Dr Lieberman is the Thad and Alice Eure Distinguished Professor of Psychiatry, Pharmacology, and Radiology and Director of the Mental Health and Neurosciences Clinical Research Center at the University of North Carolina School of Medicine at Chapel Hill.

A senior clinical editor for Advanced Studies in Medicine (AS/iM) interviewed Dr Lieberman to discuss first episode and acute psychoses, in addition to critical issues in early intervention.

AS/iM: In the management of the more severe patients who present with first-episode psychosis, what would be your first priority?

Dr Lieberman: The first priority is making a thorough and complete diagnostic assessment of the patient, which includes reviewing the patient’s current symptoms and onset of the presenting illness, developmental history, genetic or family history, and obtaining any appropriate diagnostic tests that are important, whether it is laboratory chemistries, an MRI (magnetic resonance image), or any type of neuropsychologic assessment. All of this information is then formulated into a working diagnosis, or at least a list of possible diagnoses, the so-called differential diagnoses. When it is a first-episode patient, there is always going to be a greater index of uncertainty than there is with somebody who is not presenting for the first time but is having a recurrence of illness or is presenting to a new clinician after having been ill for some time. Therefore, with the first-episode patient, you are trying to establish a diagnosis with the lowest amount of uncertainty.

AS/iM: It is difficult to make a differential diagnosis when someone is acutely psychotic. How does the clinician begin to approach making a diagnosis when this is the case?

Dr Lieberman: The first step would be to do a clinical assessment of the patient in terms of behavior and current mental and physical status, and then try to supplement that with information provided by an informant. You would try to get a history of how the presenting illness came about, what the individual is experiencing, and any past relevant information from the patient. However, if this is a psychotic disorder, if the patient is in a florid condition, then the individual may not be that cooperative, forthcoming, insightful, or accurately descriptive of what has been happening and what he or she is currently feeling. In this case, getting information from an informant would be very important. Informants can be family members, significant others, a treating physician such as a psychiatrist or primary medical doctor, or a therapist who can provide additional information to supplement the clinical assessment.

AS/iM: How reliable is information from the patient versus a family member?

Dr Lieberman: The reliability of the patient’s history is correlated with the acuity of the patient’s symptoms. The greater the severity of the symptoms, the less reliable the patient’s information.

AS/iM: What is the next step after the initial assessment?

Dr Lieberman: Immediately after the assessment of a patient and the gathering of information, a differential or a working diagnosis needs to be developed. After it is developed, the next question that needs to be addressed is a treatment plan.
**AS/iM:** How do you manage the patient and what is the immediate plan for treating this patient?

*Dr Lieberman:* This is something that obviously flows from the clinical assessment and diagnosis. If the patient has psychotic symptoms or has symptoms of agitation, then an antipsychotic drug is often the first treatment, or among the first treatments, considered. The atypical antipsychotic drugs are a very good option, if not the preferred option, because they are as effective or more effective compared to the older-generation drugs and they have a lower side-effect profile, particularly under acute treatment circumstances, in that they have little propensity to cause extrapyramidal side effects. Their major side effects (ie, weight gain and metabolic effects) are not problems that occur immediately, but take longer to develop.

**AS/iM:** And, in the long term?

*Dr Lieberman:* In the long term, the atypical antipsychotic drugs are also a good option because they are effective and generally well tolerated. The question becomes, how do you refine the diagnosis to determine whether the longer-term or maintenance treatment needs to be the same as the acute treatment? If you are managing someone for the first time who is floridly psychotic or highly agitated and you are considering schizophrenia, schizoaffective disorder, or bipolar disorder as your diagnosis, there would be a high likelihood that you would want to manage the patient acutely with an antipsychotic drug, probably an atypical antipsychotic drug. If, thereafter, you have a strong belief that the patient is likely bipolar or principally suffers from an affective disorder, you may consider whether that patient should be potentially maintained on a nonantipsychotic drug, such as a mood stabilizer.

**AS/iM:** What are the biggest dangers in these patients: harming themselves or harming others?

*Dr Lieberman:* The biggest danger for patients who are at risk for psychotic or manic behaviors is that they will produce significant disruptions in their lives. People can do things that can cause them to lose their jobs, lose their spouses, lose their friends, squander their resources, or injure themselves or other people through aggressive, reckless, or misguided behavior. They can also, in the course of the acute illness, ingest large amounts of intoxicants or use bad judgment and hurt themselves.

**AS/iM:** What are the demographics on first-episode psychosis?

*Dr Lieberman:* First-episode psychosis generally affects males and females equally. Onset is typically between the ages of 15 and 30 years; between 15 and 35 years maximally. In women, it occurs 2 to 5 years later compared to men. It tends to affect all ethnic and racial groups comparably. First-episode psychosis may occur in a setting of substance abuse.

**AS/iM:** Are there any common comorbidities that would typically present in a first-episode psychosis?

*Dr Lieberman:* The most common comorbidity is substance abuse.

**AS/iM:** Are first episodes common in the geriatric population?

*Dr Lieberman:* Generally not. People with dementia can develop psychosis when their dementia worsens. You can also see people developing a kind of late-life psychosis, which used to be called paraphrenia or late-onset schizophrenia. These late-life psychoses do occur, but to a much less frequent extent. You can see an initial presentation of a psychotic disorder that includes symptoms similar to delusions, hallucinations, or schizophrenia occurring later in life, but it is fairly unusual and runs a somewhat different course, often nondeteriorating, compared to normal adult-onset schizophrenia. You can also see people who had prior histories of depression experiencing possibly a first manic episode later in life, although this is also fairly uncommon. When first episodes do occur in the elderly, they often reflect some underlying new organic pathology, including stroke, inflammation, infection, or other condition. Patients with Huntington's disease may develop new-onset psychosis associated with mania or depression that precedes their dementia.

**AS/iM:** Early intervention in the treatment of psychosis is associated with better outcomes in first-episode schizophrenia. Is this also true of bipolar disorder?

*Dr Lieberman:* It hasn't been as carefully studied in bipolar disorder, but I think there is a reasonable expectation that this would be the case. In fact, one of the influential theories regarding bipolar disorder proposed by Robert Post, MD, is the kindling hypothesis of bipolar disorder, which is similar to what is seen in epilepsy. If the kindling model is accurate, then that
would clearly suggest that the quicker you intervene, the better the response in treatment and outcome.

ASiM: Is there research under way to try and prevent first-episode psychosis or future directions to help make a better differentiation in these patients? Dr Lieberman: Yes, there are methods of early identification and intervention that are being developed (eg, how not to wait for people to come to the emergency room or present in an already florid, acutely symptomatic condition, but to identify these individuals before the illness has progressed into a clinical syndrome or an emergent state). Also, there is an effort to try and develop new and novel treatment approaches for which you can identify people and you can use medications that are more specific to the pathophysiologic process. Therefore, I think we will be seeing compounds that are not just “me too” drugs, but drugs that are novel and will be more pharmacodynamically specific in targeting the substrates of the particular disorders.

ASiM: I know you have done some work with neuroimaging. Is there any relationship here to being able to predict behavior using neuroimaging? Dr Lieberman: I think so, but that is probably in the more distant future in terms of using it as a diagnostic measure or as a measure of treatment response or predicting what treatment should be used. However, I think that laboratory-assisted diagnosis is not too far in the offing and that measures of treatment effects on brain function and brain structure are methods that will be used to help the management of patients.