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An Interview with William Carpenter, Jr., M.D.

Maju Koola, M.D.
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The following is an interview with William Carpenter, Jr., M.D., on "Psychotic Disorders and DSM-V," conducted by Maju Koola, M.D. Dr. Carpenter is a Professor of Psychiatry and Pharmacology at the University of Maryland School of Medicine, Director of the Maryland Psychiatric Research Center, and Editor-in-Chief of Schizophrenia Bulletin. Dr. Carpenter is also a member of the APA DSM-V Task Force and Chair of the APA DSM-V Psychotic Disorders Work Group. Dr. Koola is a third-year psychiatry resident at the University of New Mexico, Albuquerque, and this month's Issue Editor.

Dr. Koola: What are your goals as the Chair of psychotic disorders for DSM-V?

Dr. Carpenter: Well, initially it was to get a diverse group of smart people who would be real workers to tackle the problem, with the goal being to create a new paradigm with a focus on targets of clinical action that will simultaneously alter the future research agenda.

Dr. Koola: Is there a place for cognitive impairments in the diagnostic criteria? What would be the instrument to measure cognitive impairments?

Dr. Carpenter: Probably not in the psychotic disorders for the diagnostic criteria per se. Patients will have various levels of cognitive performance, and neither the level nor profile is definitive for differential diagnosis. But it is a core feature for schizophrenia, and we need to have more information about the nature of cognition in a number of other psychotic disorders. So this is much more likely to be used as a dimension rather than as a diagnostic criterion per se. We expect DSM-V to have simultaneous assignment to a diagnostic class and ratings along a number of key dimensions. So this

would be a dimension. To make it useful and applicable in the wide variety of settings of DSM-V, it will have to be based on a clinical interview and not on a detailed neuropsychological testing. This might be backed up with an easy, quick-to-administer test of something such as the Digit Symbol Test, which measures processing speed. It tends to have a pretty high correlation with other aspects of cognition impairment and can be administered in a couple of minutes. The clinical interviews are being worked out. By the time DSM-V comes out, we will probably know if it can be reliably and validly done.

Dr. Koola: Will primary negative symptoms be added in the diagnostic criteria and how can clinicians be trained to differentiate between primary and secondary negative symptoms?

Dr. Carpenter: I think we are likely to stay with just the negative symptom language, with the text clarifying the importance of making the distinction, but this hasn't been settled yet. Hopefully, clinicians who are evaluating a patient who doesn't express much emotion in their face have to figure out

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if the person is depressed, if it's akinesia caused by a drug, or if it's a primary lack of emotional experience. The treatment implications are very different for these conditions. So a differential diagnosis needs to be done at the clinical level, and we don't know how reliably that will get done. We hope the text can give some emphasis to the importance of making a differential diagnosis to sort out what might be primary to the disease process per se versus secondary to these associated features.

Dr. Koola: The umbrella term "general psychotic syndrome" has been recently suggested. In your view, what are the merits and pitfalls of combining schizophrenia and bipolar disorder under such an umbrella term?

Dr. Carpenter: I think it's unlikely that they will get combined. This would be a major change, and the compelling evidence simply doesn't exist. Also, moving bipolar to schizophrenia would down-

play the relationship of bipolar disease to other mood disorders and would up-play the role of psychosis. Many bipolar patients do not have a psychotic experience. Some bipolar I patients may or may not have a psychotic experience once or occasionally during episodes, but this illness pattern is really dominated by the mood disturbance. At the phenomenological level, I think it would lose emphasis from the difference in the nature of thought disorder. The disorganized thought in schizophrenia is unlike the pressured thinking of mania. Combining the two would also play down the pattern differences. Cognition, for example, seems to decrease very early in life in schizophrenia, and it is a long lasting trait phenomenon. It's closer to a state-like phenomenon in bipolar illness, although recent studies in euthymic patients and biological relatives do suggest subtle trait impairments in bipolar disorder. The pharmacological treatments are substantially different for the two disorders. So we would be ignoring key differences and have inadequate evidence for combining the disorders despite the similarity that is observed. The

overlapping genetic contributions may be associated with features that are common to both but are not decisive to differential diagnosis. For example, psychosis occurs in many different disorders that have remarkably different etiologies, and psychosis itself is simply not definitive in the diagnostic grouping. But the genetic vulnerability to psychotic experience may cross these diagnostic boundaries.

Dr. Koola: What are the current limitations of DSM-IV schizoaffective disorder diagnosis and what are the advantages of retaining it with some modifications?

Dr. Carpenter: Everything I am saying now is my personal view and not representing the official decisions of the DSM-V Work Group. There are two limitations to schizoaffective disorder as a class. One is that we have no reason to think it is a valid existing diagnostic category in nature. The way it's defined, some patients really have schizophrenia and some patients really have mood disorder. We have no way to know if there is a third group who actually have schizoaffective disorder rather than just one of the parent disorders with overlapping features. And keep in mind that affective disturbances are very common in persons with schizophrenia, particularly in the earlier episodes. The other problem is that it is simply not a very reliable diagnosis the way it is made. Timing the relationship between mood disorder and schizophrenia symptoms creates complex criteria and does not relate well to natural history. The advantage of a schizoaffective disorder class is that it is tremendously useful clinically. It serves the function of placing patients in a holding category rather than reaching a definitive diagnosis. This increases the likelihood of clinicians considering the full range of treatment that might be appropriate for mood as well as psychotic disturbances. So there is a real need for it. With DSM-V, we will either need to figure out an alternative way of dealing with it or how to provide criteria to make a more reliable diagnosis. We are toying with the idea of using dimensions for depression, mania, and anxiety in a way that dimensions might capture the important aspects and not to rely on

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having a separate diagnostic category. But I am not sure how that will work out in the end.

Dr. Koola: After three decades of neuro-imaging research and about a decade long of genetics research, are we close to using these findings to make a diagnosis?

Dr. Carpenter: No, I don't think we are close at all. There are several problems. One is that most studies do not include all the relevant comparative groups. Many studies, for example, would compare schizophrenia subjects with normal controls. Other studies compare bipolar patients with normal controls. There are very few studies on brief psychotic disorder, psychosis not otherwise specified, and delusional disorder. So we don't really have the basic comparative information that we need. The second reason is that the findings to date, which are very interesting, lack the specificity and sensitivity to have positive predictive power to make a diagnosis in an individual. So it's easy to say that there is substantial evidence for the diminished size of the hippocampus structure in schizophrenia. But you cannot measure the size of the hippocampus in an individual and tell whether or not he has schizophrenia. It is true with the genes. Genes make some contributions to the overall manifestations of the illness. The alleles are commonly found in the general population. So for the purpose of diagnosis, most people with the dis-

ease would not have the alleles and most people with the alleles will not have the disease. And it is just nowhere close to application for diagnostic purposes.

Dr. Koola: What are the advantages and disadvantages of having separate criteria for researchers and clinicians?

Dr. Carpenter: I think for clinicians, we have to end up with something that is practical. This should be usable by a wide range of clinicians throughout the world. In that regard, it will have to be straightforward and easy to understand and apply. Researchers will have much more specific interest and questions that are not exactly the diagnostic questions per se. They will have the resources to do a more detailed evaluation for the questions of interest. So the needs can be very different, and we need to meet clinician needs. I don't think we will have separate criteria for researchers, and that is a question that is not resolved. If we move to a dimensional system, it will probably reshape the future of research in a way that ties much closer to specific pathologic dimensions and less closely to the overall diagnostic category per se. This paradigm shift to domains of psychopathology may be closer to the issues of importance to clinicians and investigators.

Dr. Koola: How should the prodromal phase or early detection syndrome be handled in DSM-V?

Dr. Carpenter: This is something that

is hotly debated in our work group. My own view is that it's extremely important to clinicians to have a way to identify persons at risk for developing psychosis. There is enough evidence that this can be validly done with a reasonable predictive power. The problem that immediately arises is that you are talking about late adolescence/early adult populations, where in the non-ill population these behavioral traits are frequently observed. The key to identifying cases that merit diagnosis and clinical care would be that they are associated with help seeking and the experience of stress, dysfunction, and/or disability. So with the protection of identifying cases because there is distress, dysfunction, and disability, it seems to me that we need to be very eager to have a category that clinicians can use to identify this group. We will have to be careful that we don't do more harm than good. One concern is that it will lead to the use of antipsychotic drugs and have a greater risk-to-benefit ratio at that stage of the illness. So there will be many things to be dealt with in the debates that will surround this. But in the end, we have to recognize the importance of early detection and intervention. This may provide a diagnostic handle that enables clinicians to recognize and to have a way to record it in the relationship to third-party pairs. It is possible that other risk syndromes will be identified, and a new category could be created rather than assigning each to a "parent" group of disorders. Mild cognitive impairment is an example.

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In addition to this online edition of the Resident's Journal, there is an e-mail portion delivered each month. This month's e-mail highlights transdiagnostic CBT and eating disorders and psychiatric evaluation and bariatric surgery.

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Dr. Koola: DSM-III and DSM-III-R had the course specifier “chronic,” which was dropped by DSM-IV. Clinicians and researchers continue to use this term. Is there an advantage to reintroducing this specifier?

Dr. Carpenter: There might be an advantage, but I expect that it is not the most heuristic way to go. An alternative way would be to have dimensions serve the purpose of specifiers. A diagnosis of schizophrenia with avolition is importantly distinguished from a diagnosis of schizophrenia without avolition. Schizophrenia subgroups without primary negative symptoms are much more likely to have depressive components or excessive emotional expressivity. Here, the differential diagnosis is between bipolar and schizophrenia. In some way, we should separate psychotic patients into those with a mood disorder pattern, those with mood disturbance and a schizophrenia pattern, and those with a schizophrenia pattern and restricted emotion. Something like this might be more informative than specific specifiers.

Dr. Koola: If a psychotic disorder meets full criteria for schizophrenia but is thought to be etiologically related to severe trauma, should it still be diagnosed as schizophrenia?

Dr. Carpenter: Two things to say about this. First of all, schizophrenia is a syndrome. There will be different etiologies associated with it. As we try to understand the etiology of people who fit in this category, the fact that they have an etiology that is different from other cases will not be decisive in terms of whether or not they belong in the syndrome. On the other hand, if it's simply a matter of having psychotic symptoms that meet criteria but are known to have another cause, then there are categories where psychosis associated with Alzheimer's disease is not considered schizophrenia. So the real issue is what is the nature of the trauma that justifies separating the illness from the schizophrenia syndrome. If there is a history of childhood physical and/or sexual abuse and the person now has a schizophrenia pattern and meets schizo-

phrenia criteria, that case will stay in schizophrenia. If it's remarkable psychological trauma that has happened recently and the person appears to be more like a posttraumatic stress disorder (PTSD) patient with psychosis, then that would belong in PTSD. Psychosis following closed-head injury is another category. So there is a differential diagnosis, and schizophrenia still remains principally psychotic conditions that are not clearly explained by a known etiological factor.

Dr. Koola: Are the traditional subtypes useful for clinical or research purposes?

Dr. Carpenter: There are formidable problems associated with traditional subtypes, and we will consider dropping them all together. The problems include that the cases often shift from one category to another over time. This suggests that they are not really marking things that are critically important in terms of etiology and pathophysiology or even treatment. The second is that catatonic schizophrenia is probably just an unfortunate designation because most people with catatonia do not have schizophrenia. The treatments for catatonia are very different than the treatments for schizophrenia, and in fact using antipsychotic drugs can be dangerous to people with catatonia. Catatonia is more frequently associated with mood disorders and general medical conditions. So some of the subtypes are just challenged for the validity, others have been more like state phenomena. The use of dimensions will be far more informative than attempting to use traditional subtypes to provide additional clinical information.

Dr. Koola: In your view, should Schneiderian symptoms have extra weight compared with other psychotic features in DSM-V?

Dr. Carpenter: We found long ago in the International Pilot Study of Schizophrenia that Schneiderian first-rank symptoms occurred in other psychotic disorders. It has been disproven that they are pathognomonic for the presence of schizophrenia. On the other hand, they tend to be more bizarre psychotic experiences than mood congruent psychotic experiences, and they help in discriminating between schizophrenia disorders and other psychotic disorders. I think it's fair

for some of them to have extra weight, but it has to be appreciated that most first-rank symptoms do not occur in most patients. Individual first-rank symptoms may occur only in 20% to 30% of cases. So they are not an adequate system. The real problem has been that reality distortion has been greatly emphasized over disorganization of thought and negative symptoms as core components of schizophrenia. So in terms of psychotic features, Schneiderian symptoms may deserve extra weight. But first-rank symptoms have had an unfortunate effect of moving the schizophrenia concept away from Kraepelin and Bleuler and creating a reality distortion syndrome.

Dr. Koola: Traditionally, delusional disorder has been recognized. Similarly, should hallucinatory disorder also be considered?

Dr. Carpenter: Well, we have not looked into that question yet in our process. I don't know enough to have an opinion on that now. It will be interesting to see if there is sufficient literature to justify this. There is a high correlation between delusions and hallucinations in individuals, and most people experiencing hallucinations also form false beliefs around them. It could be that the high correlation justifies just having one disorder and it is possible that delusional disorder might be considered delusional/hallucinatory disorder. But we will have to look at the data and see if there is enough evidence to justify having two separate categories.

Dr. Koola: What is the most appropriate title for this group in DSM-V, i.e., psychotic disorders or schizophrenia and other psychotic disorders or schizophrenia spectrum disorders?

Dr. Carpenter: I think schizophrenia spectrum disorders would be completely wrong because we don't have much evidence that many of the psychotic disorders are closely tied to schizophrenia. For example, brief psychotic disorder and delusional disorder may be minimally related to schizophrenia. The schizophrenia spectrum includes schizotypal personality and minor schizophrenia-like features

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observed in biological relatives. Schizophrenia and other psychotic disorders are problematic as a title for the group because it gives emphasis to schizophrenia when a number of the other psychotic disorders are not especially related to schizophrenia. I would think that a group of psychotic disorders would likely be the best category. But we will have to make clear that this is excluding many disorders that are associated with psychoses and that the group is based on psychotic features that are not linked to a known etiology.

Dr. Koola: The International Pilot Study of Schizophrenia emphasized the importance of insight in psychotic disorders. Will DSM-V have insight as a dimension?

Dr. Carpenter: I don't think so for two reasons. One is that insight can be a problem in a number of different disorders, even though it was clinically important in schizophrenia and turned out in our study to be one of the three leading differential pathologies among people with psychotic disorders differential in favor of schizophrenia. It's not clear how it would be defined in a way that would capture that in DSM-V, particularly when you think the nature of the lack of insight may be very different in a bipolar patient than in a schizophrenia patient. How to define that and to be sure it's a reliable differential would be problematic. The other reason I think is just the practical consideration. If we move to dimensions in addition to categories, there will be a limited number that are practical to use. And I don't think insight will be high enough on the list to make it into final consideration.

Dr. Koola: How can dimensional assessments be combined with categorical

classification and what are the key dimensions that you are considering?

Dr. Carpenter: We don't yet know how, but this will get done. There is a general agreement that we need to do dimensions in a way that they are parallel to diagnostic category in importance. So this would at least imply that dimensions would be a mandatory part of the evaluation. It would not be like having an axis V that is generally ignored. Dimensions would be the required components of evaluation. There are seven dimensions that we are considering from the point of view of the Psychosis Work Group. We think we would need to turn the diagnostic criteria for schizophrenia into dimensions. We will have reality distortion, disorganization, and negative symptom dimensions. This is important because we need to know more about how those dimensions are occurring in the other psychotic disorders, and they also represent therapeutic targets. The other four dimensions we are considering are cognition impairment, depression, mania, and anxiety. These give real emphasis to clinical therapeutic targets that are commonly observed in people with psychotic disorders. These dimensions would help clinicians identify therapeutic targets. This will help shift the paradigm for future research studies into looking at specific dimensions or domains of pathology rather than at the syndrome classification level. The additional comment I should add is that we will have to consider dimensions that are relevant and cut more broadly across DSM-V. And I don't know what will happen yet. Having suicidal ideation can be assessed as a dimension. Insomnia, common in many disorders, needs special attention therapeutically and may be another dimension. So there will be others that come into consideration from other groups. But at the moment, these are the ones that we are proposing.

Dr. Koola: What other challenges do you foresee?

Dr. Carpenter: I think the most important challenge is how to make dimensions be dominant in the system, i.e. how DSM-V represents a real paradigm shift. This is close to my heart because in a paper in 1974, with Drs. John Strauss and John Bartko, we argued that schizophrenia was best conceptualized as three domains of psychopathology. Each domain required separate attention from an etiologic and a therapeutic point of view. I am eager to see dimensions help move the paradigm to these basic behavioral traits that tend to cut across syndrome boundaries. This needs to be the focus for research study and therapeutic action. So how to really make the dimensions work as a system will be a big challenge. A second challenge is to make DSM-V a dynamic document. We hoped that by DSM-V we would have sufficient evidence to include biomarkers and other diagnostically relevant variables as criteria for classification. On the whole, we are simply not there yet. But as we have more evidence, we need DSM-V to be a modifiable document. Then we don't have to wait an additional 10 to 20 years before new information that is relevant to diagnostic category or dimensional assessment can be put into play. So creating a dynamic document will be important. And the third thing I would mention is the importance of getting it right around the prodrome or the high-risk cases. We need an effective clinical tool to address serious needs without getting too far into the non-ill population. We must avoid an adverse benefit-to-risk ratio in terms of initiating therapeutics. It will be a real challenge to get this one right.

Please send feedback/critique about psychotic disorders and DSM-V to Dr. Koola at majujuju@yahoo.com.

A Novel Project in Student Education (NPSE): Motivating Residents to Teach Medical Students

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Objective

Medical students receive their clinical training from a variety of sources, including residents during informal teaching sessions and attending physicians during more formalized rounds. Since managed care has reduced the amount of time available for formal teaching, many medical schools are emphasizing clinical experience over lectures (1). With this, the role of the resident as teacher has increased.

Wilson (2) reported that medical students receive 20% to 70% of their teaching from residents, and Weissman et al. (3) estimated that residents contribute up to one-third of medical students' total knowledge. It is also well-documented that an effective resident teacher can influence the future career choice of a medical student (4-6). Moreover, there is evidence that better resident teachers can help students become better learners (7) and that resident teaching can improve residents' clinical skills (8).

Despite these benefits, many residents shy away from teaching. According to Morrison and Haffler (7), one possible reason for this is that residents undervalue teaching. Wilson (2) also reported that obstacles to resident teaching include the lack of recognition of teaching efforts, the lack of role modeling by faculty, the lack of knowledge of teaching objectives, and the lack of resident interest. In an interview of experienced medical teachers, it appeared that receiving encouragement to teach was a common point in the acquisition of teaching skills (9). Katz and McCarty (10) reported that an incentive-based pilot program to encourage residents to teach had positive results on resident participation and enthusiasm. Similarly, a program at Northwestern University Medical School that rewards faculty with points for teaching has resulted in increased faculty morale (11).

Novel Project in Student Education

(NPSE) focuses on improving residents' motivation and attitudes toward teaching medical students. The project was purposed to eliminate many of the barriers to resident teaching by providing role modeling, clear objectives, and recognition of teaching efforts.

Method

In NPSE, each 6-week psychiatry clerkship during students' third year of medical school is set up as a fantasy football game in which "teams," comprised of three or four residents, compete against each other to accumulate the most points over the 6-week rotation. Clerkship objectives have an attached point total that is awarded to a team when a particular objective (e.g., teaching a mental status exam) is taught or reviewed by a resident. Awards might be 2, 3, or 7 points, depending on the level of complexity. Each team is "owned" by a faculty member in the department who has been identified as a role model for teaching. We hypothesized that the motivation as well as the confidence of residents to teach would be increased through this intervention of friendly competition. Essential components of this project include associating residents' names with faculty members who are held with high regard and recognizing effective resident teachers.

To test our hypothesis, all residents were asked to complete short surveys prior to and following the academic year. The preintervention surveys contain 10 questions, several of which assess residents' motivation to teach and their own confidence in their teaching abilities. The postintervention surveys have two additional questions assessing resident perceptions about the project. Average Likert scores are compared pre- and postintervention to determine whether participation in NPSE affects residents' motivation to teach. Additionally, feedback is obtained from medical students at the end of their rotations in order to

identify effective resident teachers. These resident teachers are recognized with a plaque at the end of the academic year.

Results

Nineteen of the 22 residents who participated in our most recent NPSE assessment completed the surveys (response rate: 86%). Preliminary data indicate that residents' confidence in their teaching abilities improved with their participation, which suggests that the experience of teaching may have beneficial effects on a resident's self-perception of his or her teaching skills. Markers of confidence improved from an average of 2.58 to 3.44 on a 5-point Likert scale. However, early data do not show any effects on residents' overall motivation to teach. It is also pertinent to note that, on average, residents found the project to be an enjoyable activity.

Conclusion

With increasing demands placed on academic medicine, creative approaches implemented into residency training are needed to ensure that residents are motivated to teach medical students. Literature addressing this concern has identified some of the barriers to resident teaching of medical students. Our project was purposed to create an atmosphere of friendly competition, while trying to minimize some of the identified barriers to resident teaching. Although there was a trend toward increased confidence in teaching among residents in our most recent assessment, a similar trend was not observed regarding their motivation to teach.

One of the major limitations to the most recent NPSE assessment was the small sample size. More data are needed to determine if participation in NPSE results in a statistically significant increase in residents' confidence in their teach-

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ing abilities or their overall motivation to teach. NPSE is ongoing, and more data will be analyzed through the end of 2009. Some possibilities for the expansion of the project include assessing a possible correlation between 1) medical student ratings of resident teaching abilities and residents' confidence with teaching and 2) medical student ratings of resident teaching abilities and residents' motivation to teach. It would also be worthwhile to assess any gender differences in perceived effectiveness of this "fantasy football" model of enhancing residents' motivation to teach.

Ultimately, we hope to create a model that will help residents overcome some of the existing barriers to teaching medical students. This, we believe, will help to improve teaching and supervision of medical students, foster a passion for learning and teaching among residents, and enhance medical student interest in psychiatry as a career.

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We would like to invite all residents to participate in a focus group taking place at the 2009 APA Annual Meeting in San Francisco. Editor-in-Chief Robert Freedman, M.D., along with the Committee on Residents and Fellows and select Deputy Editors, will solicit thoughts on the Residents' Journal and ideas on how *The American Journal of Psychiatry* can be of further use to residents. The meeting is scheduled for Tuesday, May 19, 2009 (time and location TBA). For further information please contact AJP@psych.org

For information on the 2009 APA Annual Meeting, including registration and housing, visit

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An Interview with Barry Reisberg, M.D.

Nauman Ashraf, M.D.
New York University

The following is an interview with Barry Reisberg, M.D., on the "Significance of Geriatric Psychiatry and Advances in Alzheimer's Disease Treatment," conducted by Nauman Ashraf, M.D. Dr. Reisberg is the Director of the Clinical Core of the New York University (NYU) Alzheimer's Disease Center, Clinical Director of the Aging and Dementia Research Center of the Silberstein Institute of NYU School of Medicine, and Professor of Psychiatry at NYU School of

Medicine. Dr. Reisberg was the first to describe many of the most important symptoms of Alzheimer's disease and the characteristic clinical course of the disease. His work has been instrumental in the worldwide development of all major current pharmacological treatment modalities for Alzheimer's disease (memantine, risperidone, rivastigmine, and donepezil). Dr. Ashraf is a first-year psychiatry resident at NYU Medical Center.

Dr. Ashraf: What motivated your interest in geriatric psychiatry and geriatric mental research?

Dr. Reisberg: When I finished my residency I was certain that I wanted to do psychiatric research. Initially, in my first faculty position at a Veterans Administration hospital, I found a mentor who was a psychopharmacologist and electrophysiologist. After 2 years of part-time research, with substantial full-time clinical and teaching responsibilities, I decided to do psychiatric research on a full-time basis. I took a job at the Neuropsychopharmacology Research Unit at the NYU Medical Center and Bellevue Hospital. One aspect of the studies was the psychopharmacology of the aging brain. I immediately became involved in this work and discovered a field about which very little was known. I was certain that I could make an impact in this epidemiologically substantial but scientifically neglected area.

Dr. Ashraf: Why is geriatric psychiatry relevant and why should residents go into geriatric psychiatry?

Dr. Reisberg: Older persons, in general, require a significant proportion of all medical care. This is also true of geriatric psychiatry. The challenges and opportunities associated with the psychiatric care of older persons are substantial and, indeed, extremely interesting. Older persons commonly have cognitive changes, which occur in a broad spectrum, from subjective changes to very severe dementia. Affective and other behavior changes also commonly occur. Concurrent medical illnesses in this population make the practice of geriatric psychiatry very exciting from an intellectual and research perspec-

tive. Many of the changes that occur are remediable, and older persons and their families are generally very appreciative of efforts made on the patient's behalf.

Dr. Ashraf: What are the major issues in geriatric psychiatry?

Dr. Reisberg: There are two major issues in geriatric psychiatry. One is Alzheimer's disease and its antecedents. Another is affective disturbances. Other major issues include vascular changes associated with infarcts and less overt conditions such as white matter brain changes. Additionally, we now know that various medical conditions interact with the three major psychiatric presentations. These other medical conditions include obesity, heart disease, hypertension, and diabetes, among others. Consequently, geriatric psychiatric conditions are generally not unitary but are part of a broad brain and body spectrum.

Dr. Ashraf: Why did you become interested in Alzheimer's disease?

Dr. Reisberg: As I noted previously, when I became involved in geriatric mental research in 1978, Alzheimer's disease and cognitive aging were extraordinarily neglected. So-called senile dementia and brain atherosclerosis were undescribed and neglected entities. I was seriously interested in psychiatric observation, which I termed phenomenologic study. I realized that the continuum of aging and Alzheimer's disease had not been well described and was amenable to description. This resulted in my describing the evolution of aging and Alzheimer's disease in seven major stages and, subsequently, in a total of 16 characteristic stages and sub-

stages. Therefore, Alzheimer's disease is a much more characteristic process than other mental illnesses and indeed, then, perhaps any other illness process. The reasons for this cannot be covered. Some of the reasons are related to the observation that many aspects of Alzheimer's disease reverse normal human development in remarkably precise ways. We are now beginning to recognize that a major aspect of this developmental reversal is progressive metabolic decrements. Clearly, all of this is extraordinarily interesting.

Dr. Ashraf: What are the recent advances in the treatment of Alzheimer's disease?

Dr. Reisberg: There are three recent advances in the pharmacologic treatment of Alzheimer's disease. The most important of these is the development of memantine as the first medication for more advanced Alzheimer's disease and the first N-methyl-D-aspartic-acid receptor antagonist treatment for Alzheimer's disease. Fifteen years ago, we had described many aspects of advanced Alzheimer's disease, which was largely neglected by the research community. Merz, a small company in Frankfurt, Germany, came to me with data on a study conducted in Latvia, which was conducted in what were called state hospitals and which studied severely impaired demented patients. The Latvian study used the Global Deterioration Scale, which I had developed, and other measures that were not internationally known. I looked over the data, and they seemed very promising. Briefly, I and my associate Steven Ferris designed the first Food and Drug Administration approvable trial for severe dementia patients. As principal investigator, I was respon-

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sible for all aspects of this study. The medication was effective and resulted in our study being published in the New England Journal of Medicine and, subsequently, the medication being approved as the first medication for more advanced Alzheimer's disease. This has been very important in decreasing the burden and neglect of millions of advanced dementia patients around the world. Subsequently, using our design, Pfizer conducted studies that showed that Aricept was effective for advanced dementia. Consequently, we now have two medications that have

been recently approved for this very burdened population. A fellow of ours in the early 1980s, Ravi Anand, went on a decade later to become responsible for the development of one of the first cholinesterase inhibitors: rivastigmine for Novartis pharmaceuticals. Ravi turned to his former mentors at NYU, myself, and Steven Ferris to help him design a trial of this medication. Six of the measures I had developed were used in these early pivotal trials. The result was that rivastigmine was approved for treatment of Alzheimer's disease at the beginning of the new millennium. Recently, rivastigmine has been approved as the first patch

treatment for Alzheimer's disease and is serving many of these patients. Apart from pharmacologic treatment, nonpharmacologic treatments and appropriate management are also very important for Alzheimer's disease patients. There are many aspects to this, including decreasing behavioral disturbances and decreasing physical morbidity. Our findings regarding developmental reversals in the process of Alzheimer's disease and corresponding care needs have been very important in understanding and alleviating these significant burdens associated with the advance of Alzheimer's and related dementias.

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Black Tar Heroin in Northern New Mexico: Socio-Cultural Factors Contributing to a Rise in Heroin Overdose Deaths

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Nestled between the Jemez and Sangre de Cristo Mountains in Northern New Mexico lies the Espanola Valley, a region steeped in tradition, with family ties stretching back to old Spanish land grants. Chimayo, a town in this region, is known in the Catholic world as one of the spiritual capitals of the Southwest. Each year during Holy Week, tens of thousands of pilgrims flock to El Santuario de Chimayo, located in the city's center. Some pilgrims walk hundreds of miles barefoot across scenes of red and white painted sandstone and sage brush (1).

Behind this sacred and picturesque landscape lies not only a rich socio-cultural landscape, but also a tragic tradition. Over the past several decades, Chimayo, Espanola, and the surrounding Rio Arriba County have served as an epicenter for heroin use. In addition, these areas represent the highest accidental overdose death rates in the United States. Despite the region's sparse, rural population, it has witnessed the profound effect of drug use and its sequelae.

In 2003, data revealed that the average accidental overdose death rate across the United States was 7.5 deaths per 100,000 individuals (2). In the same year, data also showed that the accidental overdose death rate in New Mexico was more than double that of the national rate, at 17.5 deaths per 100,000 individuals. Moreover, New Mexico showed an increase in the rate of overdose deaths by almost 277% between 1990 and 2005. At the center of this regional epidemic is Rio Arriba County, which showed a staggering drug overdose death rate of 42.5 per 100,000 individuals, averaged per year between 2001 and 2005 (3).

When looking for the cause of this steep rise in deaths, some have identified a dramatic increase of prescription opiates and multiple drug use across the nation. New Mexico data echo this national trend of increased prescription opiates and multidrug overdose rates, demonstrating a

150% growth in rate between 1990 and 2005. However, in addition to these rates, pure heroin overdose deaths have increased even more, with a 160% growth within the same time period.

Some attribute this growth of heroin overdose rates in New Mexico to an increasing purity of black tar heroin, which is a dark, resinous form of Mexican heroin (4) that dominates the drug market of the Western United States. Others attribute this epidemic to a deteriorating environment and to increased drug misuse in rural areas (5), areas where people are less likely to call for help (2). Underlying these trends in New Mexico are the complex dynamics of a rich socio-cultural landscape, mostly centered in the Espanola Valley.

Rio Arriba County is inhabited by a largely impoverished, undereducated, minority population living in small rural communities, juxtaposed to a more vibrant and thriving Los Alamos and Santa Fe. The average annual income in Rio Arriba County during the late 1990s was approximately \$14,000, with some small villages averaging close to only \$5,000, and 20.3% of individuals in the county living below the national poverty line (6). In contrast, Los Alamos, a city boasting one of the highest number of individuals with Ph.D. degrees per capita in the United States (7), had an average annual income that surpassed \$93,000 during that same time period, with only 2.9% of residents living below the poverty line (6). These conditions closely resemble what Phillip Bourgois (8) documented as the social and structural dynamics that set the scene for endemic illicit drug use in New York City and San Francisco during the 1990s (9). Bourgois described the phenomenon of bordering a neighborhood of wealth with a neighborhood of contrasting poverty, in which the dynamics between the two social classes tend to result in the decline of the latter. These once vibrant and healthy communities

often degenerate through what Bourgois identifies as forces of "racism and class segregation," which he describes as "political-economic structural forces, historical legacies, cultural imperatives, and individual actions" (8, p. 318). He goes on to state that "substance abuse is... not the root of the [problem, but] the epiphenomenal expression of deeper, structural dilemmas" (8, p. 319).

Similar to the labor markets of the more affluent parts of New York City and San Francisco, Los Alamos National Laboratory has created a vast demand for low-wage workers (9). With little available employment opportunity in Rio Arriba, residents of Espanola and Chimayo are often forced to commute to the Highlands to fill these jobs. In addition, Los Alamos now sits on land once owned by the ancestors of the residents of Rio Arriba County. Their ancestors were once prominent land owners, ranchers, and farmers, but the current residents are now often confined to vast tracts of trailer parks and low-income housing (9). Bourgois proposed that in these circumstances, not only does monetary incentive drive people into the business of drug trafficking but also the cultural imperative of garnering and reclaiming respect. This may be part of the antagonism of a 100-year-old battle over property rights between the residents of the Espanola Valley and Los Alamos, which has continued to play out in the form of low-wage jobs and income disparity and is now manifested in the use and trade of black tar heroin.

Geographically, the proximity of Espanola Valley to the Interstate 25 (I-25) corridor has also likely played a role in the development of widespread heroin use in the area. This interstate currently runs along the footsteps of the nation's oldest and longest continually used highway: Camino Real (9). Dating as far back as the 17th century, the highway has served

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to transport European settlers, goods, and Latin culture into the United States. Opium, which was one of the goods transported, passed across the border until the early 1900s (1). It wasn't until the 1970s that Mexico began to produce black tar heroin in large quantities. New Mexico has since become a major heroin gateway to the Western United States (1).

In this socio-cultural and economic milieu, a striking and unique social bond has recently formed among the close-knit extended families of the region: they have learned to share and support each other in a tradition of familial and communal heroin use. Manuel Anaya, who was addicted to heroin for 26 years, stated, "We start our addiction getting high with our uncles, then we turn on our own nephews" (3). In a recent article, Angela Garcia (9), an anthropologist originally from Rio Arriba County, stated, "Addiction can become a source of bonding between parents and their children." Mata, a resident of Espanola Valley, stated, "The drug life can be scary. When you got your mom by your side, you feel, I don't know, less afraid, less embarrassed...I think she felt that way too" (9). But this intimacy and tradition of shared heroin experience comes at a price. In an interview, Mary Ramirez, a heroin user of 20 years, described how "over the past 5 years, [she has] buried a husband and brother, both overdose victims," and how in the prior year, her eldest daughter overdosed but survived (9).

This is a tradition that has become a part of the local culture over the past several decades and has turned on the commu-

nity. Local leaders are trying to cope with this growing problem and have turned to unique solutions to involve the community in its own recovery. These solutions range from community rehab centers, focused on bringing families back to the land in agrarian projects (1), to needle exchange programs and the distribution of Narcan to families of users (3). Data show that these interventions, in combination with more mainstream biomedical methods, have made a significant difference in the short-term (10). However, greater community efforts in both support and growth are needed to combat this growing epidemic of overdose deaths.

Northern New Mexico represents a complex and beautiful landscape with an emerging tragedy—that of an insidious cultural tradition that has lost control. In this region, the holy center of the Southwest ironically serves as the epicenter of a major heroin overdose epidemic. It is where abutting neighborhoods of extreme poverty and wealth meet. A major gateway of Hispanic culture for 400 years is now burdened by a cultural epidemic. The socio-cultural and historical context is essential to understanding heroin use in New Mexico. A unique and complex deteriorating socio-cultural environment in the Espanola Valley has enabled heroin use, abuse, and its sequelae to flourish. Local leaders as well as practitioners who treat individuals with substance use problems have recognized the importance of augmenting biomedical methods of recovery with reclaiming a sense of community, reclaiming cultural and spiritual roots, and involving the entire community structure to combat this growing problem.

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D-Cycloserine: A Novel Pharmacological Agent for Treating Anxiety Spectrum Disorders

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In 1927, Pavlov reported that associative learning underlies the development, intervention, and relapse of clinical fears and anxiety. In classical conditioning, an intrinsically nonthreatening stimulus (i.e., conditioned stimulus) evokes a fear response because of an earlier experience in which the conditioned stimulus predicted an aversive event (i.e., unconditioned stimulus). Most psychotherapeutic approaches to anxiety target this fear inducing association. In a typical fear extinction procedure, an individual is continuously exposed to a conditioned stimulus without the resultant unconditioned stimulus, which leads to an extinction of the fear response (1).

Historically, traditional therapies, such as exposure therapy, were thought to exert their effects by extinguishing the fear memory. However, the finding that fear can re-emerge after extinction led to the alternative theory that there is formation of a new overlying or competing memory. The new extinction memory is the conditioned stimulus without the unconditioned stimulus, which competes with the initial fear arousing memory (2). Novel interventions for anxiety disorders are being developed with this recent theory in mind. One such novel pharmacological intervention is D-cycloserine, which has shown promise in treating anxiety disorders. Originally used in humans to treat tuberculosis, D-cycloserine is not associated with significant side effects at clinically effective doses of 50 mg to 500 mg (1). Initially, D-cycloserine had the potential of being an adjuvant for treating negative symptoms of schizophrenia, but results were modest at best (3). The drug has been resurrected as a novel intervention for the treatment of anxiety disorders. D-cycloserine is a partial agonist at the strychnine-insensitive glycine binding site on the N-methyl-D-aspartic-acid (NMDA) receptor (4). Inhibition of the NMDA receptor in the amygdala inhibits fear extinction (5-7).

Thus, NMDA receptor stimulation enhances fear extinction.

Research shows that D-cycloserine has no effect on anxiety when administered chronically to subjects over weeks or months. However, when administered acutely in combination with exposure therapy, pilot studies have suggested that the drug enhances fear extinction. A recent meta-analysis (4) revealed a robust effect in animal studies and a small but significant effect in human studies. The pilot studies conducted with humans examined healthy individuals (8, 9) as well as subjects with specific phobias (10), social phobia (11, 12), panic disorder (13), and obsessive compulsive disorder (OCD) (14-16). The meta-analysis revealed that 50 mg of D-cycloserine was sufficient to enhance extinction learning and that the efficacy of the drug was greatest when administered immediately before or after exposure therapy (4).

Of the 10 pilot human studies included in the meta-analysis (4), three showed no effect of D-cycloserine. Of these, two were conducted among populations that did not meet criteria for clinical anxiety disorders (college students with arachnophobia and healthy individuals) (8, 9). These negative findings may be explained by the ceiling effect, in which mildly phobic individuals or healthy subjects would not require extensive extinction training in order to show improvement. The other negative study (15) examined subjects with OCD. Patients with OCD received twelve weekly sessions of exposure therapy and 250 mg of D-cycloserine 4 hours prior to their sessions. The study was an outlier, compared with the other two studies, examining subjects with OCD in terms of 1) a relatively high dose (250 mg), 2) the significant lag time between the dose and exposure therapy (4 hours), and 3) the duration of treatment (12 weeks). There are several possible explanations for the negative outcome in this study. The dose of the drug may

have been too high, thereby activating the antagonist properties of the NMDA partial agonist. Alternatively, D-cycloserine may have been administered too early, thereby preventing the peak drug effect from coinciding with the learning process. Finally, the high number of exposure procedures may have led to all subjects improving, thereby preventing the authors from being able to appreciate the effect of D-cycloserine (4).

Current treatments for anxiety disorders are suboptimal and thus new approaches are needed. In addition, current pharmacological approaches fail to provide relief for many patients, and many patients do not respond to existing exposure-based treatments. Combining exposure therapy with D-cycloserine has the potential to treat patients who are refractory to existing treatments. The drug might have the capacity to increase or accelerate the efficiency of exposure therapy. The results of the pilot studies are promising. However, larger-scale, randomized, double-blind and placebo-controlled studies will need to be conducted before any definitive conclusions can be drawn.

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