Melvin Konner

Fernand Khnopff, I Lock My Door upon Myself, *1891*

The Many Faces of Madness

Drawn and tense, his limbs twitching nervously, a man of about twenty-five appears in the emergency clinic of a big city hospital, accompanied by his mother. It is July, the month when hordes of medical students are suddenly transformed into doctors (or so their patients are told), and one of these—call him Dr. Newbody—approaches the pair. "He's gettin' bad again," the woman explains. Dr. Newbody asks some questions, realizes he may have a very crazy patient on his hands, and does what any red-blooded American intern would do: he runs off to find the patient's record, hoping for some clue about how to respond.

As he flips through the files, finding nothing, he hears a commotion behind him and turns to find his patient standing in the center of the crowded waiting room, pointing at people and shouting. "Devil is here! Devil is here everywhere! Coming to get me! Krishnabuddhajesus! Gemme Krishnabuddhajesus! Coming to gemme now-now-now-now!" As the tirade becomes incomprehensible, a couple of nurses converge on the patient. "This boy needs some vitamin H," one of them says, referring to haloperidol, a drug used to bring psychotic breaks under control. Dr. Newbody nods nervously (the nurse knows a lot more than he does) and helps restrain the patient while she injects the drug into his buttock. A few moments later, four security guards pin the young man to the floor while the drug mounts toward his brain and begins to calm him.

Dr. Newbody, feeling courageous but confused, finally finds the hospital record, which reveals that the patient has been through at least six similar episodes in recent years. Since being diagnosed as schizophrenic, at age seventeen, he has been treated with a variety of neuroleptic drugs, including chlorpromazine, the prototype of the class. These have helped stabilize his mind but have recently begun to take a toll on his nervous system, causing occasional muscle convulsions and paralysis. The psychotic breaks, referred to in the record as "acute schizophrenic attacks" or "acute paranoid reactions," have usually occurred when he cut back on his medicine or neglected to take it at all. At least six psychiatrists have offered the same diagnosis over the years —each calling the young man's affliction a classic case of "remitting," or "fluctuating," schizophrenia—and Dr. Newbody, not a psychiatrist himself, sees no reason to question their judgment. So he scribbles a note in the patient's record and prescribes more of the same treatment, presuming that the attending psychiatrist will find the whole matter quite routine.

Not Dr. Baffler, who happens to be on duty that night. Has the patient really had periods of *complete* remission? he asks, perusing the young man's chart. Has he had periods of depression? And what about his family history? Is there any record of depression or alcoholism among his close relatives? Any suicide attempts? Affirmative answers to these questions convince Dr. Baffler this is not schizophrenia at all, but mania. The patient needs to be stabilized, yes, but he should then be hospitalized for a trial on lithium, the accepted treatment for manic-depressive illness and a far less dangerous drug than those the man has been receiving.

What is Dr. Newbody to make of all this? Dr. Baffler could be incompetent, of course. Or he could be European (schizophrenia has always been defined more narrowly on that side of the Atlantic). Or he may have studied under Michael A. Taylor and Richard Abrams, psychiatrists now based at the Chicago Medical School. For the past fifteen years or so, Taylor and Abrams have been chipping away at the broad, American definition of schizophrenia, asserting that it has become an all-purpose diagnosis—an official-sounding term for a lot of disorders, many of which no one really understands.

American psychiatrists tend to think of schizophrenia as the cancer of mental ill-

ness—as an organic disorder, or perhaps a group of closely related ones, whose devastating symptoms may all be vanquished once the underlying cause (presumably genetic) is identified. So it is hardly surprising that Taylor and Abrams's critique, developed in a series of papers during the mid-1970s, remains a source of bitter contention. If they are right, diagnosed schizophrenics do not share a uniform brain disorder; there is no single solution to their problems; and many of those receiving neuroleptic drugs might derive equal benefit from less noxious treatments.

Today's broad categories of psychotic illness can be traced at least to 1899, when the German physician Emil Kraepelin distinguished what had been termed *dementia praecox*, or premature dementia—a thought disorder that leads inevitably to complete incompetence—from manic-depressive psychosis, a *mood* disorder that, however severe, is usually not degenerative. The meticulous classification of somatic illnesses had brought new rigor to surgery and internal medicine during the nineteenth century, and Kraepelin sensed the possibility of making psychiatry equally scientific. Identifying various forms of mental illness would, he hoped, lead to an understanding of their causes and eventually to effective treatments.

Twelve years later, a Swiss psychiatrist named Eugen Bleuler used the general term *schizophrenia*—literally, a psychic splitting—to describe any severe disintegration of thought or disjunction of thought from emotion. Bleuler's schizophrenia, like Kraepelin's dementia praecox, was set apart from manic-depressive illness. But whereas Kraepelin had based the distinction largely on the course of illness (dementia praecox was degenerative, manic depression episodic), Bleuler emphasized the nature of the symptoms. His schizophrenia came in four varieties—paranoid, catatonic, hebephrenic, and simple—but was always "cool," or cognitive, at root. Manic-depressive illness, on the other hand, was affective, its disordered thought emotional, or "warm."

Bleuler's notion of schizophrenia had important implications. Kraepelin had assumed that dementia praecox, with its cruelly predictable course, was a unified disease with a single biological cause. Bleuler's schizophrenia, by contrast, was no more than a syndrome, a set of symptoms that might have any number of causes. It was not even clear that the cause or causes were biological. Indeed, Bleuler allowed that the disorder might be purely psychic in origin.

It is perhaps no coincidence that Bleuler's terminology gained currency just as Sigmund Freud was conceiving his revolutionary psychology. Freud had recently developed a talking cure for the treatment of hysteria, and had gone on to devise a brilliant system for exploring not only the neurotic, or mildly disturbed, personality but also its near cousin, the normal psyche.

Freud, to his credit, was pessimistic about the power of psychoanalysis to alleviate psychoses, the complete breaks with reality that had concerned Kraepelin and Bleuler. But a number of his intellectual descendants—including Carl Jung, Melanie Klein, and Harry Stack Sullivan, who himself spent time in a mental hospital after a psychotic break—believed such treatment was possible. In any event, psychoanalysis became such a powerful force that virtually all mental disorders were discussed in its terms.

Then, during the early 1950s, two French psychiatrists, Jean Delay and Pierre Deniker, discovered the effects of the drug chlorpromazine on psychotic patients, and psychiatry entered a new era. With this treatment, hundreds of thousands of chronically hospitalized patients were able to return to the community and take up lives that, if not always productive, were at least somewhat independent. Just how the drug worked its magic remains unclear, but its very effectiveness suggested that schizophrenic psychosis is biological at root and not simply an exaggerated neurosis to be mastered through self-scrutiny.

Over the past thirty years, dozens of antischizophrenic drugs have been developed, all of which share the effect of blocking the brain's use of the neurotransmitter dopamine (one of the chemicals that transmit signals between cells). And experiments have confirmed the relationship between the drugs' dopamine-suppressing tendencies and their clinical effectiveness—suggesting, if not confirming, that excessive dopamine activity is a factor in schizophrenia. Further evidence of a connection has come from the discovery that sufferers of Parkinson's disease, a condition associated with *insufficient* dopamine production, sometimes develop hallucinations or delusions when receiving the dopamine *enhancer* L-dopa. These observations hardly constitute a causal explanation of schizophrenia (it is unknown, for example, whether the problem involves excessive production of dopamine, an abnormality in the cellular structures that absorb it, or some other defect altogether), but they convinced many American psychiatrists that schizophrenia is a biochemical entity.

Two further developments helped bolster this view. First, during the late 1950s, the German psychiatrist Kurt Schneider developed a clinical formula for determining whether a person is in fact schizophrenic. According to Schneider, anyone experiencing certain "first-rank symptoms"—"voices heard arguing" or "commenting on one's actions," "diffusion of thought," "delusional perception," or any feelings, impulses, or actions that result from the imagined influence of others—could be termed schizophrenic, regardless of his case history, as long as he was not suffering from some known organic brain disorder, such as epilepsy. Schneider's permissive definition was widely adopted in the United States, and the identification of first-rank symptoms was seen as another step toward the goal of making schizophrenia as coherent and real as other medical entities. It also had the effect of discouraging the diagnosis of manic-depressive illness, which, it was felt, could be eliminated from consideration if first-rank symptoms were present.

The second development was the appearance of numerous studies suggesting that schizophrenia, or at least a susceptibility to it, could be inherited. The most elegant of these was reported in a 1968 monograph by Seymour S. Kety, a psychiatrist at the National Institute of Mental Health (and later with Harvard University and McLean Hospital, in Boston). Working out of Denmark, a country noted for its meticulous epidemiological records, Kety identified a group of adult psychotics—schizophrenics, under the broad, Schneiderian definition—who had been adopted during infancy and raised away from their kin. He then surveyed the subjects' relatives, both biological and adoptive, and found that the biological relatives suffered higher rates of schizophrenia than did the adoptive relatives or the general population. In short, schizophrenia seemed to run in families, even dispersed families.

These ideas never caught on in Europe to the extent that they did in the United States. European psychiatrists had no quarrel with the notion that mental illness might be heritable, but they still thought of schizophrenia as a quite rare disease, for they had never given up Kraepelin's system of classification for Bleuler's. They tended to restrict the term *schizophrenia* to chronic thought disorders, and to diagnose acute, nondegenerative psychoses as manic-depressive illness. And as diagnosis differed, so did therapy. British and Continental psychiatrists often gave their patients lithium, which, despite possible adverse side effects, does not cause tardive dyskinesia, the severe muscle disorder associated with dopamine blockers.

The stage was thus set for the publication of Taylor and Abrams's extraordinary series of papers. Beginning in 1973, they conducted a number of groundbreaking studies and reviewed the

research of others in relation to one hypothesis: that American psychiatrists overdiagnose schizophrenia by a large margin, and underdiagnose manic-depressive illness with comparable frequency. In fact, when Taylor and Abrams reexamined patients previously diagnosed as schizophrenic on the basis of first-rank symptoms, taking into account family history, course of illness, and response to different drugs—all mainstays of diagnosis in other medical specialties—they found that many (from twenty to fifty percent in different studies) looked like classic cases of manic-depressive illness and responded well to lithium treatment.

By 1978, Taylor and Abrams were pointing out with some urgency that they were talking about more than a diagnostic label. "Patients who receive a diagnosis of schizophrenia when in fact they have another condition (e.g., affective disorder)," they wrote in the *American Journal of Psychiatry*, "may be subjected erroneously and unnecessarily to chronic administration of neuroleptic drugs, with their high risk of permanent neurologic damage" and may be "deprived of appropriate treatment with lithium."

Other research psychiatrists—notably Harrison G. Pope and Joseph F. Lipinski, who were based, like Seymour Kety, at Harvard's McLean Hospital—had by now come to share Taylor and Abrams's view. In a paper published in the *Archives of General Psychiatry*, in 1978, Pope and Lipinski seconded the opinion that the tendency to diagnose severe mental disorders as schizophrenia could be exposing "large numbers of patients to increased social stigma, inferior treatment, and potentially irreversible neurological damage." They went on to argue in other papers that schizo-affective disorder—the term that American psychiatrists had been applying to patients who qualified as schizophrenics on the basis of first-rank symptoms but who also showed signs of manic-depressive illness—was essentially meaningless. "Since course, family history, and treatment response do not distinguish schizoaffective disorder... from manic disorder," they wrote in 1980, "there would seem to be no adequate reason on clinical grounds to make the former diagnosis. Such a diagnosis can only lead to confusion."

Eventually, these arguments persuaded the American Psychiatric Association to narrow its definition of schizophrenia. The new designation, adopted in 1980, does not automatically exclude all disorders with an affective component (as Taylor and Abrams would), but it restricts the diagnosis to chronic, unremitting illnesses and excludes acute, or fluctuating, ones.

Having made these gains in the debate over what constitutes schizophrenia, the revisionists went on to challenge the contention that it runs in families. In a study published in 1982, Pope and Lipinski, as well as others, reviewed the family histories of the thirty-nine definite schizophrenics admitted to their research ward between 1974 and 1977—patients who suffered chronic, nonaffective psychoses and thus could not possibly be manic-depressives—and found not a single case of schizophrenia among two hundred of the patients' close relatives. And the next year, Abrams and Taylor reported similar results, concluding that "if familial transmission of narrowly defined schizophrenia occurs, it is either limited to a subgroup yet to be defined" or simply "weak."

Needless to say, these claims were met with criticism and counterevidence. In June of 1983, Kety mounted a spirited defense of his original study, arguing in the *American Journal of Psychiatry* that, by excluding disorders with affective symptoms from the spectrum of those they were willing to call schizophrenia, his critics were diluting the trend he had identified. He rejected the notion that so-called schizo-affective patients are really manics, saying many are in fact clinically indistinguishable from definite schizophrenics, and he stood by his finding that the biological relatives of schizophrenics are at significantly higher risk than the rest of the population. If no concentration of mental illness was evident in the small, restrictive groups the newcomers had studied, he said, one could draw two alternative conclusions: that schizophrenia is indeed "a rare disorder with no evidence for familial or genetic transmission"—or that the researchers themselves "arbitrarily narrowed the definition of schizophrenia to the point where it is no longer particularly valid or useful."

Today, the debate over Michael Taylor's original question—"Is schizophrenia a syndrome representing a group of illnesses... or is it a specific disease with a defined onset, clinical picture, and natural history?"—continues unabated, each camp accusing the other of ignoring sound evidence in order to defend a prejudice. Some studies—including one led by Kenneth Kendler, of the Medical College of Virginia; another by Peter McGuffin, now at the University of Wales, in Cardiff; and a third by Samuel Guze, of Washington University, in Saint Louis—have continued to find evidence of a genetic basis for schizophrenia, suggesting that it is in fact a disease and not just a ragbag of symptoms. But other recent findings—the demonstration, for instance, that some forms of manic-depressive illness are associated with a gene on chromosome 11, while other forms of what we consider the *same disease* are associated with a gene on the X chromosome—suggest that even if schizophrenia is genetic at root, it may not be a single disease.

If schizophrenia is eventually found to comprise a number of identifiable illnesses, the current debate over diagnostic labels may seem rather silly in retrospect. It has had important benefits, of course. As the definition of schizophrenia has narrowed, American psychiatric practice has shifted markedly toward the European model, with more diagnosis of manic-depressive illness and less of schizophrenia. As a result, it is becoming the rule among psychiatrists recently trained in this country that every patient with a fluctuating psychosis, with some features of manic-depressive illness, or with a family history of affective disorders deserves a trial on lithium or some other mood-altering drug. Only if these prove inadequate should the patient resort exclusively to dopamine blockers, which, however appropriately used, still pose a grave risk of neurological damage.

With that resolved, though, there is little to be gained from further debate over the merits of a diagnostic label. We may discover that what we now call schizophrenia and schizo-affective disorder are in fact seven different genetic defects, each producing a biochemically different mental illness, and that some forms of these disorders have no genetic component at all. How all these afflictions are grouped—whether we call four of them schizophrenias and three manias, or vice versa—will not matter at all.

If schizophrenia is the cancer of mental illness, then it may, like cancer, be protean. Cancers share a few general attributes—they all cause cells to grow uncontrollably, and many of them respond to the same crudely effective treatments—but beyond that they are extremely varied. It is only by bearing down on individual strains of the disease that researchers have begun to understand their different causes—recognizing, for example, that retinoblastoma is likely genetic in origin; that the vast majority of lung cancers result from cigarette smoking; that cervical cancer may stem from the papilloma virus, which is also responsible for genital warts. Fortunately for the science of oncology, few ideological voices have been raised to complicate the search for such truths, though they surely could have been. Perhaps psychiatry will have come of age when its practitioners achieve a similar consensus on what's worth arguing about. ●

MELVIN KONNER's new book, BECOMING A DOCTOR: A JOURNEY OF INITIATION IN MEDICAL SCHOOL, *will be published by Viking in August.*