MODULE 1: CLINICAL PRESENTATION

HISTORY OF THE CONCEPT OF SCHIZOPHRENIA
CURRENT DEFINITIONS AND CRITERIA (ICD AND DSM)
DIFFERENTIAL DIAGNOSIS
LABORATORY WORK-UP
PSYCHOSOCIAL EVALUATION
COURSE AND OUTCOME
CROSS-CULTURAL ISSUES

This module is designed to provide information about the clinical presentation of schizophrenia to a broad range of clinicians: medical students, residents in psychiatric training, primary care physicians, psychiatrists in clinical practice, clinicians in academic settings, and investigators who work in other fields but wish to learn about schizophrenia. Clinicians who work at the most advanced level--i.e., investigators in academic medical centers who work with schizophrenia on a daily basis--will be familiar with most of the material in this module.

HISTORY AND CONCEPTUAL ISSUES

The Essence of Schizophrenia

Schizophrenia is typically a catastrophic illness that begins in adolescence or early adulthood. Although severe psychotic disorders have been recognized for centuries, as evidenced by descriptions in medical writings and literary portrayals, the classification of psychotic disorders into specific forms such as manic-depressive illness or schizophrenia only occurred approximately one hundred years ago.

Because the symptoms of schizophrenia often produce severe incapacity, the illness was originally called "dementia praecox" by Emil Kraepelin. Schizophrenia was initially delineated in the late nineteenth century by him and a team of psychiatrists who worked with him, which also included Alois Alzheimer. Schizophrenia, or dementia praecox, was originally distinguished from dementia in the elderly (later named Alzheimer's disease) on the basis of age of onset. It was also distinguished from manic-depressive illness on the basis of course, with dementia praecox tending to be more chronic and persistent while manic-depressive illness was intermittent and prone to spontaneous remission. A few years after Kraepelin's original definition, Eugen Bleuler suggested renaming this disorder "schizophrenia," which means "fragmented mind."

Schizophrenia is characterized by a mixture of signs and symptoms, no one of which is necessarily present. In this sense, it differs from many other psychiatric disorders, which are typically defined by a single prominent feature. Depression, for example, is characterized by dysphoric mood, mania by elevated mood, and panic disorder by the presence of panic attacks. The absence of a single defining feature for schizophrenia sometimes makes this disease difficult for beginning students to conceptualize.

Symptoms of Schizophrenia

The disorder is essentially defined by the presence of several from a group of characteristic symptoms, accompanied by a significant deterioration in functioning for a relatively sustained period of time (ranging from one to six months, depending on the definition that is being used). Much of the time, the characteristic symptoms are present for much longer, and often a few symptoms persist for the remainder of the person's life. The combination of significant incapacity, onset early in life, and chronicity of illness makes schizophrenia a particularly tragic disorder in many people who suffer from it. Further, it is quite common, occurring in between .5 and 1 percent of the population. This combination of being common, severe, and pervasive in its effects makes schizophrenia "the cancer of psychiatry."

It is sometimes helpful to think of schizophrenia as a disease that affects multiple systems of emotion, personality, and cognition. In this sense, it is similar to other multi-system disorders in medicine, such as systemic lupus erythematous, multiple sclerosis, or syphilis.

In order to make this complex disorder somewhat simpler and easier to understand, clinicians sometimes divide the symptoms of schizophrenia into two broad groups: positive and negative. The concept of positive and negative symptoms was originally proposed by Hughlings Jackson, who proposed that the symptoms of psychosis could be explained by thinking of brain organization as evolutionary and hierarchical:

> *Disease is said to "cause the symptoms of insanity." I submit that disease only produces negative mental symptoms answering to the dissolution, and that all elaborate positive mental symptoms (illusions, hallucinations, delusions, and extravagant conduct) are the outcome of activity of nervous elements untouched by any pathological process; that they arise during activity on the lower level of evolution remaining.*

In current usage, positive symptoms include delusions, hallucinations, disorganized speech, and disorganized and bizarre behavior. These symptoms represent distortions or exaggerations of normal cognitive or emotional functions. Hallucinations are abnormalities in perception (i.e., hearing voices without a stimulus); delusions are a distortion in inferential thinking (i.e., misinterpreting information, often in a way that suggests danger or harm); disorganized speech is a disruption in language and communication, probably reflecting an underlying disorganization in thinking; disorganized behavior is a disruption in motoric or behavioral monitoring and control. These positive symptoms are sometimes further subdivided into two groups. Delusions and hallucinations are classified as representing a psychotic dimension, while disorganized or bizarre speech and behavior are thought of as representing a disorganization dimension.

According to most current definitions, some positive symptoms are always present in schizophrenia, but the pattern may vary. One particular patient may be especially psychotic and experience hearing voices and feeling persecuted. Another patient may be more disorganized, speaking in an incoherent manner, and displaying abnormalities in behavior such as agitation, wearing strange clothing, or making clearly inappropriate sexual overtures.

The negative symptoms of schizophrenia reflect a loss or diminution of functions that are normally present. Negative symptoms include alogia (marked poverty of speech, or speech that is empty of content), affective flattening (diminution in the ability to display expression of emotion), anhedonia (inability to experience pleasure, loss of interest in social interaction), and avolition (inability to initiate or persist in goal-directed behavior.) While the positive symptoms of schizophrenia are often colorful and draw attention to the patient's illness, the negative symptoms tend to impair the person's ability to function in normal daily life. These symptoms tend to prevent patients with schizophrenia from having normal family relationships, attending school, holding a job, or forming friendships and intimate relationships.

In addition to these "classic" symptoms involving psychotic, disorganized, and negative dimensions, a variety of other symptoms are also frequently noted. These include impairment in attention, lack of insight, and catatonic motor behavior. Further, many of the more general symptoms, such as delusions, may assume a broad range of specific types. Delusions, for example, may involve various themes, such as persecution, jealousy, grandiosity, and religiosity. Hallucinations may affect many different modalities, including auditory, visual, tactile, or olfactory. Auditory hallucinations are, however, by far the most common type.

Historical Concepts of Schizophrenia

Among the various disorders that psychiatrists treat, schizophrenia has a particularly long history. Kraepelin's definition of this disorder, which crystallized its conceptualization, has been used for approximately 100 years. Inevitably, a disorder that is as inherently complex as schizophrenia and that has such a long history will be subject to variation in conceptualization across time and space, as different aspects of the disorder are emphasized by different clinicians. While many great clinicians have made important contributions to our thinking about the nature of schizophrenia, three should be highlighted, since each has contributed a different and important component. These three figures are Kraepelin, Bleuler, and Schneider. Each has enriched the concept of schizophrenia by stressing a slightly different aspect. Examining their different points of view helps illustrate why the concept of schizophrenia is so hard to "get one's mind around" and to summarize in a simple way.

Emil Kraepelin: Course and Outcome

Kraepelin's conceptualization stressed the aspects of severity and chronicity. The syndrome that he defined, dementia praecox, tended to begin relatively early in life ("praecox") and to produce a pervasive and persistent impairment in many different aspects of cognitive and behavioral function ("dementia"). While Kraepelin repeatedly stressed the diversity of signs and symptoms occurring in dementia praecox, and suggested that abnormalities in volition and affect were especially important, he found a chronic course and a poor outcome to be the characteristic defining features. His concept evolved over time, however, as he received feedback from other experts and his own ongoing clinical experience. He was a devoted empiricist with two years of training in Wundt's laboratory in Leipzig early in his career. Over his long career he was able to follow up a large sample of patients, and he observed that 12.5% of these recovered. Consequently, he later agreed with Bleuler that some patients with dementia praecox could recover.

Eugen Bleuler: Fundamental Symptoms and the Group of Schizophrenias

Kraepelin's original formulation was rapidly complemented by the work of Bleuler, who suggested that the term "dementia praecox" should be superseded by "the group of schizophrenias." Bleuler emphasized a different aspect of this large syndrome. While Kraepelin thought about course and outcome, Bleuler pondered the nature of the characteristic symptoms. He was particularly interested in trying to identify which among the multiplicity of symptoms could be considered to be most basic or fundamental.

For Bleuler, the most important symptom was a fragmentation in the formulation and expression of thought, which he interpreted in the light of the associational psychology prevailing at the time and referred to as "loosening of associations." He renamed the disorder "schizophrenia" to emphasize the fragmenting of associations as the fundamental feature of this disorder.

Bleuler also identified a variety of other signs and symptoms that he regarded as fundamental. Since all these symptoms begin with the letter "A," they have been referred to as the "Bleulerian four A's." In fact, however, Bleuler identified six different symptoms as fundamental: associations (i.e., dissociations in thought processes), ambivalence, autism, affective blunting, avolition, and attentional impairment.

In trying to determine which symptoms were most important or characteristic, Bleuler tended to use two different criteria. One involved trying to identify symptoms that were relatively specific to schizophrenia and that did not occur in other disorders. For example, he believed that the dissociative thought processes tended to occur only in the group of schizophrenias. He contrasted this abnormality in thinking with the psychotic symptoms, such as delusions and hallucinations, that also occur in other disorders, including manic-depressive illness, delirium, and even dementia. As Bleuler himself stated:

> *certain symptoms of schizophrenia are present in every case and at every period of the illness even though, as with every other disease symptom, they must have attained a certain degree of intensity before they can be recognized with any certainty. . . .for example, the peculiar association disturbance is always present, but not each and every aspect of it. . . .besides these specific permanent or fundamental symptoms, we can find a host of other, more accessory manifestations such as delusions, hallucinations, or catatonic symptoms. . . .as far as we know, the fundamental symptoms are characteristic of schizophrenia, while the accessory symptoms may also appear in other types of illness.*

Thus Bleuler believed not only that fundamental symptoms were specific to schizophrenia, but he also believed that they tended to persist rather than to wax and wane, and that they therefore reflected a more fundamental or basic process.

The Bleulerian concept of schizophrenia has dominated the conceptualization of schizophrenia throughout the world for much of the past century. Bleuler's view of the disorder leads to a somewhat broader construct than that of Kraepelin, since it does not require the presence of psychotic symptoms and places less emphasis on chronicity and deterioration. Only one of the positive symptoms, formal thought disorder, or disorganized speech and thinking, is among Bleuler's fundamental symptoms. From the Bleulerian perspective, negative symptoms are the core features. Another important component of Bleuler's thinking about schizophrenia was his emphasis on the "the group of schizophrenias." Within the context of his broad conceptualization, Bleuler believed that "the schizophrenias" were a heterogeneous group of disorders that could be produced by a variety of different factors. He was not, of course, the first to point to the heterogeneity of schizophrenia. In his textbook on dementia praecox, Kraepelin also observed:

> *The presentation of clinical details in the large domain of dementia praecox meets with considerable difficulties because a delimitation of the different clinical pictures can only be accomplished artificially. There is certainly a whole series of phases which frequently return, but between them there are numerous transitions so that in spite of all efforts it appears impossible at present to delimit them sharply and to assign each case without objection to a definite form.*

An Emphasis on Psychosis: The Schneiderian System

The views of a third European psychiatrist, Kurt Schneider, have also been very influential in conceptualizations of schizophrenia. Like Bleuler, Schneider was interested in identifying pathognomonic symptoms. He developed a description of a set of "First Rank Symptoms" (FRS), which he believed to be specific to schizophrenia and diagnostic of it. Schneiderian First Rank Symptoms have been very influential because they were included in the first widely used structured interview, the Present State Examination (PSE), which was used in the World Health Organization (WHO)-sponsored International Pilot Study of Schizophrenia (IPSS). As used in this context, FRS have perhaps been given a significance beyond his original intent, since Schneider himself was deeply interested in understanding the personal experience of the individual patient. Within the context of structured diagnostic interviews and the WHO studies, they are treated as highly specific indicators of the diagnosis of schizophrenia.

Schneiderian FRS are specific types of delusions and hallucinations, such as thought insertion, thought broadcasting, delusions of control, or voices commenting. They tend to be tied together by the common thread that the patients perceive themselves as losing the autonomy of their thoughts, feelings, and bodies. This "loss of ego-boundary" hypothesis was not, however, the basis for Schneider's claim that these symptoms carried a major diagnostic weight for schizophrenia. Rather, Schneider's emphasis on these symptoms was derived from clinical observations and an underlying phenomenological perspective closely related to the thinking of Karl Jaspers.

Schneiderian FRS have enjoyed their popularity for several reasons. They tend to be all or none phenomena. Unlike the Bleulerian four A's (or six A's), which seem to be on a continuum with normality, Schneiderian delusions and hallucinations are discrete phenomena that are clearly pathological. In fact, they are sometimes referred to as "bizarre." Because of this discontinuity from normality, investigators have believed that Schneiderian FRS could be defined much more reliably than could the Bleulerian four A's. Thus, these symptoms have enjoyed substantial use in recent criterion-based diagnostic systems, which attempt to identify symptoms that are highly reliable (i.e., likely to produce similar results during two independent observations). Therefore, they have been introduced into widely used structured interviews, such as the Present State Examination or the Schedule for Affective Disorders and Schizophrenia (SADS), and they also play a prominent role in the criteria for schizophrenia in the International Classification of Disease (ICD).

These three ways of thinking about schizophrenia - the Kraepelinian, the Bleulerian, and the Schneiderian - co-exist in contemporary thinking about the nature of schizophrenia. Individual clinicians tend to vary in the value and emphasis that they place on these three perspectives, sometimes leading to clinical debates as to whether a patient "really has schizophrenia." Some clinicians base their diagnosis primarily on a Kraepelinian emphasis on chronicity and poor outcome, while others stress Bleulerian negative symptoms and thought disorder, and yet others insist on the presence of florid and prominent psychotic symptoms. These differing perspectives reflect a very real debate about the basic essence of schizophrenia. This debate is not likely to reach closure until the disorder can be defined in terms of its pathophysiology and etiology.

Some Fundamental Questions about the Nature of Schizophrenia

The competing perspectives on schizophrenia reflect four main issues:

1) What are the characteristic symptoms?
2) What are the boundaries of the concept?
3) Is the disorder a single illness or multiple disorders?
4) If it is multiple disorders, what are the best methods for subdividing or subtyping it?

Characteristic Symptoms

As outlined above, several different perspectives compete with one another. The Schneiderian point of view (as distilled through structured interviews such as the PSE) emphasizes that the characteristic symptoms are positive; they typically involve the psychotic dimension, which is comprised of delusions and hallucinations, as manifested in their most extreme or bizarre form. A Schneiderian dogmatic would argue that these symptoms occur **only** in schizophrenia and are never seen in other disorders with psychotic features, such as manic-depressive illness or an organic delirium. During the past several decades, a number of investigations have found enough exceptions to the "Schneiderian rule" to call this dogma into question.

The Bleulerian perspective would emphasize the importance of fragmentation of thinking and personality. Among the various Bleulerian symptoms, "formal thought disorder" - a disorganization in the structure and presentation of thinking and speech rather than in its content - has been considered to be most important. Formal thought disorder is manifested through various forms of disorganized speech, such as loosening of associations or derailments, where ideas slip off the track and the patient's line of reasoning seems to move continually from one topic to another without any (or minimally) coherent links. When thought disorder is very severe, it also may manifest itself as incoherence, where the speech is so disorganized that it is jumbled and sounds like "word salad." The following quotation illustrates this phenomenon:

> Interviewer: *What do you think about energy conservation?*
> Patient: *They 're destroying too many cattle and oil just to make soap. If we need soap when you can jump into a pool of water, and then when you go to buy your gasoline, my folks always thought they should, get pop, but the best thing to get is motor oil, and money. May, may as well go there and, trade in some, pop caps and, uh, tires, and tractors to group, car garages, so they can pull cars away from wrecks, is what I believed in.*

The following Danish example of thought disorder, in which a young man speaks of his fiancee, illustrates components of ambivalence and illogicality:

> *Her beautiful-ugliness attracts my ability for repulsion. That is why I cannot live with her any longer.*

Bleuler also stressed the importance of other symptoms that reflected a disorganization in the structure of thinking or in the ability to relate realistically to the external world: ambivalence, an autistic retreat into fantasy, avolition or severe loss of drive, affective blunting, and attentional impairment.

A third point of view, which is the most dominant one in current thinking, is that no single symptom or group of symptoms can be identified as specific to schizophrenia or characteristic of it. Just as psychotic

symptoms occur in mania or delirium, so too may many of the Bleulerian or negative symptoms occur in other disorders. Disorganization of thinking and speech may be quite prominent in mania, and the negative symptoms tend to occur in depression, although in that context they may seem qualitatively different. The most widely-held current concept tends to stress that schizophrenia should be conceptualized as a multi-system disease that has pervasive manifestations in many aspects of thinking, emotion, and interpersonal relationships.

The Boundaries of the Concept

The boundaries of the concept of schizophrenia have expanded and contracted over time and space. Kraepelin's original construct was relatively narrow, emphasizing an early age of onset, progressive deterioration, and a mixture of relatively severe positive and negative symptoms (although he did not use that specific terminology). In an ongoing dialogue that he maintained with Bleuler, he eventually broadened his concept somewhat and agreed that certain cases might show a later onset and a marked improvement or even full recovery. Bleuler, who did not stress deterioration, nevertheless believed that patients with true schizophrenia were unlikely to have a full recovery, referred to as *restitutio ad integrum*. Kraepelin summed up the problems well in one of the later editions of his textbook of psychiatry:

> *Whether dementia praecox in the extent here delimited represents* one uniform disease, *cannot be decided at present with certainty....it is certainly possible that its borders are drawn at present in many directions too narrow, in others perhaps too wide.*

The boundary of the concept of schizophrenia is unclear on two different frontiers. On the one hand, schizophrenia shares a border with the affective disorders. In this instance, the concept of schizoaffective disorder has served as a buffer zone since the condition was originally defined by Kasanin in 1933. The definition of schizoaffective disorder has varied over time. Some definitions stress the simultaneous concurrence of affective and schizophrenic symptoms. Since many patients with classic core schizophrenia develop depressive symptoms, particularly when they acquire insight about the nature of their illness, the concept of schizoaffective disorder can itself be quite broad. A mixture of affective and psychotic symptoms has been recognized for many years and by many skilled clinicians and researchers as a "good prognosis" form of schizophrenia. Sometimes schizoaffective disorder is viewed as synonymous with good prognosis schizophrenia. Other good prognostic indicators include late or acute onset, family history of affective disorder, good premorbid functioning, intact emotional responsiveness, and the presence of insight.

One factor that has impinged on the concept of schizoaffective disorder has been availability of lithium and the effectiveness of antidepressant medications. As lithium became increasingly available for the treatment of psychotic syndromes, clinicians observed that many patients who had been called schizophrenic or even schizoaffective seemed to do well on lithium alone. This led to a conceptual revision, with a suggestion that such patients might not have schizophrenia at all, but might have a psychotic form of affective illness. While response to treatment cannot be used as a means of identifying specific disease categories (i.e., many different specific diseases respond to steroids or to aspirin), some clinicians believe that a highly effective response to lithium alone makes a diagnosis of schizophrenia less likely.

The second major boundary territory for schizophrenia is the group of conditions that are characterized by oddities in behavior, poor social functioning, and a chronic course, in the absence of florid positive or psychotic features. In the pre-neuroleptic era, mild nonpsychotic forms of schizophrenia were gradually added to the concept with a variety of different names: latent, pseudoneurotic, borderline, and simple schizophrenia. Current ICD-10 nomenclature recognizes these disorders as schizotypal disorder and simple schizophrenia, while DSM-IV classifies them as schizotypal personality disorder and simple deteriorative disorder (which appears in an appendix but not in the diagnostic manual).

The broadening of the concept of schizophrenia to include these nonpsychotic forms was consistent with a Bleulerian perspective. It was frequently observed that these patients did not respond particularly well to psychotherapy, leading clinicians to decide that they had some form of schizophrenia rather than a neurosis. When neuroleptic medications became available, however, some of these patients with mild syndromes did not show striking improvement either. As the risk of tardive dyskinesia became more apparent, pressure mounted to narrow the concept of schizophrenia to prevent the excessive or inappropriate use of neuroleptics. Another source of concern leading to a narrowing of the concept in recent years, and to the requirement of prominent positive or psychotic symptoms, was the practice of using the diagnosis of schizophrenia to justify political abuses. In this context, requiring a stringent set of relatively narrow criteria seemed appropriate to many clinicians.

Single Illness or Multiple Disorders?

Given the breadth and diversity of the symptoms that characterize schizophrenia, it is only natural to wonder whether this disorder is truly homogenous or whether it represents a related group of different disorders.

Again Kraepelin, who was an astute clinician, was one of the earliest to raise this issue, in the quotation cited above. Bleuler also raised the issue when he subtitled his book "the group of schizophrenias."

This issue can ultimately be resolved only when the pathophysiology of schizophrenia is identified. Conventionally, discrete disorders in medicine are identified on the basis of their pathophysiology. Some disorders, such as the dementias, share a common clinical presentation, at least at the superficial level, but are subdivided into specific types on the basis of pathophysiology. For example, we distinguish between Alzheimer's disease and multi-infarct dementia based on the presence of plaques and tangles in the former and multiple infarcts secondary to stroke in the latter. As the example of the dementias illustrates however, identifying discrete disease entities tends to become increasingly complex as our knowledge advances. Studies of the neuropathology of Alzheimer's disease are currently beginning to suggest that the distinction between it and dementias secondary to other neuropathological lesions may not be precise; for example, the Lewy bodies considered to be characteristic of Parkinson's disease have been frequently noted in Alzheimer's disease, suggesting that these two types of dementia may in fact overlap at the neural level. On the other hand, investigators are also considering the possibility that Alzheimer's disease should be further subdivided, since patients appear to fall into several different natural groups with differing ages of onset, course, and severity.

Furthermore, our understanding of "pathophysiology" grows steadily more sophisticated as it progresses from the syndromal to the cellular to the molecular levels. Diabetes melletis, once seen as a single disorder, is divided into juvenile and adult onset forms, each of which has different cellular manifestations as well as a different onset and course. Growing knowledge concerning the molecular basis of diabetes suggests that the disorder will have further subdivisions. For example, even a classic genetically-caused biochemical and metabolic disorder such as phenylketonuria has been found to have two different types, based on two different abnormalities in DNA sequencing.

Compared to these disorders, our understanding of the homogeneity or heterogeneity of schizophrenia remains exceedingly primitive. Several different competing models have been proposed in order to resolve this issue. One model, sometimes referred to as the "single disease entity" model, suggests that schizophrenia is a single disorder. According to this point of view, schizophrenia is similar to other illnesses that have multiple and diverse manifestations that are due to a single cause. The most striking example of a single disease entity with multiple manifestations is syphilis. Multiple sclerosis or systemic lupus erythematosis may be other examples.

A second model that has been proposed is the "multiple disease entities" model. This model suggests that schizophrenia is similar to mental retardation. That is, like mental retardation the clinical heterogeneity of schizophrenia is based on heterogeneity at the etiological level, and the illness is therefore a related group of illnesses that represent a final common pathway leading to a syndrome that we refer to as schizophrenia, but which should more properly be called the "group of schizophrenias." Many forms are likely to be multifactorial, combining both genetic (and probably polygenetic) and a broad array of environmental factors. Purely genetic forms may also exist, analogous to phenylketonuria, as well as purely environmental forms, analogous to fetal alcohol syndrome or virally induced illnesses. According to this model, the varying clinical manifestations reflect the time of injury or insult within the developmental and maturational process, as well as the various parts of the central nervous system that are affected by the process.

A third model, sometimes referred to as the "multiple domains of psychopathology" model, assumes that the various symptoms of schizophrenia represent discrete pathophysiological processes leading to different specific symptom domains. Current applications of this approach often divide the symptoms of schizophrenia into three broad domains or dimensions. Positive symptoms are subdivided into two dimensions; one is composed of psychotic symptoms such as delusions and hallucinations, while a second reflects disorganization and is composed of positive thought disorder (disorganized speech), bizarre and disorganized behavior, and inappropriate affect. Negative symptoms form the third dimension. According to this model, each of these dimensions is due to a different disease process. For example, disease process A leads to the first dimension, disease process "B" leads to the second dimension, and so on. A given patient may have one or more of the different disease processes, thereby producing the clinical heterogeneity that is observed in schizophrenia.

Methods for Subdividing or Subtyping

Each of these three models attempts to explore the heterogeneity of schizophrenia by beginning with the empirically-observed clinical presentation of the illness, sometimes referred to as its "phenomenology." Strategies that begin with the clinical presentation are sometimes said to begin by exploring the "phenomenotype." The phenomenotype is composed of a variety of clinical descriptors, including types of symptoms, severity of symptoms, longitudinal course, mode of onset, cognitive function, psychosocial adaptation, and response to treatment.

Studying the "biotype," which is composed of a variety of pathophysiological measures, has also been proposed as an alternate approach to teasing apart the possible heterogeneity of schizophrenia. According to this strategy, any one of a number of biological measures is used in order to divide patients designated as having "schizophrenia" into subgroups. Measures that are used to assess the biotype include genetic loading, exposure to birth and pregnancy complications, exposure to viral risk factors such as influenza epidemics, and various

neurophysiological, neurochemical, or neuroimaging measures. Examples include increased saccades measured by eye tracking, increased D2 receptor density measured in postmortem tissue or with Positron Emission Tomography (PET), or decreased size of the hippocampus measured with Magnetic Resonance Imaging (MRI) or postmortem tissue.

At present several clinical systems are used for subtyping schizophrenia. Perhaps the most widely used involves the traditional subtypes originally described by Kraepelin and Bleuler. These emphasize dividing patients based on their prominent symptoms, which may provide useful clinical information about course and outcome. The traditional subtypes include the paranoid, disorganized or hebephrenic, catatonic, and undifferentiated forms. These traditional subtypes are used in the standard diagnostic systems, DSM-IV and ICD-10 (See criteria in section 2 below). These traditional subtypes have been validated largely by their ability to predict social and occupational functioning, prognosis, and response to treatment. The paranoid type tends to have the best social and occupational functioning and best prognosis, while the hebephrenic (disorganized) type has the worst. The catatonic type is rare in industrialized or Western European countries, but much more common in non-industrialized, Asian, or African countries. It may have a relatively acute onset and in some forms has a relatively good prognosis as well.

An alternate approach to subtyping has also been proposed, which emphasizes the positive and negative dimensions of schizophrenia. This approach to subtyping has blended a description of course and prognosis with speculations about underlying pathophysiological mechanisms. According to this approach, patients may be classified as positive, negative, or mixed, depending on which features are most prominent. Patients with prominent positive symptoms may have a more acute onset, a better premorbid adjustment, more intact cognitive functioning, better response to treatment, and a better outcome; it has been hypothesized that this form of schizophrenia is primarily due to a biochemical mechanism, such as overactivity in the dopamine system. At the other extreme, patients with prominent negative symptoms are more likely to have poor premorbid functioning, an insidious onset, cognitive impairment, and a worse outcome; this set of features has been hypothesized to be due to abnormalities in brain structure rather than brain chemistry, which accounts for the irreversibility or refractoriness of the syndrome. The majority of patients have a mixture of positive and negative symptoms, however, making the application of this approach somewhat difficult. Further, it is now clear that structural abnormalities may also be present in patients with prominent positive symptoms. Thus, both types of symptoms may be explained by the broad range of biological processes (e.g., viral, genetic, toxic) that affect neural development, making a dichotomous etiology highly unlikely. Similar problems tend to occur with the traditional subtypes as well. As a consequence, identifying subtypes of schizophrenia remains a vexing clinical and research problem.

CRITERIA FOR MAKING THE DIAGNOSIS OF SCHIZOPHRENIA AND OTHER SPECTRUM CONDITIONS

Two systems are widely used in order to make the diagnosis of schizophrenia and other related spectrum conditions.

The first is the International Classification of Disease, which is currently in its 10th edition (ICD-10). ICD-10 is the standard nomenclature that is used throughout the world. As such, it must be flexible and meet the needs and conceptualizations of a wide range of clinicians. Historically, the ICD has comprised a list of conditions that could be used for international epidemiological studies and that would facilitate coding. In response to the increasing emphasis on providing detailed descriptions of disorders and using criteria to enhance reliability, however, ICD now provides versions that contain a substantial amount of additional information. The most recent version of ICD, ICD-10, contains a range of detail in its guidelines and descriptions. At the simplest level, disorders are listed by name. The volume titled, "Clinical Descriptions and Diagnostic Guidelines" has more detail, including at least a paragraph of description and sometimes brief criteria. The most detailed version, the research criteria, specifies the precise algorithms that should be used to make a diagnosis.

The second major system that is widely used throughout the world is the Diagnostic and Statistical Manual of the American Psychiatric Association, currently in its 4th edition (DSM-IV). The third edition of this manual, published in 1980, was the first clinical diagnostic system that specified criteria for making diagnoses. Because specified criteria improve reliability, clarify the construct, and facilitate communication, these diagnostic criteria have been widely used. The most recent revision of this manual, DSM-IV, appeared in 1994.

The two sets of criteria are listed below.

ICD-10 Criteria

F20 - F29 SCHIZOPHRENIA, SCHIZOTYPAL AND DELUSIONAL DISORDERS

F20 SCHIZOPHRENIA

This overall category includes the common varieties of schizophrenia, together with some less common varieties and closely related disorders.

F20.0 - F20.3

General criteria for Paranoid, Hebephrenic, Catatonic, and Undifferentiated type of Schizophrenia:

G1. Either at least one of the syndromes, symptoms and signs listed below under (1), or at least two of the symptoms and signs listed under (2), should be present for most of the time during an episode of psychotic illness lasting for at least one month (or at some time during most of the day).

(1) At least one of the following:

a) Thought echo, thought insertion or withdrawal, or thought broadcasting.

b) Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception.

c) Hallucinatory voices giving a running commentary on the patient's behavior, or discussing him between themselves, or other types of hallucinatory voices coming from some part of the body.

d) Persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, superhuman powers and ability (e.g., being able to control the weather, or being in communication with aliens from another world).

(2) Or at least two of the following:

e) Persistent hallucinations in any modality, when occurring every day for at least one month, when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas.

f) Neologisms, breaks or interpolation in the train of thought, resulting in incoherence or irrelevant speech.

g) Catatonic behavior, such as excitement, posturing or waxy flexibility, negativism, mutism and stupor.

h) "Negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (it must be clear that these are not due to depression or to neuroleptic medication).

G2. Most commonly used exclusion criteria: If the patient also meets criteria for manic episode (F30) or depressive episode (F32), the criteria listed under G1.1 and G1.2 above must have been met before the disturbance of mood developed.

G3. The disorder is not attributable to organic brain disease, or to alcohol - or drug-related intoxication, dependence or withdrawal.

Comments: In evaluating the presence of these abnormal subjective experiences and behavior, special care should be taken to avoid false-positive assessments, especially where culturally or sub-culturally influenced modes of expression and behavior, or a subnormal level of intelligence, are involved.

In view of the considerable variation of the course of schizophrenic disorders it may be desirable (especially for research) to specify the **pattern of course** by using a fifth character. Course should not usually be coded unless there has been a period of observation of at least one year.

Pattern of course

F20.x0 Continuous (no remission of psychotic symptoms throughout the period of observation);
F20.x1 Episodic, with a progressive development of 'negative' symptoms in the intervals between psychotic episodes;
F20.x2 Episodic, with persistent but non-progressive 'negative' symptoms in the intervals between psychotic episodes;

F20.x3 Episodic (remittent) with complete or virtually complete remissions between psychotic episodes;
F20.x4 Incomplete remission;
F20.x5 Complete or virtually complete remission;
F20.x8 Other pattern of course.
F20.x9 Course uncertain, period of observation too short.

F20.0 Paranoid schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3 above) must be met.

B. Delusions or hallucinations must be prominent (such as delusions of persecution, reference, exalted birth, special mission, bodily change or jealousy; threatening or commanding voices, hallucinations of smell or taste, sexual or other bodily sensations).

C. Flattening or incongruity of affect, catatonic symptoms, or incoherent speech must not dominate the clinical picture, although they may be present to a mild degree.

F20.1 Hebephrenic schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3) above must be met.

B. Either (1) or (2):

(1) Definite and sustained flattening or shallowness of affect;

(2) Definite and sustained incongruity or inappropriateness of affect.

C. Either (1) or (2):

(1) Behavior which is aimless and disjointed rather than goal-directed;

(2) Definite thought disorder, manifesting as speech which is disjointed, rambling or incoherent.

D. Hallucinations or delusions must not dominate the clinical picture, although they may be present to a mild degree.

F20.2 Catatonic schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3 above) must eventually be met, though this may not be possible initially if the patient is uncommunicative.

B. For a period of at least two weeks one or more of the following catatonic behaviors must be prominent:

(1) Stupor (marked decrease in reactivity to the environment and reduction of spontaneous movements and activity) or mutism;

(2) Excitement (apparently purposeless motor activity, not influenced by external stimuli);

(3) Posturing (voluntary assumption and maintenance of inappropriate or bizarre postures);

(4) Negativism (an apparently motiveless resistance to all instructions or attempts to be moved, or movement in the opposite direction);

(5) Rigidity (maintenance of a rigid posture against efforts to be moved);

(6) Waxy flexibility (maintenance of limbs and body in externally imposed positions);

(7) Command automatism (automatic compliance with instructions).

C. Other possible precipitants of catatonic behavior, including brain disease and metabolic disturbances, have been excluded.

F20.3 Undifferentiated schizophrenia

A. The general criteria for Schizophrenia (F20.0 - F20.3) above must be met.

B. Either (1) or (2):

(1) There are insufficient symptoms to meet the criteria of any of the sub-types F20.0, .1, .4, or .5;

(2) There are so many symptoms that the criteria for more than one of the subtypes listed in B(1) above are met.

F20.4 Post-schizophrenic depression

A. The general criteria for schizophrenia (F20.0 - F20.3 above) must have been met at some time in the past, but are not met at the present time.

B. At least four of the following 'negative' symptoms have been present throughout the previous twelve months:

(1) Psychomotor slowing or underactivity;

(2) Definite blunting of affect;

(3) Passivity and lack of initiative;

(4) Poverty of either the quality or the content of speech;

(5) Poor non-verbal communication by facial expression, eye contact, voice modulation or posture;

(6) Poor social performance or self-care.

F20.6 Simple schizophrenia

A. Slowly progressive development over a period of at least one year, of all three of the following:

(1) A significant and consistent change in the overall quality of some aspects of personal behavior, manifest as loss of drive and interests, aimlessness, idleness, a self-absorbed attitude, and social withdrawal;

(2) Gradual appearance and deepening of "negative" symptoms such as marked apathy, paucity of speech, under-activity, blunting of affect, passivity and lack of initiative, and poor non-verbal communication (by facial expression, eye contact, voice modulation and posture);

(3) Marked decline in social, scholastic, or occupational performance.

B. Absence, at any time, of the abnormal subjective experiences referred to in G1 in F20.0 - F20.3, and of hallucinations or well-formed delusions of any kind, i.e., the subject must never have met the criteria for any other type of schizophrenia, or any other psychotic disorder.

C. Absence of evidence of dementia or any other organic mental disorder listed in section F0.

F20.8 Other schizophrenia

F20.9 Schizophrenia, unspecified

F21 SCHIZOTYPAL DISORDER

A. The subject must have manifested, over a period of at least two years, at least four of the following, either continuously or repeatedly:

(1) Inappropriate or constricted affect, subject appears cold or aloof;

(2) Behavior or appearance which is odd, eccentric or peculiar;

(3) Poor rapport with others and a tendency to social withdrawal;

(4) Odd beliefs or magical thinking influencing behavior and inconsistent with subcultural norms;

(5) Suspiciousness or paranoid ideas;

(6) Ruminations without inner resistance, often with dysmorphophobic, sexual or aggressive contents;

(7) Unusual perceptual experiences including somatosensory (bodily) or other illusions, depersonalization or derealization;

(8) Vague, circumstantial, metaphorical, over-elaborate or often stereotyped thinking, manifested by odd speech or in other ways, without gross incoherence;

(9) Occasional transient quasi-psychotic episodes with intense illusions, auditory or other hallucinations and delusion-like ideas, usually occurring without external provocation.

B. The subject must never have met the criteria for any disorder in F20 (Schizophrenia).

F22 PERSISTENT DELUSIONAL DISORDERS

F22.0 Delusional disorder

A. The presence of a delusion or a set of related delusions other than those listed as typical schizophrenic under F20 G1.1b or d (i.e., other than completely impossible or culturally inappropriate). The commonest examples are persecutory, grandiose, hypochondriacal, jealous (zelotypic) or erotic delusions.

B. The delusion(s) in A must be present for at least three months.

C. The general criteria for schizophrenia (F20.0 - F20.3) are not fulfilled.

D. Persistent hallucinations in any modality must not be present (but transitory or occasional auditory hallucinations that are not in the third person or giving a running commentary, may be present).

E. If affective symptoms are present during a part of the episode, the delusions must persist unchanged with regard to content in their absence.

F. Most commonly used exclusion criteria: There must be no evidence of primary or secondary brain disease as listed under F0, or a psychotic disorder due to psychoactive substance use.

Specification for possible subtypes: The following types may be specified, if desired: persecutory type; litigious type; self-referential type; grandiose type; hypochondriacal (somatic) type; jealous type; erotomanic type.

F22.8 Other persistent delusional disorders

This is a residual category for persistent delusional disorders that do not meet the criteria for delusional disorder (F22.0). Disorders in which delusions are accompanied by persistent hallucinatory voices or by schizophrenic symptoms that are insufficient to meet criteria for schizophrenia should be coded here. Delusional disorders that have lasted for less than three months should, however, be coded, at least temporarily, under F23.

F22.9 Persistent delusional disorder, unspecified

F23 ACUTE AND TRANSIENT PSYCHOTIC DISORDERS

G1. An acute onset of delusions, hallucinations, marked disorder in the form of thought, or any combination of these. The time intervals between the first appearance of any psychotic symptoms and the presentation of the fully developed disorder should not exceed two weeks.

G2. If transient states of perplexity, misidentification, or impairment of attention and concentration are present, they do not fulfill the criteria for organically caused clouding of consciousness as specified in F05 A.

G3. The disorder does not meet the symptomatic criteria for manic episode (F30), depressive episode (F32), or recurrent depressive disorder (F33).

G4. No evidence of recent psychoactive substance use sufficient to fulfill the criteria of intoxication. The continued moderate and largely unchanged use of alcohol or drugs in amounts or frequencies to which the subject is accustomed does not necessarily rule out the use of F23; this must be decided by clinical judgment and the requirements of the research project in question.

G5. Most commonly used exclusion criteria: absence of organic brain disease (F0) or serious metabolic disturbances affecting the central nervous system (this does not include childbirth).

A fifth character should be used to specify whether the acute onset of the disorder is associated with acute stress (occurring within two weeks prior to evidence of first psychotic symptoms).

F23.x0 without associated acute stress
F23.x1 with associated acute stress

For research purposes it is recommended to further specify the onset of the disorder from a non-psychotic to clearly psychotic state as either:

abrupt (onset within 48 hours), or
acute (onset in more than 48 hours but less than two weeks).

F23.0 Acute polymorphic psychotic disorder without symptoms of schizophrenia

A. The general criteria for acute and transient psychotic disorders must be met.

B. The symptomatology is rapidly changing in both type and intensity from day to day or within the same day.

C. The presence of any type of either hallucinations or delusions, for at least several hours, at any time since the onset of the disorder.

D. Symptoms from at least two of the following categories, occurring at the same time:

(1) Emotional turmoil, characterized by intense feelings of happiness or ecstasy, or overwhelming anxiety or marked irritability;

(2) Perplexity, or misidentification of people or places;

(3) Increased or decreased motility, to a marked degree.

E. Any of the symptoms listed in Schizophrenia F20, G1.1 and G1.2 that are present, are only present for a minority of the time since the onset, i.e., criterion B of F23.1 is not fulfilled.

F. The total duration of the disorder does not exceed three months.

F23.1 Acute polymorphic psychotic disorder with symptoms of schizophrenia

A. Criteria A, B, C, and D of acute polymorphic psychotic disorder (F23.0) must be met.

B. Some of the symptoms specified for schizophrenia (F20.0 - F20.3) must have been present for the majority of the time since the onset of the disorder, but not necessarily meeting these criteria completely i.e., at least:

(1) any one of the symptoms in F20, G1.1a to d,

or

(2) any one of the symptoms in F20, G1.2e to g.

C. The symptoms of schizophrenia in B above do not persist for more than one month.

F23.2 Acute schizophrenia-like psychotic disorder

A. The general criteria for acute and transient psychotic disorders (F23) must be met.

B. The criteria for schizophrenia (F20.0 -F20.3) are met, with exception of the duration criterium.

C. The disorder does not meet the criteria B, C, and D for acute polymorphic psychotic disorder (F23.0).

D. The total duration of the disorder does not exceed one month.

F23.3 Other acute predominantly delusional psychotic disorder

A. The general criteria for acute and transient psychotic disorders (F23) must be met.

B. Relatively stable delusions and/or hallucinations are present, but they do not fulfill the symptomatic criteria for schizophrenia (F20.0 - F20.3).

C. The disorder does not meet the criteria for acute polymorphic psychotic disorder (F23.0).

D. The total duration of the disorder does not exceed three months.

F23.8 Other acute and transient psychotic disorders

Any other acute psychotic disorders that are unclassifiable under any other category in F23 (such as acute psychotic state in which definite delusions or hallucinations occur but persist for only small proportions of the time) should be coded here. States of undifferentiated excitement should also be coded here if more detailed information about the patient's mental state is not available provided that there is no evidence of an organic cause.

F23.9 Acute and transient psychotic disorder, unspecified

F24 INDUCED DELUSIONAL DISORDER

A. The subject must develop a delusion or delusional system originally held by someone else with a disorder classified in F20-F23.

B. The two people must have an unusually close relationship with one another, and be relatively isolated from other people.

C. The subject must not have held the belief in question prior to contact with the other person, and must not have suffered from any other disorder classified in F20 - F23 in the past.

F25 SCHIZOAFFECTIVE DISORDERS

Note: This diagnosis depends upon an approximate "balance" between the number, severity and duration of the schizophrenic and affective symptoms; so long as an approximate balance is maintained, this diagnosis can therefore be made at more than one degree of severity if required.

G1. The disorder meets the criteria of one of the affective disorders of moderate or severe degree, as specified for each sub-type.

G2. Symptoms from at least one of the symptom groups listed below, clearly present for most of the time during a period of at least two weeks (these groups are almost the same as for schizophrenia (F20.0 - F20.3)):

(1) Thought echo, thought insertion or withdrawal, thought broadcasting (F20 G1.1a)

(2) Delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions or sensations (F20 G1.1b)

(3) Hallucinatory voices giving a running commentary on the patient's behavior, or discussing him between themselves; or other types of hallucinatory voices coming from some part of the body (F20 G1.1c)

(4) Persistent delusions of other kinds that are culturally inappropriate and completely impossible, but not merely grandiose or persecutory (20 G1.1d), e.g., has visited other worlds; can control the clouds by breathing in and out; can communicate with plants or animals without speaking, etc.

(5) Grossly irrelevant or incoherent speech, or frequent use of neologisms (a marked form of F20 G1.2f)

(6) The intermittent but frequent appearance of some forms of catatonic behavior, such as posturing, waxy flexibility and negativism (F20 G12.2g)

G3. Criteria G1 and G2 must be met within the same episode of the disorder, and concurrently for at least some time of the episode. Symptoms from both criteria G1 and G2 must be prominent in the clinical picture.

G4. Most commonly used exclusion criteria: the disorder is not attributable to organic brain disease (F0), or to psychoactive substance-related intoxication, dependence or withdrawal (F1).

F25.0 Schizoaffective disorder, manic type

A. The general criteria for schizoaffective disorder (F25) must be met.

B. Criteria of a manic disorder must be met (F30.1 or F31.1).

F25.1 Schizoaffective disorder, depressive type

A. The general criteria schizoaffective disorder (F25) must be met.

B. The criteria for depressive disorder, at least moderate severity, must be met (F32.1, F32.2, F31.3 or F31.4).

F25.2 Schizoaffective disorder, mixed type

A. The general criteria for schizoaffective disorder (F25) must be met.

B. The criteria for mixed bipolar affective disorder must be met (F31.6).

F25.8 Other schizoaffective disorders

F25.9 Schizoaffective disorder, unspecified

F28 OTHER NONORGANIC PSYCHOTIC DISORDERS

Psychotic disorders that do not meet the criteria for schizophrenia (F20.-) or for psychotic types of mood [affective] disorders (F30 - F39), and psychotic disorders that do not meet the symptomatic criteria for persistent delusional disorder (F22.-) should be coded here (such as persistent hallucinatory disorder). Include here also combinations of symptoms not covered by the previous categories of F20, such as delusions other than those listed as typical schizophrenic under F20 G1.1b or d (i.e., other than completely impossible or culturally inappropriate) plus catatonia.

DSM-IV Criteria

F20-SCHIZOPHRENIA

A. **Characteristic Symptoms:** At least two of the following, each present for a significant portion of time during a one month period (or less if successfully treated).

(1) delusions
(2) hallucinations
(3) disorganized speech (e.g., frequent derailment or incoherence)
(4) grossly disorganized or catatonic behavior
(5) negative symptoms, i.e., affective flattening, alogia, or avolition

[Note: only one A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other].

B. **Social/Occupational Dysfunction:** For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations or self-care is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. **Duration:** Continuous signs of the disturbance persist for at least six months. This six-month period must include at least one month of symptoms that meet criterion A (i.e., active phase symptoms), and may include prodromal and/or residual periods when the A criterion is not fully met. During these periods, signs of the disturbance may be manifested by negative symptoms or two or more symptoms listed in criterion A present in an attenuated form (e.g., the total duration of the active and residual periods).

D. **Schizoaffective Disorder and Mood Disorder with Psychotic Features have been ruled out** because either: (1) no major depressive or manic episodes have occurred concurrently with the active phase symptoms; or (2) if mood episodes have occurred during the psychotic episode, their total duration has been brief relative to the duration of the psychotic episode (i.e., the total duration of the active and residual periods).

E. **Substance/General Medical Condition Exclusion**: The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Schizophrenia Subtypes

Paranoid Type

A type of Schizophrenia in which the following criteria are met:
A. Preoccupation with one or more delusions and/or frequent auditory hallucinations
B. None of the following is prominent: disorganized speech, disorganized behavior, flat or inappropriate affect or catatonic behavior.

Disorganized Type

A type of Schizophrenia in which the following criteria are met:
A. All of the following are prominent:
(1) disorganized speech
(2) disorganized behavior
(3) flat or inappropriate affect
B. Does not meet criteria for Catatonic type

Catatonic Type

A type of Schizophrenia in which the clinical picture is dominated by at least two of the following:

(1) motoric immobility as evidenced by catalepsy (including waxy flexibility) or stupor
(2) extreme agitation (excessive motor activity that is apparently purposeless and not influenced by external stimuli)
(3) extreme negativism (an apparently motiveless resistance to all instructions or a maintenance of a rigid posture against attempts to be moved) or mutism
(4) peculiarities of voluntary movement as evidenced by posturing (voluntary assumption of inappropriate or bizarre postures), stereotyped movements, prominent mannerisms, or prominent grimacing
(5) echolalia or echopraxia

Undifferentiated Type

A type of Schizophrenia in which symptoms meeting criterion A are present, but the criteria are not met for Paranoid, Catatonic, Disorganized types.

Residual Type

A type of Schizophrenia in which the following criteria are met:

A. Criterion A for Schizophrenia (i.e., active phase symptoms) is no longer met.

B. There is continuing evidence of the disturbance, as indicated by the presence of negative symptoms or two more more symptoms listed in criterion A for Schizophrenia, present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences)

F20.8 SCHIZOPHRENIFORM DISORDER

A. Meets criteria A, D, E, and F of Schizophrenia

B. An episode of the disorder (including prodromal, active, and residual phases) lasts less than six months. (When the diagnosis must be made without waiting for recovery, it should be qualified as "provisional.")

Specify:

Without Good Prognostic Features
With Good Prognostic Features as evidenced by at least two of the following:

(1) onset of prominent psychotic symptoms within four weeks of first noticeable change in usual behavior or functioning
(2) confusion or perplexity at the height of the psychotic episode
(3) good premorbid social and occupational functioning
(4) absence of blunted or flat affect

F25. SCHIZOAFFECTIVE DISORDER

A. An episode during which, at some time, there is either a major depressive episode* or manic episode concurrent with symptoms that meet criterion A for Schizophrenia.

*Major depressive episode must include A (1) depressed mood

B. During the same episode, there has been a period of delusions or hallucinations for at least two weeks in the absence of prominent mood symptoms.

C. Symptoms meeting criteria for a mood episode are present for a substantial portion of the psychotic episode (including active and residual periods).

D. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specify type:

Manic Type: if manic episode
Depressive Type: if depressive episode

F22.0 DELUSIONAL DISORDER

A. Non-bizarre delusions (i.e., involving situations that occur in real life, such as being followed, poisoned, infected, loved at a distance, having a disease, being deceived by one's spouse or lover) of at least one month duration.

B. Absence of other features characteristic of the active phase of Schizophrenia, i.e., none of the following for more than a few hours: hallucinations, disorganized speech, grossly disorganized or catatonic behavior; or negative symptoms (i.e., affective flattening, alogia, or avolition).

[Note: Tactile and olfactory hallucinations are not excluded if related to delusional theme.]

C. Apart from the impact of the delusion(s) or its ramifications, functioning is not markedly impaired and behavior is not obviously odd or bizarre.

D. The delusional disturbance is not better accounted for by a Mood Disorder With Psychotic Features (i.e., to diagnose Mood Disorder with Psychotic Features, delusions have not been present for more than two weeks in the absence of prominent mood symptoms).

E. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Specify type: (the following types are assigned based on the predominant delusional theme)

Erotomanic Type: delusions that another person, usually of higher status, is in love with the individual

Grandiose Type: delusions of inflated worth, power, knowledge, identity, or special relationship to a deity or famous person

Jealous Type: delusions that one's sexual partner is unfaithful

Persecutory Type: delusions that one (or someone to whom one is close) is being malevolently treated in some way

Somatic Type: delusions that the person has some physical defect or general medical condition

Mixed Type: delusions characteristic of more than one of the above types but no one theme predominates

Unspecified Type

298.8 BRIEF PSYCHOTIC DISORDER

A. Presence of at least one of the following symptoms:

(1) delusions

(2) hallucinations

(3) disorganized speech (e.g., frequent derailment or incoherence)

(4) grossly disorganized or catatonic behavior

Note: do not include a symptom if it is a culturally-sanctioned response pattern.

B. Duration of an episode of the disturbance is at least one day and no more than one month, with eventual full return to premorbid level of functioning. (When the diagnosis must be made without waiting for the expected recovery, it should be qualified as "provisional.")

C. Not better accounted for by a Mood Disorder (i.e., no full mood syndrome is present) or Schizophrenia, and not due to the direct effects of a substance (e.g., drugs of abuse, medication) or a general medical condition.

Specify if:

With Marked Stressor(s) (Brief Reactive): if symptoms occur shortly after and apparently in response to events that, singly or together, would be markedly stressful to almost anyone in similar circumstances in the person's culture.

Without Marked Stressor(s): if psychotic symptoms do not occur shortly after, or are not apparently in response to events that, singly or together, would be markedly stressful to almost anyone in similar circumstances in the person's culture.

With Postpartum Onset: if onset within 4 weeks postpartum.

297.3 Shared Psychotic Disorder (Folie a Deux)

A. A delusion develops in an individual in the context of a close relationship with another person(s), who has an already established delusion.

B. The delusion is similar in content to that of the person who already has the established delusion.

C. Not better accounted for by another Psychotic Disorder (e.g., Schizophrenia) or a Mood Disorder with Psychotic Features and is not due to the direct effects of a substance (e.g., drugs of abuse, medication) or a general medical condition.

293.8X PSYCHOTIC DISORDER DUE TO A GENERAL MEDICAL CONDITION

A. Prominent hallucinations or delusions.

B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct physiological consequence of a general medical condition.

C. The disturbance is not better accounted for by another mental disorder.

D. The disturbance does not occur exclusively during the course of a delirium.

Code based on predominant symptoms:
.x1 **With Delusions:** if delusions are the predominant symptom.
.x2 **With Hallucinations:** if hallucinations are the predominant symptom.

SUBSTANCE-INDUCED PSYCHOTIC DISORDER

A. Prominent hallucinations or delusions. Note: Do not include hallucinations if the person has insight that they are substance-induced.

B. There is evidence from the history, physical examination, or laboratory findings of substance intoxication or withdrawal, and the symptoms in A developed during, or within a month of, significant substance intoxication or withdrawal.

C. The disturbance is not better accounted for by a psychotic disorder that is not substance-induced. Evidence that the symptoms are better accounted for by a psychotic disorder that is not substance-induced might include: the symptoms precede the onset of the substance abuse or dependence; persist for a substantial period of time (e.g., about a month) after the cessation of acute withdrawal or severe intoxication; are substantially in excess of what would be expected given the character, duration, or amount of the substance used; or there is other evidence suggesting the existence of an independent non-substance-induced disorder (e.g., a history of recurrent non-substance-related episodes).

D. The disturbance does not occur exclusively during the course of Delirium or Dementia.

Code: (Specific substance) Psychotic Disorder
9291.5 Alcohol, with delusions; 291.3 Alcohol, with hallucinations; 291.11 Amphetamine [or Related Substance], with hallucinations; 291.11 Cannabis, with delusions; 291.12 Cannabis, with hallucinations; 291.11 cocaine, with delusions; 291.12 cocaine, with hallucinations; 291.11 Hallucinogen, with delusions; 291.12 Hallucinogen, with hallucinations; 291.11 inhalant, with delusions; 291.12 Inhalant, with hallucinations; 291.11 Opiod, with delusions; 291.12 Opiod, with hallucinations; 291.11 Phencyclidine [or Related Substance], with delusions; 291.12 Phencyclidine [or Related Substance], with hallucinations; 291.11 Sedative, Hypnotic or Anxiolytic, with delusions; 291.12 Sedative, Hypnotic or Anxiolytic, with hallucinations; 291.11 Other [or Unknown] Substance, with delusions; 291.12 Other [or Unknown] Substance, with hallucinations)

Coding note: also code substance-specific Intoxication or Withdrawal if criteria are met.

Specify if:
with onset during intoxication
with onset during withdrawal

298.9 PSYCHOTIC DISORDER NOT OTHERWISE SPECIFIED

This category should be used to diagnose psychotic symptomatology (i.e., delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior) about which there is inadequate information to make a specific diagnosis, or about which there is contradictory information, or for psychotic presentations that do not meet the criteria for any of the specific psychotic disorders defined above.

Examples include:

1) postpartum psychosis that does not meet criteria for Mood Disorder With Psychotic Features, Brief Psychotic Disorder, Psychotic Disorder Due to a General Medical Condition, or a Substance-Induced Psychotic Disorder.

2) persistent auditory hallucinations in the absence of any other features.

3) persistent non-bizarre delusions with periods of overlapping mood episodes that have been present for a substantial portion of the delusional disturbance.

4) psychoses with confusing clinical features that make a more specific diagnosis impossible.

5) situations in which the clinician has concluded that a psychotic disorder is present but is unable to determine whether it is primary, due to a general medical condition, or substance-induced.

Comparison of ICD-10 and DSM-IV

The overall diagnostic algorithm for the diagnosis of schizophrenia is simpler in ICD-10 than in DSM-IV. The ICD criteria require that the characteristic symptoms of the disorder be present for one month and that the symptoms are not attributable to either a mood disorder or "organic" causes. ICD-10 does not require evidence of social or occupational dysfunction in order to make the diagnosis of schizophrenia, while DSM-IV does.

The two systems differ in terms of the symptoms that are regarded as characteristic (i.e., listed in the A criterion). ICD places greater emphasis on Schneider's First Rank Symptoms, many of which are specifically listed in the criteria. The listing of symptoms in ICD is also much more specific and relatively more complex than in DSM-IV, which refers primarily to general categories of symptoms (i.e., delusions, hallucinations, disorganized speech).

At a more fundamental level, however, the algorithm implied in the list of characteristic symptoms in the two manuals is in fact highly comparable. Both require that the characteristic symptoms must be present for much of the time over a one month period; DSM-IV mentions that the clinician may use his or her judgment about this duration requirement if the patient has been successfully treated, while ICD makes no mention of treatment, but presumably would permit the use of clinical judgment as well. Both systems give increased diagnostic weighting to certain types of delusions and hallucinations (i.e., only one such symptom is required), and these "special symptoms" are of the general Schneiderian type. In the absence of these types of delusions and hallucinations, two characteristic symptoms are required, and the list is quite similar across the two systems.

The major difference between the two systems is that ICD-10 does not require an overall duration of six months for a diagnosis of schizophrenia (criterion C in DSM-IV). In ICD-10, one month of characteristic symptoms fully satisfies the overall duration. A corollary to this is that ICD does not place any emphasis on the concept of prodromal or residual symptoms.

The boundary between schizoaffective disorder and mood disorder varies to some extent across the two systems. If a full mood syndrome has been present, ICD requires that schizophrenia be diagnosed only if the psychotic symptoms preceded the onset of the mood syndrome, rather than stressing the overall duration of the two types of symptoms (i.e., mood and psychotic) as in DSM-IV.

Overall, the concept of schizophrenia in ICD-10 is broader in some ways than DSM-IV and narrower in others. ICD-10 is broader in that it only requires a one month duration, and also in that it includes non-psychotic forms of schizophrenia (i.e., simple schizophrenia) within the general category. ICD is narrower, however, in that it emphasizes the importance of florid psychotic symptoms, and especially the relatively narrow concept of Schneiderian First Rank Symptoms, while the overall list of characteristic symptoms in DSM-IV is somewhat broader.

ICD also shows greater specificity in its description of various types of reactive psychoses and the various manifestations of brief psychotic disorders. This emphasis on the importance of particular categories of brief psychotic syndromes reflects the clinical weight that is given to these specific syndromes in various parts of the world. ICD has been designed to meet a broader group of needs and is based on extensive international input. DSM-IV, on the other hand, was designed primarily by American psychiatrists and placed more emphasis on an appeal to empirical research evidence in its development. The developers of both systems worked closely with one another, however, and attempted to achieve as much congruence between the two systems as possible. In most cases, diagnoses made using either of the systems are likely to be quite similar.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of the schizophrenia spectrum conditions involves boundaries with mood disorders and non-psychotic personality disorders, as well as with substance-induced psychotic disorders and psychotic disorders due to a general medical condition.

The conceptual boundaries with mood disorders and schizotypal disorder have been discussed above. The clinical distinction between schizophrenia and a mood disorder can be extremely difficult, particularly early in the illness. Many young people experiencing symptoms of psychosis react to their experience with feelings of fear, anxiety, and sadness. The symptoms of loss of energy and interest can be attributed to schizophrenic avolition and anhedonia or to an affective syndrome. Timing, pattern, and severity of symptoms may provide some clues, as may the patient's level of insight. For example, the person who has avolition and social withdrawal in the absence of intense painful affect is much more likely to have schizophrenia, while the person who displays intact affect and engages the interviewer's empathy is more likely to have a mood disorder. Likewise, symptoms such as disorganized speech may be seen in both mania and schizophrenia. Again, the timing and pattern of symptoms will assist in the differential diagnosis. In general, if either the positive or negative symptoms of schizophrenia persist for a substantial period of time in the absence of abnormalities of mood, the diagnosis of schizophrenia is much more likely. Sometimes longitudinal observation for several years will be required in order to make a differential diagnosis with confidence.

Psychotic disorders may be precipitated by the use of a variety of drugs, such as amphetamines, marijuana, or hallucinogens. If the psychosis is clearly secondary to the drug use (e.g., it began shortly after the drug was used, or it disappeared quickly after the drug use stopped), then the differential diagnosis is relatively simple. Some patients who abuse drugs and appear to have an acute psychotic condition initially may eventually become chronically psychotic; when this occurs, especially if the patient can be evaluated in a restricted setting where he has no access to drugs of abuse, then the probability that the patient has schizophrenia is increased. There is no firm guideline as to the appropriate length of the drug-free period in order to solidify a diagnosis; drug-free periods ranging from two to six weeks have been suggested.

A variety of medical conditions can also present with psychotic symptoms. Some of the most common include temporal lobe epilepsy, tumor, stroke, brain trauma, endocrine/metabolic disturbances, infectious processes (e.g., general paresis, AIDS), multiple sclerosis, and autoimmune diseases. The differential diagnosis is usually dependent upon obtaining a careful history and ordering the appropriate laboratory tests. In general, an atypical presentation is the more likely indicator that the illness is not within the schizophrenia spectrum. Examples include an unusual age of onset (especially if coupled with an existing medical illness) or an unusual pattern of symptoms (e.g., prominent visual hallucinations in the absence of any negative symptoms).

PSYCHOSOCIAL EVALUATION

Assessing psychosocial functioning is an important aspect of evaluating patients with schizophrenia and related spectrum conditions. Information about psychosocial functioning can assist both in formulating a diagnosis and in determining prognosis. In evaluating psychosocial functioning, the clinician should examine the following domains: relationship to parents, relationship to siblings, relationship to peers, sexual adjustment, educational history, work history, and recreation/activities and interests. These various aspects of psychosocial functioning should be evaluated both prior to the onset of symptoms (i.e., premorbid assessment) and concurrently.

Relationship with family members, such as parents and siblings, will provide information about early indications of developmental abnormalities, psychological stresses that may contribute to onset of symptoms, and the availability of social supports. It is often useful to compare the social and developmental history of the patient with his or her siblings, who provide a socially and educationally matched "comparison sample." Parents will often have noted early "soft" indicators of abnormality. For example, the patient may have been more shy, more developmentally slow, or more emotionally sensitive. Sometimes the onset of schizophrenia will occur at a time when disruptions of family structure produce stress, such as when parents separate or divorce. Sometimes a parent will have been aloof or abusive; contrary-wise, sometimes the patient will have been noticeably aloof or irritable in comparison with other siblings.

After schizophrenia becomes an established condition, it typically produces considerable stress on family members, including both parents and siblings. Parents may find it difficult to accept the emotional, social, and cognitive disruptions that are occurring in their child, and they themselves may need considerable psychological support. Some families have been observed to have a style of coping or relating that may be prone to induce subsequent relapses. These families, who are high on "expressed emotion," may need assistance in learning new ways to deal with the patient's symptoms and to minimize their over-involvement and tendency to make critical comments. (See the section on psychosocial treatment below.) Living with a psychotic brother or sister may also produce considerable stress on siblings.

Depending on all the circumstances, the clinician will need to make a determination as to whether the patient will benefit more from living at home or living independently. Some families work well with patients with schizophrenia, while others have considerable difficulty. There appear to be some international differences as

well. Patients with schizophrenia have a better prognosis in developing countries, perhaps in part because family structures are more accepting of patients with severe mental illness.

The psychosocial evaluation must also assess relationships with peers. Premorbidly, the patient may have been noticeably more shy or lacking in social skills and to have had few friends. Even patients who had a good relationship with peers prior to onset of illness may have difficulty making or maintaining friendships after the onset, since the symptoms often make the individual suspicious or difficult to relate to. Patients with schizophrenia may reply, upon questioning, that they have a number friends; more intensive querying indicates that these friends are in fact seen very infrequently and that the relationship is quite superficial.

Sexual adjustment is often poor in schizophrenia. In fact, many patients have little or no sexual experience throughout their lives, and the majority of patients with schizophrenia do not marry. Some patients have a limited interest in sex, while others have a normal level of sexual interest. On occasion a patient with schizophrenia will develop a delusional relationship with a "fantasy lover," and in extreme cases the object of this fantasy love will be at risk from the patient. Patients with schizophrenia who have a predominantly disorganized syndrome may behave in ways that are considered sexually inappropriate, such as masturbating in public.

The educational history of patients with schizophrenia can be quite variable. Some patients have normal to high educational function until the onset of symptoms and decline precipitously thereafter, finding themselves unable to return to school and achieve at their previous level. Other patients continue to do well, although this is less common. Some patients have early indicators of educational impairment, especially when compared with their siblings. Some patients are subjectively aware of an impairment in their ability to think clearly and to achieve at previous levels; when this occurs, the patient may become quite depressed and be at high risk for suicide.

Work history also tends to be variable. The majority of patients with schizophrenia are not able to work at the same level as their parents or siblings, leading to the phenomenon referred to as "downward drift." That is, patients with schizophrenia typically have a lower socioeconomic level than their parents, as measured both by educational and work achievements. The work history will often indicate this downward drift, particularly in patients who began at a relatively high level of functioning. The patient may have been able to hold a job for a number of years, but may become steadily more handicapped if the illness persists. A subset of patients are, however, able to maintain an adequate work history.

Recreational activities and interests should also be assessed during the clinical work-up. One approach to this assessment involves having the patient describe "a typical day" or a "typical evening" or a "typical weekend." The description will often indicate that the patient spends large amounts of time sitting alone and doing very little. Recreational activities and interests tend to be solitary and passive, such as watching television. To the extent that a high level of recreational activities and interests are present, the prognosis is better.

LABORATORY WORK-UP

There is no "boiler plate" set of laboratory evaluations for schizophrenia, as there may be for other medical disorders such as hypertension or chest pain. Depending on the clinical presentation, mode of onset, and past history, the clinician may wish to select from a variety of possible laboratory tests in order to assist in decisions about diagnosis and treatment. Some laboratory tests that are commonly obtained include a complete blood count (CBC), urinalysis, evaluation of endocrine function, evaluation of hepatic function, electroencephalogram (EEG), computed tomography (CT) or magnetic resonance (MR), neuropsychological tests, and projective tests.

A CBC and urinalysis are commonly obtained in most patients when they are admitted to a hospital. These are useful screening tests in order to provide clues as to whether some underlying medical condition may be producing the symptoms. Examples include an infectious process, which could affect the white count or sedimentation rate. A subset of patients with chronic schizophrenia often develop a "water intoxication syndrome," characterized by high fluid intake and low specific gravity of the urine. The frequency with which infectious processes may be observed will vary widely depending on the setting. For example, patients in developing countries may present with a psychotic picture secondary to an infectious process endemic there, such as toxoplasmosis, while these syndromes are relatively rare in Europe or the United States.

Other laboratory tests that may be useful in a differential diagnosis between schizophrenia and spectrum conditions and other medical conditions include blood tests to assess endocrine and liver function, an EEG, and neuroimaging techniques such as CT or MR. These tests may be helpful in identifying conditions such as myxedema (e.g., "myxedema madness"), syndromes due to tumors or head injuries (e.g., subdural hematoma), multiple sclerosis, or the lesions of HIV or syphilis.

A variety of clues may alert the clinician to the need for ordering additional or more complex laboratory tests. These include the presence of confusion, an atypical clinical picture, or an atypical onset. For example, the most typical age of onset for schizophrenia is in the late teens to early 20s. An onset outside this age range may suggest the presence of a pathophysiological process other than schizophrenia, such as head injury, infection, or tumor. The need to rule out other "nonschizophrenic" syndromes is heightened if confusion is present, since the sensorium is classically "clear" in schizophrenia (although some patients who are severely psychotic or very chronically ill may be confused and may show disorientation or memory impairment). Further,

although the clinical picture of schizophrenia may be quite variable, some types of symptoms are much less common. For example, hallucinations are usually auditory, although they may be visual, tactile, or olfactory. The more the hallucinations diverge from the typical auditory presentation, the more likely it is that they could be due to some other syndrome. For example, visual hallucinations are more characteristic of intoxication with drugs such as the hallucinogens or with the delirium tremens that occurs as a consequence of alcohol withdrawal. Olfactory hallucinations may suggest a syndrome such as temporal lobe epilepsy. Marked disorganization of speech should alert the clinician to considering the possibility of aphasia and ruling out a syndrome such as stroke or tumor. Marked silliness and shallowness of affect, accompanied with disorganization of speech, may suggest frontal lobe lesions such as tumors. Any of these unusual presentations will make the need for further laboratory tests more likely.

Neuropsychological and projective tests may also be useful in assessing patients with schizophrenia. Neuropsychological tests permit the clinician to determine the patient's level of cognitive function and to assist in the diagnosis by determining whether the level of function is below that expected for the person's educational achievement or social class. More detailed psychological tests may help in identifying areas of function or dysfunction and may assist in rehabilitative planning. Projective tests may be useful in determining the degree of thought disorder or conceptual disorganization. In particular, they may be helpful in eliciting delusional thinking or disorganization in thinking that is not evident in a typical clinical interview.

COURSE AND OUTCOME

Studies by investigative teams working with Bleuler, Huber, and Ciompi represent some of the major long-term outcome studies of the course of schizophrenia. The work of Bleuler and Ciompi has examined patients in Switzerland, while Huber has studied patients in Germany. However, in the 1930s, prior to these studies, studies on a large number of patients who left the hospital were reported in the U.S.A. by Malamud and by Rupp and in Japan by Hayashi. There are also follow-up studies in which patients with schizophrenia were compared to patients with other disorders (e.g., affective disorders, physical disorders, etc.) as a control group in order to clarify the course and outcome of schizophrenia, such as the Iowa 500 study. Since the end of the 1970s, follow-up studies have been conducted using subjects selected according to operational diagnostic criteria such as DSM-III.

One of the crucial issues in describing the course and outcome of schizophrenia involves determining the effects of treatment. The early "founding fathers" based their descriptions on the natural history of the disorder, but this has almost certainly been altered by the availability of treatments such as electroconvulsive therapy or neuroleptic medications. Many different studies of outcome have been conducted, which can be related to the introduction of various treatment techniques. These results are summarized in terms of social outcome, and they indicate that the introduction of drug therapy appears to have improved social outcome. The percentage of patients who are either self-supportive or semi-self-supportive has increased steadily, while the percentage requiring hospitalization has steadily decreased, as has the percentage of deaths.

Studies of outcome, must of course consider not only levels of social adjustment, including personal relationships and vocational ability, but also levels of clinical psychiatric symptoms. The WHO Division of Mental Health established the International Pilot Study of Schizophrenia (IPSS). Using the PSE (already described above), they reported the two-year symptomatic outcome and compared course in developing and developed countries. Overall, course is better in the developing countries. In either case, however, the two-year outcome reported in this study indicates that some degree of remission (as measured by severity of symptoms) occurs in more than half of the patients studied at a two year period, although many may have psychotic exacerbations within that time period. The long-term outcome, as assessed for longer time periods and on the basis of both social and symptomatic remission, is probably somewhat poorer.

Nakane and colleagues of Nagasaki University have summarized the pattern of clinical course and social outcome of schizophrenic patients included in a WHO collaborative study that was conducted after the IPSS at the points of two years, five years and ten years. The symptomatic course during this time period indicates a relatively poor long-term outcome. By the time of ten-year follow-up, only 4% of patients were in complete remission, while 25% were in remission with past psychotic exacerbations, providing an overall "good recovery" rate of around 30%. Approximately 20% were chronically psychotic during the entire 10-year interval, and the remainder (approximately 50%) were in incomplete remission. Using the Disability Assessment Schedule (DAS) which was also developed by WHO, the course of social outcome of the subjects was classified into four levels based on their condition during six months prior to the evaluation: 'very favorable', 'favorable', 'unfavorable' and 'very unfavorable' and 'hospitalized.' Then they were grouped into three groups, a group with 'good outcome' including patients with 'very favorable' and 'favorable' outcome, one with 'poor outcome' including those with 'unfavorable' and 'very unfavorable' outcome and one being 'hospitalized.' By the ten-year follow-up, approximately 30% of the patients were hospitalized, while approximately 35% had either good or poor outcome. These results are quite similar to the frequently-cited "rule of thirds:" that one third of patients remain severely ill, one third show considerable improvement, and one third are improved but still markedly impaired.

There have been many attempts to identify those characteristics which are likely to predict outcome in a given patient. At the clinical level, the question that patients or family members are most likely to ask is: "What can we expect in the future?" Prognostic indicators represent an attempt to try to develop a rational answer to that question. Some of the factors considered to be more predictive of a poor outcome include male gender, insidious onset, poor premorbid personality, premorbid social isolation, low educational achievement, low parental social class, and negative symptoms. None of these factors can be considered predictive in isolation, however; in general, the more that are present, the more likely that the course will be chronic.

CROSS-CULTURAL ISSUES

There are similarities and differences between schizophrenic patients originating from various different cultures. Studies conducted in different countries have shown that the symptoms of schizophrenia are found in all cultures, and more or less in the same proportion. However, the content of these symptoms may vary considerably. The similarities between schizophrenic patients from various cultures are represented mainly by negative symptoms, especially cognitive impairment, but also thought disorders. The differences can be observed in delusional ideas. For example, a schizophrenic patient from a Western country is more likely to have delusions about laser beams or atomic bombs, while a patient from a sub-Saharan African country will take the components of his delusions from his own cultural source: sorcery, witchcraft, possession.

The number of acute psychotic episodes observed in developing countries is remarkably high, compared to the Western ones. These episodes may be reactive or secondary to organic problems. This is due, among other things, to insufficiency of medical coverage in these countries, as well as high prevalence of infectious diseases and malnutrition, which can provoke organic brain syndromes, which create an important differential diagnosis with schizophrenia.

The difference observed in course and outcome of schizophrenia in developed and developing countries has already been mentioned. This is a paradoxical result, since patients from industrialized countries usually receive more technical help from mental health workers than the ones from developing countries. Nevertheless, these findings are probably accounted for by a variety of cultural differences.

The traditional social structure of many developing countries may play a major role in producing a better outcome. The availability of large extended families gives patients more social supports. Many of the schizophrenic patients who need hospitalization in developing countries are in fact treated within their families. Another aspect which could explain the better outcome in developing countries is the less intense pressure on the patient to be efficient in working, producing, and socializing. The sophistication needed in order to survive in urban regions is much greater than in smaller villages or rural areas, creating a handicap for the schizophrenic patient who suffers from cognitive disabilities. Finally, the traditional image of mental illness may be also less stigmatized in developing countries, since in many cultures it is seen as a link with the supernatural world, or even sometimes being of a religious value.

Family structures may also have a negative impact on outcome. For example, the tolerance shown usually in traditional extended families can be a handicap for the patients, if the mental illness is denied or not recognized. It happens sometimes that a schizophrenic patient is seen by a psychiatrist for the first time 10 or 20 years after the onset of his illness; meanwhile, the family has consulted numerous traditional healers.

The situation in Japan also presents some interesting cross-cultural paradoxes, since this country is the only one in the world that is increasing steadily the number of its psychiatric beds, and yet it also espouses very traditional family structures. The increases in hospitalization are probably explained by the fact that family members are very busy with their work and do not have enough time to look after ill family members, especially when they are chronic. The high population concentration in Japan may also make it more difficult for families to care for psychotic patients within the home, since living space is relatively crowded and the population tends to be concentrated in urban areas.

In developing countries, the situation is rapidly changing, especially in the cities. The social solidarity among the members of extended families is decreasing steadily, and the tolerance towards mental patients will probably diminish in the future. Psychiatric institutions will therefore have to play an increasing role in order to substitute for this deficiency.

Contributors: Nancy C. Andreasen, Driss Moussaoui, and Yoshibumi Nakane