7

Psychosis

1. A 19-year-old male college student was brought to the emergency room. It was noted that he had become progressively distracted and withdrawn and had suffered from severe insomnia for the past two or three months. Initially, this behavioral change had been thought to be due to the breakup with his girlfriend that had occurred several months earlier. When he started to converse with a nonexistent person in his room, however, and accused his roommate of homosexual advances, his friends persuaded him that he needed help for his "nerves."

2. A 26-year-old married woman was brought to the psychiatric clinic by her husband. Over the past several weeks, she had become irritable and argumentative and had stayed awake most of the night arranging and re-arranging furniture. She had several arguments with her husband about her conviction that he was having an extramarital affair even though there was no objective evidence that he was. On psychiatric examination, it was found that for the past two months she had been taking large doses of amphetamines to lose weight. She was a pharmacist and had ready access to the amphetamines.

3. Dear Family Fridori and Family Graf or Schmidli!

Here in this smith-house it doesn't go very well. This is indeed no parish-house or even a poor-house but in this place there is noise, anger, grumbling—sunny—heavenly-knells all year round. Many a small and large landowner, wind-bag or poor drunk from Thalweil, Addisweil, from Albis, from Salz, from Seen, from Rorbach, from Rorbas have never again returned to their own homes, etc., etc., etc.

Greetings to all who are still alive.

My own relatives no longer exist.

Anna

[From Eugen Bleuler's Dementia Praecox or The Group of Schizophrenias, translated by J. Zinkin. New York, International Universities Press, 1950. Reprinted with permission.]

4. A 65-year-old married salesman became agitated and argumentative in the surgical recovery room following a cholecystectomy. He accused the nurses of conspiring to rob him of his property—in fact, he was convinced that the hospital was a front for organized crime. When his wife came to see him, he accused her of being in cahoots with the "crooks." He stated that he actually saw the director of the hospital meeting in his room with well-known organized crime figures. He claimed that he overheard their conversation plotting to rob him and kill him.

When the psychiatric consultant examined his medical chart, the onset of the patient's behavioral problems was found to coincide with the administration of meperidine for his surgical pain. When the pain medicine was changed, the behavioral problems subsided rapidly.

PSYCHOSIS, MADNESS, AND INSANITY

Perhaps everyone recognizes that psychosis is a serious illness, sometimes referred to in lay terms as craziness or madness. We know, however, that we can all feel crazy sometimes, especially under stress or under the influence of drugs. In fact, Freud (1900) pointed out that even normal persons exhibit thinking processes and engage in behaviors in dreams that would be considered quite psychotic in the awake state. Some people deliberately seek experiences resembling psychosis by ingesting drugs such as mescaline or LSD. Rosenhan (1973), in an often-cited study, arranged to have eight apparently normal people present themselves to a number of different mental hospitals with feigned psychotic symptoms including hallucinations. They were indeed admitted under the diagnosis of schizophrenia, and even when they behaved quite normally once admitted, they had some difficulty in being discharged from the hospitals. This study, often cited as an example of inaccuracy in psychiatric diagnosis, proves quite something else if one understands the nature of psychotic phenomena—that it is quite possible for normal people to pretend to be psychotic. Psychosis is often feigned on the stage and in literature. To an extent, then, crazy behaviors associated with psychosis may be seen to be a part of the human repertoire of behaviors. What, then, distinguishes psychosis as an illness from unusual behaviors that occur within the normal range? While normal persons can feign psychosis, and can induce a crazy state by using drugs, they usually have control over whether or not they will be, or

act, psychotic. A psychotic *patient*, on the other hand, has no control over his illness unless medical help is given. This does not mean that a psychotic patient will always remain psychotic without treatment; as with any illness, there may be spontaneous exacerbations and remissions of the symptoms. The patient in the midst of a psychotic attack cannot, however, get over being psychotic by simply willing to do so.

GENERAL PHENOMENOLOGY OF PSYCHOSIS

Psychosis is a psychiatric syndrome in which there are profound and prolonged involuntary alterations in perception, affect, thinking, and behavior (Bowers, 1983). This results in a break in the patient's relationship with reality, often causing socially inappropriate or "crazy" behavior. Characteristic perceptual changes in psychosis are hallucinations and illusions. Hallucinations are perceptual experiences without any external sensory input, while illusions refer to distorted perceptions of external stimuli. For example, in vignettes 1 and 4, there is clear evidence of auditory and visual hallucinations, respectively.

Common aberrations in thought in psychosis include delusions. Delusions refer to aberrations in content of thought, e.g., fixed ideas that are not based on reality, such as delusions of persecution (vignette 4) and delusions of infidelity (vignette 2). Delusions of grandeur are also common in psychotic states associated with mania (e.g., vignette 2 in Chapter 6). Delusions are usually "logic-tight"; that is, no amount of logic will convince a delusional patient that his ideas are not true. In terms of thought *process*, psychotic patients often manifest abnormalities in formal thought process, e.g., blocking, difficulties with *associations*—the linking of one idea to another. "Loose associations" are commonly associated with schizophrenia and other psychotic states (vignette 3).

The behavioral changes that occur in psychosis reflect the patient's perceptual and cognitive state; the patient may follow a hallucinated command, or his behavior may be socially inappropriate or bizarre due to delusions or impairment of reality testing, as mentioned earlier. In fact, this impairment of the individual's relationship with reality is often considered to be the hallmark of the syndrome of psychosis. The motoric behavior of the patient may also be grossly abnormal in a psychotic state. Agitation is common, but on occasion, the patient may present with catatonia, characterized by mutism, unresponsiveness, and rigidity. When the physician changes the patient's posture by, for example, lifting up his arm, the arm remains in the new position ("waxy flexibility"). The

vital signs are usually normal in this state. This *catatonic syndrome* has been regarded as typical of a form of schizophrenia, but many other conditions and diseases can give rise to many of the features of catatonia (as in Table 6).

There are phenomenological differences between the acute psychotic state and the chronic phase of psychosis, although they both share the basic features described above. The sensorium in acute psychosis is typically hyperalert (Bowers, 1974). The behavior tends to be more agitated and floridly disruptive, and the patients are exquisitely sensitive to external stimuli, which may be interpreted in a highly personalized way (e.g., the sound of the ambulance is an indication that "the aliens are coming to get me"). In chronic psychosis, on the other hand, the patient's behavior tends to be more subdued despite the presence of delusions and hallucinations. In chronic schizophrenia, the so-called negative symptoms, such as anhedonia and paucity of thought, may predominate. It should be noted, however, that there may be episodes of florid psychosis in chronically psychotic patients.

We should, at this point, review the phenomenology and etiological theories of schizophrenia in some detail, since acquaintance with what is known about schizophrenia is essential in the evaluation and management of patients with psychosis.

SCHIZOPHRENIA—A CLASSIC PSYCHOSIS

Schizophrenia is, perhaps, the illness that most people think of when the term "psychosis" is mentioned. Schizophrenia is indeed a representative chronic psychotic illness, and most psychosis research has been conducted with the goal in mind of understanding and treating schizophrenia.

Brief History

Descriptions of psychotic phenomena date back to ancient times, but systematic investigations concerning psychosis had to wait until the 19th century, when a number of psychiatrists made systematic attempts at describing and classifying the chronic psychosis that is today known as schizophrenia.

Morel (1860), a French psychiatrist, coined the term *demence precoce* in 1856 to describe an adolescent patient who became gradually withdrawn, gloomy, and silent.

Table 6. List of Conditions Often Associated with the Catatonic Syndrome[a]

Psychiatric disorders
Schizophrenia
Affective disorders
Neuroses and related phenomena
Neurological disorders
Basal ganglia (following bilateral surgical lesions of the globus pallidus)
Limbic system and temporal lobes
Akinetic mutism
Focal temporal abnormalities
Diencephalon
Tumors and traumatic hemorrhage in the region of the third ventricle
Focal lesions of the thalamus
Other brain lesions
Frontal lobe tumors
Focal frontal lobe lesions
Anterior cerebral artery aneurysm
Arterial malformation of the posterior circulation
Diffuse brain trauma
Diffuse encephalomalacia following closed head injury
Petit mal status
Postictal phase of epilepsy
Wernicke's encephalopathy
Tuberous sclerosis
General paresis
Narcolepsy
Acute phase of encephalitis lethargica
Cerebral macular degeneration
Metabolic conditions
Diabetic ketoacidosis
Hypercalcemia from parathyroid adenoma
Pellagra
Acute intermittent porphyria
Homocystinuria
Membranous glomerulonephritis
Hepatic encephalopathy
Toxic agents
Organic fluorides
Illuminating gas
Psychotomimetic drugs
Chronic amphetamine intoxication
Phencyclidine (PCP) intoxication
Pharmacological agents
Aspirin intoxication
ACTH
High-potency antipsychotic agents

[a]After Gelenberg (1976). Reproduced with permission.

The German psychiatrist Emil Kraepelin in 1896 systematically described in his book *Psychiatry, 5th Edition,* under the rubric "Dementia praecox," the signs and symptoms of psychotic illnesses that seemed to have a course characterized by progressive deterioration in mental functioning. Dementia praecox, which means "premature losing of mind" as opposed to senile dementia, included "catatonia," described some years earlier by another German psychiatrist, Kahlbaum, and "hebephrenia," a form of psychosis that usually occurs in adolescents and young adults and in which severe regression, giggling, posturing, and other inappropriate "silly" behaviors are prominent symptoms, described by still another German psychiatrist, Hecker. According to Kraepelin, then, progressive deterioration was the hallmark of dementia praecox. He thus differentiated dementia praecox from manic–depressive illness, which did not result in a progressive deterioration (see Chapter 6 for further discussion of manic–depressive illness).

Kraepelin paid particular attention to systematic data-gathering and describing the symptoms and natural course of psychiatric illnesses. This systematic *descriptive approach* in psychiatry, often referred to as the Kraepelinian approach, forms a major foundation of modern psychiatry, side by side with the *dynamic approach* developed by Sigmund Freud.

Eugen Bleuler, a Swiss psychiatrist, radically changed the concept of dementia praecox by pointing out that not all patients with the symptoms described by Kraepelin actually had an unremitting deteriorating course. He coined the term *schizophrenia,* which means "split mind," in his book *Dementia Praecox or the Group of Schizophrenias,* published in Germany in 1911. Bleuler proposed that in schizophrenia, there are four fundamental symptoms: disturbances in (1) association and (2) affect and the presence of severe (3) autism and (4) ambivalence. These are the "4 A's" that are still used as useful diagnostic indicators of schizophrenia. Bleuler proposed that other symptoms such as hallucinations, delusions, illusions, and motoric changes (e.g., catatonia) were all accessory or secondary symptoms of schizophrenia. Bleuler was influenced by both Kraepelin and Freud, and his work represents a synthesis of both approaches.

Definition

Schizophrenia is a chronic psychotic disorder of unknown etiology. The essential features of schizophrenia, according to the DSM-III-R, are the presence of the psychotic syndrome during the active phase of the illness, characteristic symptoms involving multiple psychological processes, and deterioration from a previous level of functioning.

Clinical Features and Diagnostic Criteria

The DSM-III-R diagnostic criteria for schizophrenia are listed in Table 7.

Schneiderian First Rank Symptoms and Bleuler's 4 A's. Kurt Schneider (1959) described characteristic symptoms of schizophrenia, which he called the "first rank symptoms." They include complete auditory hallucinations such as hearing two voices conversing with each other, voices commenting on one's behavior, hearing one's thoughts spoken aloud, feeling that one's thoughts are taken away by others (thought withdrawal), feeling that others are putting thoughts into one's head (thought insertion), feeling that one's thoughts are spread to others (thought broadcasting), and delusions of control, such as the belief that one's actions are controlled by radio waves coming from spaceships. The presence of even one of the Schneiderian first rank symptoms in a patient warrants a serious consideration of the diagnosis of schizophrenia.

The important features of the Schneiderian first rank symptoms are auditory hallucinations and delusions. These symptoms are related to Bleuler's *autism* (one of the 4 A's) or dereistic thinking, which means that the patient lives in a world of his own with tenuous relationship with external reality, a world determined primarily by inner psychic drives and stimuli. The patient usually withdraws emotionally and physically from social relationships, being preoccupied with unrealistic fantasies and illogical thoughts. In fact, family members or friends often notice that the patient seems to have withdrawn into a world of his or her own.

Another important feature of schizophrenia is what is known as "formal thought disorder," which means that the form or process of thinking, as opposed to the content of thought, is impaired. The most common example of such a thought disorder is *loosening of associations* of ideas, another of Bleuler's 4 A's. When associations are loosened, the connection between one idea and the next is impaired, so that the patient may skip from one topic to a completely unrelated topic without any seeming awareness that he is talking about unrelated subjects. When a patient's associations are loose, his speech may be incoherent (vignette 3). An extreme form of loose associations is sometimes called "word salad." In addition to loose associations, the schizophrenic patient may show stilted language, neologisms (making up of new words), perseveration (repetition of the same words or ideas), clang associations (words that are linked by the sound rather than the meaning, e.g., "I drank milk, and silk, and ilk, and ink, and dink, and think.") Thought blocking

Table 7. Diagnostic Criteria for Schizophrenia

A. Presence of characteristic psychotic symptoms in the active phase: either (1), (2), or (3) for at least one week (unless the symptoms are successfully treated):
   1. two of the following:
      a. delusions
      b. prominent hallucinations (throughout the day for several days or several times a week for several weeks, each hallucinatory experience not being limited to a few brief moments)
      c. incoherence or marked loosening of associations
      d. catatonic behavior
      e. flat or grossly inappropriate affect
   2. bizarre delusions (i.e., involving a phenomenon that the person's culture would regard as totally implausible, e.g., thought broadcasting, being controlled by a dead person)
   3. prominent hallucinations (as defined in (1)(b) above) of a voice with content having no apparent relation to depression or elation, or a voice keeping up a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other

B. During the course of the disturbance, functioning in such areas as work, social relations, and self-care is markedly below the highest level achieved before onset of the disturbance (or, when the onset is in childhood or adolescence, failure to achieve expected level of social development).

C. Schizoaffective Disorder and Mood Disorder with Psychotic Features have been ruled out, i.e., if a Major Depressive or Manic Syndrome has ever been present during an active phase of the disturbance, the total duration of all episodes of a mood syndrome has been brief relative to the total duration of the active and residual phases of the disturbance.

D. Continuous signs of the disturbance for at least six months. The six-month period must include an active phase (of at least one week, or less if symptoms have been successfully treated) during which there were psychotic symptoms characteristic of Schizophrenia (symptoms in A), with or without a prodromal or residual phase, as defined below.

   Prodromal phase: A clear deterioration in functioning before the active phase of the disturbance that is not due to a disturbance in mood or to a Psychoactive Substance Use Disorder and that involves at least two of the symptoms listed below.

   Residual phase: Following the active phase of the disturbance, persistence of at least two of the symptoms noted below, these not being due to a disturbance in mood or to a Psychoactive Substance Use Disorder.

   Prodromal or Residual Symptoms:
   1. marked social isolation or withdrawal
   2. marked impairment in role functioning as wage-earner, student, or homemaker
   3. markedly peculiar behavior (e.g., collecting garbage, talking to self in public, hoarding food)
   4. marked impairment in personal hygiene and grooming
   5. blunted or inappropriate affect
   6. digressive, vague, overelaborate, or circumstantial speech, or poverty of speech, or poverty of content of speech

(continued)

Table 7. *(Continued)*

   7. odd beliefs or magical thinking, influencing behavior and inconsistent with cultural norms, e.g., superstitiousness, belief in clairvoyance, telepathy, "sixth sense," "others can feel my feelings," overvalued ideas, ideas of reference
   8. unusual perceptual experiences, e.g., recurrent illusions, sensing the presence of a force or person not actually present
   9. marked lack of initiative, interests, or energy

   Examples: Six months of prodromal symptoms with one week of symptoms from A; no prodromal symptoms with six months of symptoms from A; no prodromal symptoms with one week of symptoms from A and six months of residual symptoms.

E. It cannot be established that an organic factor initiated and maintained the disturbance.

F. If there is a history of Autistic Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present.

Classification of course. The course of the disturbance is coded in the fifth digit:
   1—**Subchronic.** The time from the beginning of the disturbance, when the person first began to show signs of the disturbance (including prodromal, active, and residual phases) more or less continuously, is less than two years, but at least six months.
   2—**Chronic.** Same as above, but more than two years.
   3—**Subchronic with Acute Exacerbation.** Reemergence of prominent psychotic symptoms in a person with a subchronic course who has been in the residual phase of the disturbance.
   4—**Chronic with Acute Exacerbation.** Reemergence of prominent psychotic symptoms in a person with a chronic course who has been in the residual phase of the disturbance.
   5—**In Remission.** When a person with a history of Schizophrenia is free of all signs of the disturbance (whether or not on medication), "in Remission" should be coded. Differentiating Schizophrenia in Remission from No Mental Disorder requires consideration of overall level of functioning, length of time since the last episode of disturbance, total duration of the disturbance, and whether prophylactic treatment is being given.
   0—**Unspecified.**

[a]From DSM-III-R. Reprinted with permission from the American Psychiatric Association.

is also sometimes seen, in which the patient is completely without any thoughts in the middle of an ongoing statement or conversation.

Another common symptom of schizophrenia, and one of Bleuler's 4 A's, is the *blunting* or *flattening of affect.* Flat affect denotes a marked reduction in the intensity of affective expression, so that there is practically no evidence of expression; blunting means a less severe reduction in affective expression. With flat affect, the patient usually speaks in a monotone (if he speaks at all), and the facial muscles appear immobile. Inappropriate affect may also be exhibited in schizophrenia; for example,

the patient may giggle while talking about a sad event, such as the death of his mother.

Sense of self is often impaired in schizophrenia, such that a sense of individuality is lost. Problems with sense of identity are common. This is sometimes referred to as a loss of *ego boundaries.*

Volition, or self-initiated, goal-directed activity, is often impaired in schizophrenia. This may be associated with severe *ambivalence* regarding decision-making (this is the last of Bleuler's 4 A's). The patient may show lack of interest in activities, lack of enjoyment (anhedonia), and lack of motivation.

Positive and Negative Symptoms. The symptoms of schizophrenia may be classified into "positive" and "negative" ones (Andreasen and Olsen, 1982). The positive symptoms are the florid psychotic symptoms such as hallucinations and delusions that are commonly shared by all psychoses. The negative symptoms, on the other hand, are "deficit" symptoms that are particularly pronounced during the chronic or residual phase of the illness. They include flatness of affect, paucity of thought, anhedonia, and motoric retardation.

On the basis of symptomatology and drug-therapy response, Crow (1980) proposed that there might be two types of schizophrenia: *Type I* is characterized by mostly "positive" symptoms, probably dopamine-sensitive, and therapeutic response to antipsychotic drugs (dopamine-receptor blockers) is good (see the section on Neurotransmitters). *Type II* schizophrenia, on the other hand, is characterized by a predominance of the "negative symptoms," is dopamine-insensitive, and treatment outcome with antipsychotic drugs is poor (perhaps, with the exception of clozapine). The "negative symptoms" have been associated with cerebral ventricular enlargement on computerized tomography (Andreasen *et al.,* 1982) as well as a variety of hypothesized correlates of structural brain abnormality, including poor premorbid adjustment, early age of onset, lower educational achievement, poor performance on cognitive testing, and poor response to treatment (Andreasen *et al.,* 1990).

Clinical Types. On the basis of the predominant clinical picture, schizophrenia may be subdivided into the types described below. It should be emphasized, however, that over the course of time, the predominant presentation may change. Antipsychotic drugs may also alter the clinical picture as the "positive" symptoms respond better than the "negative" ones.

1. Disorganized (hebephrenic) type: Characterized by marked incoherence and blunted, inappropriate, or silly affect. Posturing and odd behavior are prominent. The illness typically begins in adolescence.
2. Catatonic type: Characterized by marked psychomotor disturbances, which may include catatonia, rigidity, stupor, excitement, negativism, and posturing (see also Table 6).
3. Paranoid type: Characterized by delusions of a persecutory or grandiose nature; delusional jealousy or hallucinations with persecutory or grandiose content may also occur. Generally, the onset of psychosis in this type is later than in other types of schizophrenia (late 20s to 30s). Functional deterioration in this type is usually milder than in other types of schizophrenia.
4. Undifferentiated type: Characterized by a mixed picture, such as delusions, hallucinations, and incoherence or disorganized behavior.
5. Residual type: This diagnosis is given to patients who have had at least one episode of schizophrenia and who are not floridly psychotic although certain symptoms persist, such as blunting of affect, social withdrawal, looseness of associations, and illogical thinking.

Course and Prognosis

Schizophrenia is a chronic illness, but the course is not necessarily progressively downhill as it was considered to be in Kraepelin's time. The advent of antipsychotic drugs has improved the prognosis greatly, so that with continuing therapy, reasonably satisfactory degrees of functioning can be maintained in many patients for long periods of time. There is, however, usually some deterioration in the functional capacity. The family's expectations of a patient may have to be lowered once schizophrenia has developed.

There are several factors that seem to be associated with the *prognosis* for functional adjustment of patients with schizophrenia. Factors that are associated with a good prognosis include: absence of premorbid personality disturbance, good level of premorbid social functioning, clear-cut precipitating events, abrupt onset, onset in mid-life, presence of confusion in the clinical picture, and a family history of affective disorder. A particularly poor prognostic indicator is early insidious onset with predominant "negative" symptoms.

Mortality

Psychiatric patients in general have a higher mortality rate than the general population. Affective disorders (mania and depression) and schizophrenia are particularly implicated in an increased mortality rate. In a 30- to 40-year follow-up study of patients with various psychiatric and nonpsychiatric disorders in Iowa, Tsuang and Woolson (1978) found that an excess mortality rate existed for both schizophrenia and affective disorders. While the excess mortality was most pronounced during the first ten years following hospitalization (2–4 times the control population), the increased mortality rate continued throughout the study period in schizophrenia. While the rate of suicide and accidents are increased in schizophrenia, these do not completely account for the excess mortality rate.

Epidemiological Aspects

Approximately 100,000 new schizophrenic patients receive care each year in the United States. At any given time, about 0.5–3.0% of the population seems to be afflicted with schizophrenia according to various community surveys (Strauss and Carpenter, 1981).

The lifetime prevalence rate based on studies in Europe and Asia that used a relatively narrow definition of schizophrenia is 0.2–1%.

Sex ratio. Schizophrenia is equally common among males and females.

Socioeconomic status. Schizophrenia is more prevalent in lower socioeconomic populations. Faris and Dunham (1939) found in their classic study in Chicago that the highest first-hospitalization rates for schizophrenia occurred in the poor, inner-city areas. Hollingshead and Redlich (1958) found in New Haven that the prevalence rates of psychotic disorders were higher in the lower socioeconomic classes, while the prevalence rates of neurotic disorders (anxiety disorders) were higher in the upper socioeconomic classes.

These socioeconomic differences in the prevalence of schizophrenia may be explained by two possibilities: (1) the *origin hypothesis* postulates that the disorganized urban ghetto environment and genetic pooling of the low socioeconomic populations give rise to the genetic and environmental conditions that cause schizophrenia; (2) the *drift hypothesis* postulates that the individuals afflicted with schizophrenia drift downward in socioeconomic status and living environment to the more impoverished areas.

Etiological Aspects

Schizophrenia is a disorder of as yet undetermined etiology, but there are considerable relevant data and many theories about aspects of its etiology.

Biological Dimension. Genetic factors. Schizophrenia clearly runs in families. The risk of developing schizophrenia in the general population is somewhat less than 1%, while the prevalence for parents of children who are known schizophrenics is 12%. The morbidity risk for schizophrenia for full siblings of schizophrenic patients is 13–14%. The risk for children with one schizophrenic parent is 8–18%. If both parents are schizophrenic, the morbidity risk for their children may be as high as 50% (Rosenthal, 1968). In the case of twins, heterozygous twins have the same risk as other siblings, while homozygous (identical) twins have a concordance rate for schizophrenia of approximately 50%. (However, there is much variability in the concordance rate depending on the study, from practically 0 to 86%.) The high rate of concordance for monozygotic twins suggests a strong genetic component in schizophrenia, but the lack of absolute concordance also proves that there are factors other than genetic ones that operate in the development of the schizophrenic syndrome.

Studies of adopted children contributed to an understanding of genetic factors in schizophrenia. In general, there seems to be an increased incidence of prevalence for schizophrenia in biological relatives of chronic schizophrenic patients, but not in their adoptive relatives. However, acute schizophrenia was not increased in these biological relatives (Gottesman and Shields, 1976; Kety *et al.*, 1968).

Smooth-pursuit eye-tracking impairment has been reported in schizophrenic patients and their nonschizophrenic relatives. This abnormality was reported to be associated with social introversion and has been suggested as a genetic marker of those who are vulnerable to schizophrenia (Holzman *et al.*, 1974; Siever *et al.*, 1982).

There are undoubtedly genetic factors that contribute to a vulnerability to schizophrenia, but the nature of the vulnerability is not yet clearly understood.

Neuroanatomical and neurophysiological considerations. Disorders in arousal (hyperarousal in acute psychosis, hypoarousal in the insidious or chronic phase) and inability to sustain attention are common in schizophrenic patients. Disturbances in the emotional life (mood and affect) also characterize most schizophrenics. From these manifestations, it is reasonable to assume that neurophysiological abnormalities in the re-

ticular activating and limbic systems are involved in schizophrenia (see Chapter 6 for a discussion of these brain areas). Some studies have demonstrated an association between certain psychophysiological measures of brain function and treatment outcome with antipsychotic drugs (Landau *et al.*, 1975; Strauss and Carpenter, 1981). Unwanted and irrelevant memories and thoughts often intrude uncontrollably into the patient's consciousness. Such phenomena may also represent a disturbance of the "filtering" function of the reticular activating system concerning extraneous stimuli. At times of such extraneous sensory inundations, the patient may be behaviorally mute and catatonic. The EEG, however, often shows a pattern of hyperarousal (low-voltage fast activity) during these episodes.

Other phenomena often seen in schizophrenia, such as feelings of unreality about the environment *(derealization)* or concerning the self *(depersonalization)*, experiences of thought insertion and withdrawal, hallucinations, and disturbances of arousal and attention, all bear some resemblance to symptoms displayed in seizure disorders (epilepsy) involving the limbic brain ("partial complex seizures" or "limbic" or "temporal lobe" seizures). Chemically induced seizures of the amygdaloid nucleus have been shown to produce chronic "psychotic" behaviors in cats, such as apparent hallucinations, inappropriate fear and attack responses, and hypervigilance (Stevens, 1973).

Ventricular enlargement on computerized tomography (CT scan) has been reported in some schizophrenic patients. There is evidence that such ventricular enlargement may be associated with the "negative" or "deficit" symptoms of schizophrenia rather than the "positive" symptoms (Andreasen *et al.*, 1982, 1990). On the basis of these findings, Andreasen and her colleagues hypothesize that there might be two types of schizophrenia: a "negative" or "defect" schizophrenia characterized by the "negative" signs and caused by diffuse atrophic changes in the brain and a "positive" schizophrenia caused by more focal brain dysfunction involving neurotransmitters, with a predominance of the "positive" symptoms. There is evidence, however, that both "positive" and "negative" symptoms exist in many patients depending on the phase of the schizophrenic illness.

Positron emission tomography (PET) scan tends to show decreased frontal lobe activity in some schizophrenic patients (Buchsbaum *et al.*, 1982).

Neurological "soft signs" (such as awkwardness in the pronation and supination of the arm) have been reported in some schizophrenic patients, particularly those with premorbid asociality (Quitkin *et al.*, 1976). The presence of these signs is thought to indicate the presence of

diffuse and general brain damage, as in "minimal brain dysfunction syndrome." There is also evidence on CT scan that the normal asymmetry in brain structures may be reversed more often in schizophrenic patients than in normals, particularly in the frontal and occipital lobes (Luchins *et al.*, 1979). Such findings seem consistent with theories that postulate disturbances in the right–left brain specialization in schizophrenia, e.g., that disturbance of logical thought in patients with schizophrenia may indicate a dysfunction of the dominant (usually left) hemisphere (Flor-Henry, 1976).

In summary, then, there is evidence suggesting disordered function of the limbic system in schizophrenia, and in some chronic schizophrenic patients with predominant "negative" symptoms, there may be diffuse atrophic changes in the brain and these may be associated with "soft" neurological signs.

Biochemical factors. The idea that biochemical factors are involved in schizophrenia receives strong support from a number of important facts. They include: (1) certain drugs can cause clinical psychotic states that are in many ways indistinguishable from some schizophrenic psychotic states (e.g., the amphetamines); (2) different chemical classes of drugs that are effective in ameliorating many of the serious symptoms of schizophrenia share common pharmacological features (e.g., ability to block postsynaptic dopamine receptors; see below); and (3) when genetic factors are involved in transmission of vulnerability to an illness, as in schizophrenia, the mediating mechanisms operate through biochemical pathways.

Drug-induced psychosis. Altered states of consciousness induced by the use of marijuana were reported over a thousand years ago in India, and Aztec Indians in Mexico used the peyote plant (which contains the psychotomimetic drug mescaline) as a part of their religious ceremonies (Snyder, 1974).

There are several classes of drugs that commonly cause psychosis—the hallucinogens (psychedelic drugs) and CNS stimulants. The hallucinogens include LSD, PCP, and mescaline; D-amphetamine and cocaine are examples of CNS stimulants. Drug-induced psychoses have been observed with high frequency in both medical and psychiatric settings since the 1960s, when self-administration of psychedelic drugs became popular throughout the world.

Some hallucinogens are structurally related to endogenous substances. For example, mescaline is chemically similar to norepinephrine. The *transmethylation theory* of schizophrenia postulates that certain hallucinogens such as bufotenine and DMT (N,N-dimethyltryptamine) are endogenously produced in some schizophrenic patients by abnormal

methylation of biogenic amines (Osmond and Smythies, 1952; Rosengarten and Friedhoff, 1976). The enzymes required to produce such transmethylated hallucinogens have been found in the human brain, and the administration of methyl donors such as methionine that would enhance such reactions have been shown to exacerbate psychotic symptoms in some known schizophrenic patients. According to the transmethylation hypothesis, the administration of methyl acceptors such as nicotinic acid should reduce schizophrenic symptoms. The results of experiments designed to test this hypothesis are conflicting and indeterminate.

In general, psychoses caused by drugs are acute psychoses with hyperalertness and severe anxiety. In many instances, they resemble the acute stage of schizophrenia (Bowers and Freedman, 1966). Amphetamine psychosis is almost indistinguishable from paranoid schizophrenia, and may be caused by the abuse of "diet pills," as in vignette 2. Drug-induced psychoses typically lack, however, the "negative" symptoms of schizophrenia and the chronic course.

Neurotransmitters. With the advent of antipsychotic drugs, a new biochemical theory emerged—the *dopamine theory of schizophrenia.* All drugs that were effective against schizophrenia (and psychosis) were shown to be blockers of the brain neurotransmitter dopamine (Snyder, 1974), while dopamine agonists like amphetamine and L-dopa often provoke psychosis. Phenothiazines (e.g., chlorpromazine) and butyrophenones (e.g., haloperidol) are examples of antipsychotic drugs that are potent dopamine antagonists. Usually, there is a general correlation between a drug's dopamine-receptor-blocking activity as manifested by extrapyramidal side effects (e.g., parkinsonian tremor and cogwheel rigidity caused by the deficiency of functional levels of dopamine in the substantia nigra) and its antipsychotic potency. One clinically useful indication of a drug's dopamine-antagonist activity rests on the fact that dopamine inhibits prolactin secretion by the pituitary; hence, a drug's ability to increase serum prolactin levels has been used as a screening test for potential new antipsychotic agents. However, as we will see later in this chapter, the locations of dopamine receptors that are important in psychoses (mesolimbic system) are not identical with those that are involved in the extrapyramidal symptoms (nigrostriatal tract) or in prolactin secretion (dopamine tract within the hypothalamus). Thus, these side effects should not be inescapable when more specific antipsychotic drugs are invented and developed.

There are some reports of finding direct evidence of increase in brain dopamine and dopamine receptors in the brains of schizophrenic patients on postmortem examination (Mackay *et al.*, 1978). The increase in dopamine levels was not related to the amount of antipsychotic drugs

used, but the increase in the number of receptors was seen only in patients who had been maintained on antipsychotic drugs for a long time (Creese and Snyder, 1982). Recently, bimodal distribution of dopamine receptors in postmortem brains of schizophrenics has been reported, a finding that is compatible with the notion that there are two types of schizophrenia (Seeman *et al.*, 1984).

There are at least four types of dopamine receptors in the brain. The D1 but not the D2 receptors stimulate adenylate cyclase activity. The D2 receptors have been shown to be increased in schizophrenic brains by 50–100% (Lee and Seeman, 1977, 1980).

However, schizophrenia cannot be explained simply on the basis of increased functional levels of dopamine in the brain. Antipsychotic drugs are not uniformly effective in all schizophrenics; in fact, there is a subgroup of patients who show little or no response to dopamine-receptor blockers (dopamine-insensitive or type II of Crow [1980]). In fact, the "negative" symptoms of schizophrenia are the most resistant to the antipsychotic drugs. Studies on dopamine turnover in the brain have so far been equivocal (Haracz, 1982). Also, it is clear that an aberration of the dopamine system is not specific for schizophrenia as opposed to other psychoses, since almost all psychotic states, regardless of cause, seem to respond to the dopamine-receptor-blocking agents.

Neurotransmitters other than dopamine have also been implicated in schizophrenia. For example, decreased serotonergic function has been suggested (Bartholini *et al.*, 1968; Bowers, 1972). Increased cholinergic activity has also been suggested for the negative symptoms in schizophrenia (Tandon and Greden, 1990).

Despite these problems, however, it is reasonable to regard dysfunction in brain dopaminergic neurons as playing an important part in schizophrenic psychoses. The specific dopaminergic system hypothesized to be involved (hyperfunctional) in schizophrenia is the mesolimbic system, which originates from the melanin-containing cells in midbrain tegmentum (ventral tegmental nucleus of Tsai) and terminates on small interneurons of the limbic striatum in the region of the nucleus accumbens (or accombens), olfactory tubercle, amygdala, and caudate nucleus (see Figure 11 [Chapter 6]).

Janice Stevens (1973) postulated, on the basis of phenomenological, neuroanatomical, and pharmacological data, that there may be dopaminergic and serotonergic push–pull servosystems in the limbic striatum that may act as a "gate" between limbic inputs and perception–behavior outputs. According to her proposal, the interneurons of the limbic striatum, on which the predominantly cholinergic axons from neocortex and limbic cortex converge, may be concerned with the selection or gating of

endogenous and exogenous stimuli that compete for access to conscious attention and for access to autonomic endocrine functions and to neural pathways that control behavior. The threshold of these normally hyperpolarized limbic interneurons, according to this theory, may be influenced by the reciprocal actions of the ascending dopaminergic and serotonergic neurons. Schizophrenic psychosis, then, could result from a chronic disorder in the aminergic regulation of this "limbic striatal filter," with some of the symptoms representing "release phenomena."

Other Substances. Monoamine oxidase. There are reports of decreased levels of the enzyme monoamine oxidase (MAO) in the blood platelets of schizophrenic patients (Wyatt *et al.*, 1980). First-degree relatives of schizophrenics have also been reported to have lower levels of MAO activity (Berrettini *et al.*, 1980), but lower platelet MAO activity has been reported in other psychiatric disorders as well, including affective disorders and alcoholism. Low MAO activity may represent a genetic marker of nonspecific vulnerability to psychiatric disorders.

Endorphins. Endorphins seem to be involved in the regulation of dopamine and serotonin synthesis. The exact nature of involvement, if any, of the endorphin system in schizophrenia is as yet undetermined (Bowers, 1980).

Prostaglandins. Disorders of prostaglandins have also been reported, but the data so far are contradictory (Bowers, 1980; Horrobin, 1977; Kafka *et al.*, 1979).

Creatine phosphokinase. The clinical significance of the increased levels of serum creatine phosphokinase (CPK) that have been reported in schizophrenia (Meltzer, 1976) is unclear.

Immune mechanisms and viral agents. Increased levels of serum immunoglobulins G and M have been reported in schizophrenia, and the possibility that schizophrenia is an autoimmune disease has been suggested (Amkraut *et al.*, 1973; Burch *et al.*, 1968). Viruslike agents reportedly have been found in the cerebrospinal fluid of schizophrenics (Crow *et al.*, 1979; Tyrrell *et al.*, 1979). Atypical lymphocytes that show stimulated features have been found in schizophrenics ("P" cells); these P cells do not seem to be related to neuroleptic medication (Hirata-Hibi *et al.*, 1982). Although the evidence of immunological changes is intriguing, no definite immunological mechanisms or viral agents have been identified as specific to schizophrenia.

Personal Dimension. Problems in cognitive and affective development may also contribute to predisposition and vulnerability to schizophrenia. In terms of the personality structure, abnormalities of *ego functions*, particularly cognitive systems, are prominent in schizophrenia (and other psychoses). From a developmental perspective, *regression* to earlier, infantile states of cognition and affect regulation characterize schizophrenic symptomatology. Evidence of regression includes illogical thought process *(primary process thinking)*, massive denial of reality, autism, and magical thinking. Some severely regressed schizophrenic patients may even assume the fetal position for long periods of time.

In general, psychological difficulties implicated in theories of etiology and pathogenesis concerning schizophrenia involve three types of theories and their combinations: *deficit theories, conflict theories,* and *maladaptive learning theories.*

Deficit theories postulate that some inborn psychological defects may be precursors of later illness. Conflict theories propose that certain early conflicts, for example, in the oral phase of development, cause a fixation in development, and that the individual may then regress back to that stage of cognition and function when confronted with severely stressful situations in (later) life. Maladaptive learning theories propose that schizophrenic behavior may be based on abnormal interpersonal behaviors and patterned thinking learned over time (Strauss and Carpenter, 1981). Lidz *et al.* (1965) emphasize the role of abnormal family patterns of interaction in shaping behaviors that will later be manifest as a part of schizophrenic psychopathology.

Studies of high-risk children (such as the offspring of schizophrenics) do indicate that premorbid cognitive and behavioral defects are present even in childhood. For example, problems with attention and reaction time to stimuli, problems with activity–passivity, and poor social relationships are common in children who later become schizophrenic (Chapman, 1979; Strauss *et al.*, 1977).

There is considerable evidence to support the fact that major psychological conflicts associated with stressful life situations may precipitate an acute schizophrenic psychosis (Bowers, 1974) regardless of the nature of the etiological factors that predispose to it.

In summary, then, we might state that in patients with schizophrenia, various combinations of psychological deficits, learned maladaptive behaviors, and intrapsychic conflicts along with biological and environmental factors may have contributed to the development of the illness. The precise sequence and nature of the interactions among these factors are not known, and their relative weights may vary in different patients and in patients with different clinical forms and stages of the disorder.

Environmental Dimension. Environmental factors that have been postulated to be associated with the pathogenesis of schizophrenia include abnormal family environment and the effect of socioeconomic milieu.

As discussed previously, the fact that the prevalence of schizophrenia is higher in the urban ghetto environment gave rise to the hypothesis that the stressful environment in these areas might be a causative factor in schizophrenia (Faris and Dunham, 1939). This finding is in part supported by the fact that the prevalence of the illness is higher in nonwhites (who predominate in urban ghetto areas) as compared to whites (Kramer, 1978). Caution is needed in interpreting such epidemiological data, since there is good evidence that schizophrenic patients drift down in socioeconomic status, and also the gene pool in the underprivileged sector may contribute to the vulnerability.

Family studies illuminate the nature of developmental factors that contribute to development of schizophrenia. *Patterns of communication* have been reported to be abnormal in schizophrenic families. The *double bind* described by Bateson *et al.* (1956) is an example of a communication deviance that if consistently characteristic of most transactions between adults and child could lead to difficulty. In it, the child is put in a "no-win" situation by the parents. For example, a mother buys two neckties for her son, one red, the other blue. When the mother sees her son wearing the red tie, she asks him, "What's the matter, don't you like the blue tie?"

If the child is exposed consistently and over time to such no-win situations, psychosis might offer the only or best "way out." Wynne *et al.* (1977) described typical patterns of communication deviance in schizophrenic families, including failure to arrive at a closure, premature closure, and lack of "visualizability." They postulated that these types of communication problems would compromise children's ability to deal conceptually with life's demands. Wynne *et al.* (1958) also described a psychological "rubber fence" that surrounds certain families of schizophrenics. Such a family isolates itself from others and provides little real contact for the child with the outside world, and the communication pattern of such a family may be "pseudomutual" (a special form of communication whereby agreement seems to occur without actual communication of concepts or facts).

Lidz *et al.* (1965) described two characteristic patterns found in families of patients with schizophrenia, *skewed* and *schismatic.* In the skewed family, one member of the family who has abnormal behavior patterns dominates the interactional patterns and sets an abnormal "norm" of behavior. In the schismatic family, the parents are severely split. Each parent is involved in hostile competition for the attention and affection of the child. Such abnormal family environments, when unremittingly consistent, can be considered to be detrimental to normal psychosocial

development and to create personality structures conducive to the development of schizophrenia.

Controlled empirical studies of families of patients with schizophrenia have demonstrated that high levels of expressed emotion in family interactions, particularly high levels of expressed hostility and aggression, correlate with increased probability of psychotic relapse of schizophrenic patients who are in remission (Brown *et al.*, 1972; Vaughn and Leff, 1976).

In summary, schizophrenia seems to be an illness in which biological, psychological, and environmental factors may all contribute to predisposition, vulnerability, and precipitation.

Dysfunction (hyperfunction) of the mesolimbic dopaminergic pathway may be a final common pathway in schizophrenic psychosis. Additionally, there might also be structural changes in the brains of schizophrenics who manifest predominantly "negative" symptoms.

NATURE OF PSYCHOSIS

We mentioned that drug-induced "model" psychosis gave rise to biochemical theories concerning schizophrenia. Many features of psychoses that are clearly nonschizophrenic, such as those induced by amphetamines, are indistinguishable from schizophrenia. Drugs that are effective in schizophrenia, e.g., the dopamine-receptor blockers, are also effective in many psychoses other than schizophrenia. Thus, theories concerning the biochemical disorder underlying psychotic symptoms in schizophrenia apply as well to practically all psychotic conditions. In fact, antipsychotic drugs such as the phenothiazines are used widely in the treatment of many acute psychotic states including mania and psychotic organic brain syndromes.

As might be expected, the "positive" or florid symptoms of schizophrenia that are sensitive to antipsychotic drugs, such as hallucinations and delusions, are symptoms that are commonly found in psychoses other than schizophrenia. "Negative" symptoms such as asociality and poverty of thought that are often resistant to antipsychotic drugs are the ones that seem to be more specifically encountered in schizophrenia. All this suggests that psychosis as a syndrome may be a *final common pathway* for expression of a number of underlying disorders including the antecedent genetic and psychological traits that characterize individuals who are predisposed and vulnerable to develop schizophrenia.

Bowers (1974) postulated that the central nervous system possesses a latent capacity for a pattern of functioning that is experientially known as human psychotic consciousness. This postulated neurobiologically altered mode may be "switched on" under certain circumstances, the most notable of which is drug ingestion. This altered mode may also be transiently operational during dreaming and under sensory deprivation conditions, when hallucinations naturally occur.

Many factors may lower the threshold for the state change to psychosis. Genetic and personality developmental factors would be long-term factors also encountered within psychiatric disorders such as affective disorders, borderline personality disorder, and drug dependence. Changes in physical and social environment may also contribute to a psychotic break, as in sensory deprivation (such as in intensive care units), and at times of severe interpersonal stress. Changes in the internal environment also contribute to psychosis, as in toxic states due to disease or drugs (e.g., endocrine diseases, neurological diseases; see Table 21 [Chapter 13]).

In conclusion, then, psychosis may be considered to be a stress-related *final common pathway* of the brain that functions in response to and expresses a variety of predisposing and contributing biological, psychological, and environmental factors.

EVALUATION OF PSYCHOSIS

Psychosis is not an uncommon phenomenon among hospitalized patients, even in medical and surgical units. Most commonly, such psychoses are due to drug toxicity (such as narcotic analgesics) or drug withdrawal, impaired circulation to the brain, or a combination of organic and environmental factors such as sensory deprivation and overload of the intensive care unit, drugs, and sleep deprivation.

It is also important to recognize that patients who *present* with psychotic symptoms to a psychiatrist may have an underlying medical or surgical disease rather than schizophrenia or another psychiatric disorder. Common among diseases that present with psychotic symptoms are endocrinopathies, neurological diseases, and metabolic diseases (Jefferson and Marshall, 1981; Leigh and Kramer, 1984).

Evaluation of the psychotic syndrome, then, must be comprehensive and include the biological, psychological, and environmental dimensions of the patient. Comprehensive evaluation of the patient naturally leads to a differential diagnosis and to an understanding of the interrelated predisposing, contributing, and precipitating factors of the psychotic syndrome.

Biological Dimension

The most important considerations in the biological dimension include the presence or absence of toxic states and medical or neurological diseases (current context). Physical and neurological examination, laboratory tests (including toxic screen), and careful medical history are obviously important. For example, evidence of sympathetic hyperactivity with increased blood pressure and the presence of amphetamines in the urine would establish the diagnosis of amphetamine psychosis (vignette 2).

Toxic psychosis is often caused by commonly used anticholinergic agents such as atropine. Signs of sympathetic overactivity and anticholinergic activity (e.g., tachycardia, dry, hot skin, mydriasis) should be present. Anticholinergic psychosis may be temporarily reversed by the intravenous administration of physostigmine (a cholinesterase inhibitor).

EEG and CT scan may yield valuable data in making the diagnosis of viral encephalitis or a space-occupying lesion causing psychosis.

In the recent context, a history of self-administered drug use or abuse (analgesics, alcohol, and hypnotics) or of medications will give clues concerning toxic or withdrawal psychoses, e.g., LSD- or PCP-induced toxic states or propranolol- or digitalis-induced psychosis or alcohol or barbiturate withdrawal.

Family history of schizophrenia or bipolar affective disorder increases the possibility that the patient may have schizophrenia or manic psychosis, respectively.

Personal Dimension

The current mental status of the patient establishes the presence of the psychotic state through such features as hallucinations, delusions, loosening of associations, and illogical thinking. The type of hallucination is often important in distinguishing schizophrenia from organic psychosis. Visual hallucinations of the unformed type are particularly indicative of organic psychosis, while auditory hallucinations are more common in schizophrenia.

Cognitive aspects of the mental-status examination often provide clues concerning the etiology of the psychotic syndrome. Disorientation and confusion are typically seen in psychoses associated with organic

brain syndrome rather than schizophrenia. Careful evaluation concerning possible toxic states, neurological conditions, and other medical diseases is called for in the presence of these symptoms.

It is also important to inquire into the history of the psychotic syndrome—onset (insidious or acute), clinical features (e.g., gradual social withdrawal, predominantly paranoid flavor), and change in functioning. The presence of characteristic clinical features of schizophrenia will help establish the diagnosis, as well as possibly give clues to the prognosis (e.g., poor prognosis in the asocial, "negative" schizophrenia).

In the background context, the premorbid personality often provides clues concerning the cause of the psychosis; the withdrawn, introverted premorbid personality is more common with schizophrenia, while a person with cyclothymic personality may develop a psychotic manic syndrome. Persons who are characterized by extreme lability in emotions and behavior and stormy relationships may occasionally develop transient psychotic episodes that seem to "seal off" spontaneously. Such patients may have *borderline personality disorder.*

There are patients who manifest both severe depression or mania *and* features of schizophrenia. These patients are classified as having *schizoaffective disorder.*

Environmental Dimension

The current social and physical environment of the patient may provide important clues concerning the causes of the psychotic syndrome. For example, a teen-ager who is in a drug culture is most likely to have a drug-induced psychosis. A cardiac patient in the coronary care unit is most likely to have an *intensive care unit syndrome* or a toxic psychosis due to analgesics or antiarrhythmic drugs. A person living alone in progressive social isolation is more likely to have schizophrenia.

Recent changes in the environment, such as breaking up with a boyfriend or girlfriend, may have precipitated a situational psychosis or an acute schizophrenic psychosis (with a better prognosis than in "negative" schizophrenia with gradual insidious onset and no precipitating factors).

Early background information concerning family relationships may reveal patterns suggesting a predisposition to psychosis such as "skewed" or "schismatic" parental relationships or consistent exposure to "double bind."

DIFFERENTIAL DIAGNOSIS OF PSYCHOSIS

On the basis of a comprehensive evaluation of the psychotic syndrome, a differential diagnosis should be performed to make appropriate plans for managing the patient.

As in the case of the depressive syndrome, it is important to distinguish between psychosis secondary to a specific cause and what might be called primary (or idiopathic) disorders, e.g., psychoses that include schizophrenia, schizoaffective disorder, and affective disorders (as well as "schizophreniform psychosis" with unknown etiology and "paranoid disorder," in which there are no associated signs of schizophrenia).

The secondary psychoses are diagnosed on the basis of an identifiable etiological factor, such as drugs, medical disease, stimulus deprivation, or major situational stress.

The primary psychoses are diagnosed first by ruling out secondary psychoses, but should also be supported by the symptomatology, clinical course, and background information such as family history of schizophrenia (see Table 7).

MANAGEMENT OF PSYCHOSIS

A comprehensive evaluation of the psychotic patient should lead to a comprehensive management strategy. Removal of the causative agent in secondary psychosis is, of course, the most important consideration. However, if the patient is acutely psychotic and agitated, immediate management of the psychotic behavior may be necessary before the causative agent can be identified and eliminated.

The treatment of psychosis should be done in collaboration with a psychiatrist, who can provide expertise in psychotherapy, environmental management, and pharmacotherapy. Once schizophrenia or any other chronic primary psychosis has been diagnosed, referral to a psychiatrist may be advisable, since protracted and ongoing specialized treatment will generally be necessary.

Biological Dimension

As previously discussed, antipsychotic drugs are effective in almost all kinds of psychoses and can be effectively used for symptomatic treatment of both primary and secondary psychoses. In general, the dose of

the antipsychotic drug may have to be much higher to treat schizophrenia as compared to secondary psychoses.

Typically, the antipsychotic drugs are phenothiazines (e.g., chlorpromazine, perphenazine, fluphenazine) or butyrophenones (e.g., haloperidol). The drugs should be titrated to control the psychotic symptoms (particularly the "positive" symptoms such as hallucinations and delusions). The neuroleptic clozapine seems to be effective for both "positive" and "negative" symptoms, but it must be used with caution because of a high incidence of agranulocytosis as a side effect. In acutely psychotic, disruptive patients, parenteral administration may be necessary, since they may be unable to take oral medications. Chlorpromazine, 25 mg intramuscularly, may be given every 4 hr, or for less sedation, haloperidol, 5 mg intramuscularly every 4 hr, may be tried until the disruptive symptoms are under control. Schizophrenic patients may require maintenance doses for protracted periods of time to prevent relapse. It should be remembered, however, that embarking on a long-term course of antipsychotic drugs for a patient is a serious business.

Tardive dyskinesia, which has been associated with long-term use of antipsychotics, is a movement disorder consisting of involuntary writhing and jerking movements in the orobuccal region that spread to the rest of the body. This often irreversible condition is probably caused by dopamine-receptor supersensitivity induced by long-term dopaminergic blockade.

The choice of antipsychotic drugs depends to a large extent on the side effects of the drugs. The common side effects that are important include: sedation, orthostatic hypotension, extrapyramidal effects (pseudoparkinsonism), photosensitivity, and occasional jaundice. Agranulocytosis is a rare but serious side effect. Different drugs have different patterns and degrees of these side effects, as discussed in Chapter 21.

Personal Dimension

Supportive psychotherapy in combination with drug therapy as outlined above is the treatment of choice in schizophrenia or any chronic psychosis (Leigh, 1983). Psychotherapy is geared to help maintain the patient's contact with reality and to provide a regular relationship with an accepting figure who will monitor the patient's symptoms and level of social function and the effect of medications. Additionally, it may offer psychosocial rehabilitation and support for further emotional growth once the acute phase is passed and a good therapeutic relationship has been established.

Reality-oriented counseling to solve immediate problems of living, such as the living situation (e.g., home vs. halfway house), is frequently necessary. The frequency and locus of psychotherapeutic sessions should be individualized. Usually, during the acute phase, hospitalization is necessary with daily contact. On discharge, patients usually require at least weekly sessions until they are stabilized and reasonably rehabilitated. Then the frequency may be reduced to once every few months with the understanding that the patient may contact the physician at any time when necessary.

Even in cases of secondary psychosis, psychotherapy is often needed in addition to the removal of the causative agent to help the patient integrate the frightening effects of the psychotic experience.

Long-term insight-oriented psychotherapy may be helpful after the acute episodes. It is highly specialized treatment and should be used only by experts in carefully selected cases, usually from among patients refractory to combined short-term hospital, drug, and supportive psychotherapy management (Fromm-Reichmann, 1948). The degree of regression and autism and the "negative" symptoms often preclude intensive psychotherapy during the acute phase of schizophrenic psychosis, but consistent presence of the therapist during this phase may set the stage for more active treatment later.

Environmental Dimension

Acutely psychotic patients are typically in a state of fear and hypervigilance. They experience and react to internal and external stimuli in a highly exaggerated fashion. Thus, it is important to provide, as much as possible, an environment of low stimuli for such patients before adequate evaluation can be performed (Bowers, 1983). A relatively dimly lit, quiet room with adequate space is an optimal setting for interviewing such a patient. The room should be free of potentially dangerous visible objects, such as scalpels and scissors, and the door should be visible to the patient with ready access and left open to reassure the patient.

On the other hand, it is equally important for the evaluating physician to feel secure. If indicated because of violent behavior, security officers may need to be called to restrain the patient before any evaluation can take place.

In secondary psychosis due to pathogenic influences in the immediate environment, as in the intensive care unit, transfer to another unit may be considered. In psychosis associated with organic brain syndrome (see Chapter 8), a multibed room with a calendar and night-lights may be therapeutic in reducing the disorientation and confusion that may

contribute to misinterpretations of environmental stimuli. Frequent visits from family members, familiar objects, and photographs of close relatives help the patient keep a hold on reality.

Hospitalization is perhaps the most important treatment in the environmental dimension for acutely psychotic patients. The indications for hospitalization include grossly disruptive behavior or violent, homicidal, suicidal, or self-destructive behavior or potential.

Family evaluation and therapy is particularly important in younger, "first-break" schizophrenics. In some cases, abnormal interactional patterns of the family may be identified and corrective measures may be instituted, which may reduce the pathogenic influence on the patient. More important, education of family members concerning the chronic nature of schizophrenia and its treatment modalities will enhance their understanding of the patient, which most patients sorely need, and ensure both the family's and the patient's cooperation and collaboration.

SUMMARY

Psychosis is a syndrome characterized by involuntary alterations in perception, thinking, and behavior. Some important symptoms include hallucinations, delusions, loosening of associations, and agitation or catatonia.

Many drugs, toxic states, and medical and neurological diseases are associated with psychosis.

Schizophrenia, which affects about 1% of the population during their lifetime, is but one type of chronic psychotic syndrome with remissions and exacerbations. Autism, association problems, affective flattening, and severe ambivalence causing problems with intentional behavior (Bleuler's 4 A's) have been described as characteristic symptomatology. Auditory hallucinations, delusions, and experiences of thought insertion, thought withdrawal, thought broadcasting, and thought control are also considered to be characteristic. Genetic, developmental, psychological, and environmental factors have been identified in its pathogenesis. The "positive" (or florid) symptoms of schizophrenia seem to be more responsive to antipsychotic drugs than the "negative" (or deficit) symptoms. Disturbances in the limbic brain, particularly in the *mesolimbic dopaminergic system,* seem to be associated with the psychotic symptoms in schizophrenia.

Psychosis may be conceptualized to be a *final common pathway* of altered consciousness the neurobiological alteration of which may be in

the mesolimbic dopaminergic system. Heredity, early family interactions, and psychological conflicts may provide varying degrees of predisposition, and severe developmental stressors including interpersonal relationships and endocrine changes (as in adolescence) may be precipitating factors. Drugs or endogenous toxins may precipitate psychosis even in persons with little constitutional predisposition to psychosis.

The *evaluation* of psychosis should consider the symptomatology, onset, and associated biological and environmental factors such as the possibility of drugs or toxins and pathogenic environments. Since acutely psychotic patients are fearful and hypervigilant, a quiet, secure, and tranquilizing environment is necessary for optimal evaluation. Before primary psychiatric disorder (or idiopathic psychosis) is diagnosed, the possibility of secondary psychosis should be considered. In secondary psychosis, treatment of the underlying cause is crucial, although symptomatic treatment with antipsychotic drugs may also be necessary initially before the primary cause can be alleviated.

Follow-up psychotherapy to reintegrate the psychotic experience with the patient's ongoing life may also be needed in managing the patient with a secondary psychosis.

In schizophrenia or other chronic primary psychosis, antipsychotic drugs in combination with supportive psychotherapy are indicated on a long-term basis. Education of the family is necessary, as well as their collaboration with the therapist whenever possible. An important consideration in the environmental dimension concerning the psychotic patient is *hospitalization,* which is often necessary during an acute episode to control disruptive, suicidal, homicidal, or otherwise self-destructive behavior.

IMPLICATIONS

For the Patient

Psychosis is a frightening experience for the patient. In secondary psychosis, it is important to be certain that the patient understands the fact that the psychotic symptoms are a part of the medical condition, drug side effect, or other cause and that he/she is not "going crazy." In schizophrenia and other primary psychosis, the patients are usually isolated from others, mistreated, and misunderstood. Thus, the availability of the physician who understands the patient's experiences sets the stage for a long-term trusting and collaborative relationship. Education of the patient concerning the nature of his illness, proposed

treatment, and the effects and possible side effects of medications will help allay irrational fears and prevent a rupture in the therapeutic relationship should any side effects occur.

For the Physician

There is a tendency for general physicians to consider all psychotic behavior to be exclusively in the domain of the psychiatrist. They should recognize that many medical and neurological diseases, drugs and their withdrawal states, and various metabolic toxic states as well as sensory deprivation can cause psychosis, especially in susceptible individuals. A comprehensive evaluation is necessary in psychosis as in depression or anxiety syndromes. Consultation with a psychiatrist concerning the evaluation, differential diagnosis, and management of the psychotic patient is usually advisable, but in the case of secondary psychosis, collaborative management with the primary physician is essential. The physician should be aware of the principles of management of the acutely psychotic patient as might be encountered in many primary-care settings as well as in the emergency room.

For the Community and the Health-Care System

The chronically psychotic patient has been historically stigmatized and isolated from the community. While this trend has been reversed in more recent years through "deinstitutionalization" of chronic patients from state hospitals, there are inadequate facilities for the patients who require long-term residential or protected treatment setting. Education of society in general is needed to provide humane treatment settings for those who require protection and to destigmatize those who have been well rehabilitated through combined effective drug therapy and psychosocial intervention and thus are able to be useful members of the community. It is imperative that society generate and implement plans to correct the problems presented by the growing population of chronically psychotic "street people." At the level of social policy, plans should now be in progress to cope with the increasing numbers of schizophrenic patients that can be anticipated from the apparently increasing incidence rate (Kramer, 1978). Medical schools and hospital training programs should educate future physicians and health-care personnel in comprehensive evaluation and initial management of the psychotic syndrome.

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RECOMMENDED READING

Bowers MB Jr: *Retreat from Sanity—The Structure of Emerging Psychosis*. New York, Human Sciences Press, 1974. This book describes the experiences of a number of patients who develop psychoses. A very readable book with vivid descriptions of the phenomena of psychosis with thought-provoking discussions.
Leigh H (ed): *Psychiatry in the Practice of Medicine*. Menlo Park, California, Addison-Wesley Publishing Co, 1983. Chapter 7, Evaluation and management of psychosis, by Malcolm Bowers, Jr, and Chapter 8, Schizophrenia, by Hoyle Leigh contain practical information concerning the clinical aspects of psychosis and schizophrenia. These chapters complement the basic information provided in this book.
Leigh H, Kramer SI: The psychiatric manifestations of endocrine disease. *Adv Intern Med* **29**:413–445, 1984. An up-to-date review of the psychiatric manifestations of endocrine and metabolic diseases. These manifestations include psychosis, anxiety, depression, and personality change, among others.

Lidz T, Fleck S, Cornelison AR: *Schizophrenia and the Family*. New York, International Universities Press, 1965. This book describes the classic Yale study on the families of schizophrenia that led to the identification of "skewed" and "schismatic" families.

Stevens JR: An anatomy of schizophrenia? *Arch Gen Psychiatry* 29:177–189, 1973. A good review of literature concerning the neurobiology and phenomenology of schizophrenia leading up to the author's conclusions that schizophrenia involves a disorder of a hypothesized dopaminergic and serotonergic "push–pull" servosystem in the limbic striatum.

Strauss JS, Carpenter WT Jr: *Schizophrenia*. New York, Plenum Press, 1981. A readable and concise book summarizing information concerning various aspects of schizophrenia, including epidemiology, etiology, course, and treatment.