably due to the reassurance as well as autonomy over the benzodiazepine dosing. The remainder of his hospital course was uneventful, and he was discharged without psychotropic medication or the need for ongoing psychiatric care.

Not all consultation cases require complex medication management or psychotherapeutic or extensive social interventions. Empathy and restoring the patient's sense of control can treat serious situations such as suicidal statements when these statements are the result of demoralization.

Dr. Pradhan is a Fellow in Consultation Liaison Psychiatry (PGY-V) at Inova Fairfax Hospital, Falls Church, Va.

Reference

1. Jacobsen J, Maytal G, Stern T: Demoralization in medical practice. Prim Care Companion J Clin Psychiatry 2007; 9:139–143

Letter to the Editor

More on States' Laws Regarding the Duty to Warn

To the Editor: I greatly enjoyed reading Dr. Seawell's excellent review of the Tarasoff case and subsequent changes in state laws regarding the duty to warn (1). Dr. Seawell inspired me to better acquaint myself with the state laws in Oregon, which is one of the states in which the physician is allowed, but not required, to warn a potential victim. Specifically, the statute indicates that potential harm to others "may" (not must) be reported and clarifies that "a decision not to disclose information under this subsection does not subject the provider to any civil liability" (2). It would be interesting to learn how many trainees know the specific laws regarding duty to warn in their state. I certainly did not and was under the impression that there was a duty to warn in Oregon. My perception is that many of my colleagues believe the same.

It seems quite reasonable to warn someone in "clear and imminent danger," as the Oregon statute reads. However, much more common seem to be situations in which patients make conditional statements, such as "if I ever track him down, I'll kill him." In these cases, the psychiatrist is unable to legally disclose the threat and must hope that the patient does not follow through. These remain extremely challenging situations for psychiatrists to navigate.

References

1. Seawell M: A residents' guide to Tarasoff. Am J Psychiatry Res J 2011; 6:7–9
2. Oregon Revised Statutes, 179.505, 2009

Jay Augsburger, M.D.

Dr. Augsburger is Chief Resident (PGY-IV) in the Department of Psychiatry at Oregon Health Sciences University, Portland, Oregon.

Response to Augsburger Letter

To the Editor: Dr. Augsburger raises several critical points. First, he draws attention to the fact that many trainees are likely unaware of the great variability in the interpretation and application of the Tarasoff warning throughout the United States and they may incorrectly assume that issuing a Tarasoff warning is a nationally mandated practice. Secondly, he highlights some of the challenges associated with clinical application of state statutes. Even seemingly concrete concepts, such as "clear and imminent danger," may have varying definitions among practitioners, and conditional threats can have varying degrees of plausibility, i.e., "If I see her again, she's dead" versus "If I win a billion dollars, the first thing I'll do is kill her." Knowledge of case law is useful in helping to navigate these and other complex clinical situations and can assist in further elucidating state-specific expectations. However, given the complexity of the Tarasoff warning and its progeny, trainees are urged to consider consultation with their institutions' legal expert(s) should there be concerns about whether or not a particular clinical scenario necessitates issuing a warning. Residents are also encouraged to follow Dr. Augsburger's example and familiarize themselves with Tarasoff interpretations in their states. He has initiated an exciting dialogue, which I am hopeful will inspire discussion among other trainees.

Monifa Seawell, M.D.

Dr. Seawell is a third-year resident in the Department of Psychiatry, Wayne State University, Detroit. Dr. Seawell is also the selected candidate for the position of Resident's Journal Associate Editor, 2011–2012.

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 Mark Sylvester, M.D., (PGY-III), Department of Psychiatry, University of Florida, Gainesville, Fla.

Question #1.
Ketamine, an agent used for the rapid treatment of depression, is most closely related to which of the following drugs?

A. Phencyclidine
B. Lysergic acid diethylamide
C. Methylene deoxymethamphetamine
D. Dimethyl tryptamine
E. Chlorazdiapoxide

Question #2.
Which of the following is not considered a favorable factor in the use of ketamine for depression?

A. Effectiveness and safety may improve with subsequent doses
B. Low cost
C. Ease of administration
D. Rapid onset of action
E. Low abuse potential

ANSWERS

Answers to March Questions. To view the March Test Your Knowledge questions, go to http://ajp.psychiatryonline.org/cgi/data/168/3/A36/DC2/1.

Question #1.
Answer: D. Fluoxetine
In a study conducted by Cornelius et al., the use of fluoxetine to treat symptoms of depression showed a statistically significant decrease in cannabis use relative to placebo.

Reference
1. Cornelius JR, Salloum IM, Haskett RF, Ehler JG, Jarrett PJ, Thase ME, Perel JM: Fluoxetine versus placebo for the marijuana use of depressed alcoholics. Addict Behav 1999; 24:111–114

Question #2
Answer: A. 42.2%
Green et al. conducted a review of 58 studies that showed cannabis use in patients with schizophrenia or psychotic disorders to be significantly higher than that found in the general population, with lifetime abuse prevalence reaching as high as 22.5%.

Reference
1. Green B, Young R, Kavanagh D: Cannabis use and misuse prevalence among people with psychosis. Br J Psychiatry 2005; 187:306–313

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. Fayad; fayad@ufl.edu.**

Author Information for *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.

May 2011
Section Theme: Child Psychiatry
Guest Section Editor: Michael Ascher, M.D.;
michaelaschermd@gmail.com

June 2011
Section Theme: No specific theme
Guest Section Editor: Deepak Prabhakar, M.D.;
dprabhakar@med.wayne.edu

July 2011
Section Theme: Suicide
Guest Section Editor: Karthik Sivashanker, M.D.
sivashanker@gmail.com

August 2011
Section Theme: Clinical Trials
Guest Section Editor: Madhav Muppa, M.D.
mmuppa@lsuhsc.edu

September 2011
Section Theme: Addiction
Guest Section Editor: Jonathan Avery, M.D.
joa9070@nyp.org

We invite residents who are interested in participating as Guest Section Editors to e-mail Dr. Cerimele at joseph.cerimele@mssm.edu. If you are interested in contributing a manuscript on any of the themes outlined, please contact the Section Editor for the specified month.