

Schizophrenia (DSM-IV-TR #295.1–295.3, 295.90)

Schizophrenia is a chronic, more or less debilitating illness characterized by perturbations in cognition, affect and behavior, all of which have a bizarre aspect. Delusions, also generally bizarre, and hallucinations, generally auditory in type, also typically occur. The original name for this illness, “dementia praecox,” was coined by Emil Kraepelin, a German psychiatrist in the late nineteenth and early twentieth century, whose description of the illness remains a guiding force for modern investigators.

Schizophrenia is a relatively common disorder, with a lifetime prevalence of about 1%. Although the overall sex ratio is almost equal, males tend to have an earlier onset than females, a finding accounted for by the later age of onset in those females who lack a family history of the disease.

ONSET

Although most patients fall ill in late teenage or early adult years, the range of age of onset is wide: childhood onset may occur, and in some instances symptoms may not appear until the sixties.

There may or may not be a prodrome before the actual onset of symptoms. In some cases the “pre-morbid personality” appears completely normal. In others, however, peculiarities may have been apparent for years or even decades before the onset. In cases where the prodrome began in childhood, the history may reveal introversion and peculiar interests. In cases where the prodrome began later, after the patient’s personality was formed, family members may recall a stretch of time wherein the patient “changed” and was no longer “the same.” Prior interests and habits may have been abandoned and replaced by a certain irritable seclusiveness, or perhaps suspiciousness.

The onset of symptoms per se may be acute or insidious. Acute onsets tend to span a matter of weeks or months and may be characterized by confusion or at times by depressive symptoms. Patients may recognize that something is wrong, and they may make some desperate attempts to bring some order into the fragmenting experience of life. By contrast, in cases with an insidious onset the patient may not be particularly troubled at all. Over many months or a year or more, evanescent changes may occur: fleeting whispers, vague intimations, or strange occurrences.

CLINICAL FEATURES

Although the clinical presentation of schizophrenia varies widely among patients, certain signs and symptoms, though present to different degrees, are consistently present, and these include *hallucinations, delusions, disorganized speech and catatonic or bizarre behavior*. “*Negative*” symptoms (e.g., flattening of affect) are often also seen but in some cases are quite mild. Generally, based on the constellation of symptoms present, one may classify any given case of schizophrenia into one of several *subtypes*, namely the *paranoid, catatonic, hebephrenic* (“disorganized”) and

simple subtypes, with a large proportion of patients, however, failing to clearly fit any subtype and being characterized as having “*undifferentiated*” schizophrenia.

Hallucinations are very common in schizophrenia. Patients may hear things, often voices, or they may see things; hallucinations of taste, touch, and smell may also occur. But of all these, the hearing of voices is most characteristic of schizophrenia.

The voices may come from anywhere. They come from the air; God or angels send them. They may come from the television or radio; wiring may emanate the voices. Special devices may be planted in the walls or furniture. Sometimes they are in clothing; often they are localized to certain parts of the body. They come from the bowels, the liver, from “just behind the ear.” They may be male or female; the patient may or may not be able to recognize the identity of the speaker. It is a sibling, or a dead parent. Most often, though, the voices are not recognized as belonging to anyone; they are from strangers. They may be clear and easily understood; sometimes they are deafening and compelling—“everything else is shut out.” At other times they may be soft, “just a mumbling,” indistinct and fading.

What the voices say is extremely varied: however, certain themes are relatively common. Voices may comment on what the patient is doing. Often two voices argue with one another about the patient. Often the voice echoes or repeats what the patient thought. Thoughts are “audible”; they are “heard out loud”; they are repeated on the television.

At times “command hallucinations,” or voices that tell the patient what to do, may be heard. At times these are imperious and irresistible; at other times they are soft, “suggestive only.” Sometimes they command innocuous things; the patient may be directed to shave again. At other times they may command the patient to commit suicide or to hurt others. Usually the commands can be resisted, but not always. Sometimes they are overwhelmingly compelling—“they must be obeyed.”

The patients generally hear only short phrases, perhaps single words. Only very rarely do the voices speak at length in a coherent way. Often the patient is tortured by the voices. Patients may hear threats of death, accusations of unspeakable sins, or announcements that the gallows are being erected.

Rarely patients are encouraged or comforted by the voices. An angel’s voice may proclaim their divinity; seductive voices may whisper enticement; their names may be praised. Unutterable joys are set aside for them. Patients who hear such voices may have a beatific countenance.

Most patients find the voices as real sounding as the voice of any other person. They may talk back to them out loud or may even argue with them. At times when the voices are

unpleasant, the patient may try to drown them out by listening to music or to the television.

In addition to hearing voices patients may also hear sounds, such as a creaking or a rattling of chains. Footsteps or a tapping on the windows is heard. Hissing and whistling also may be heard. Sometimes a ringing of church bells or an explosion is heard. Hammering means the gallows are being constructed. Very rarely the patient may hear music.

Visual hallucinations, though common, play a relatively less prominent part in the clinical picture of schizophrenia than do auditory hallucinations. They may be poorly formed, indistinct, seen only "out of the corner of the eye." They may, however, be vivid and compellingly realistic. Strange people walk the halls; the devil in violent red appears in front of the patient; heads float through the air. Reptilian forms appear in the bath; things crawl in the food; a myriad of insects appear in the bedding. The electric chair is made ready; torturers approach; a chorus of sympathetic angels is seen.

Hallucinations of smell and taste, though not common, may be particularly compelling to the patient. Poison gas is smelled; it seems to be coming from the heating ducts. The patient smells putrefied flesh, so the corpses must be buried nearby. At times inexpressibly beautiful perfumes are appreciated, a seduction seems close at hand.

Tastes, often foul and bitter, may appear on the tongue "from nowhere." Often, however, something is detected in food or drink. Patients detect something brackish, a poisonous or medicinal taste. Patients may refuse all food and drink and declare that they have had enough poison already.

Hallucinations of touch, also known as haptic or tactile hallucinations, are relatively common. Something is crawling on them; a pricking is coming from behind. At night all manner of things are felt. Fluids are poured over the body; a caressing is felt, as are lips on all parts. Electrical sensations may be felt at any time. Sometimes patients may feel things inside their bodies. Their intestines shrivel up; the ovaries burst; the brain is pressed upon.

Delusions are almost universal in schizophrenia. The content of the delusions is extremely varied: patients may feel persecuted; they may have grandiose ideas; all manner of things may refer and pertain to them; thoughts may be broadcast, withdrawn, or inserted into them; they may feel influenced and controlled by outside forces; bizarre, loathsome events may occur. These beliefs may grow in the patient slowly. At first there may be only an inkling, a suspicion; only with time does conviction occur. Conversely, sudden enlightenment may occur; all may be immediately clear. Sometimes patients may have lingering doubts about the truth of these beliefs, but for most they are as self-evident as any other belief. Occasionally patients may argue with those who disagree, but for the most part they do not press their case on the unbeliever. Most often the delusions are poorly coordinated with each other; typically they are contradictory and poorly elaborated. Occasionally, however, they may be systematized, and this is especially the case in the paranoid subtype.

Delusions of persecution are particularly common. There is a conspiracy against the patient; the FBI has coordinated its

efforts with the local police. Plain-clothes officers follow the patient. At times the surveillance is covert. Satellites are used. Listening devices have been placed in the walls; the telephone is tapped. The patient is followed by cars; headlights blink on and off to indicate that capture is imminent. The food is poisoned. Electrical currents are passed through the body at night; internal organs are horribly manipulated during sleep. Tortures are prepared; escape is not possible. Sometimes patients may stoically endure their persecution, and at other times they may fight back. To the patient, this unprovoked assault may be a justifiable defense. Other patients attempt to flee their persecutors and may move to another state. For a time they may feel less insecure, but eventually they see signs that they have been found and again the persecution begins. Some patients attempt to protect themselves against noxious influences by armoring themselves or their apartments. One patient who believed that persecutors sent electrical charges down through the ceiling at night papered the entire ceiling with aluminum foil and for a time felt protected.

Grandiose delusions also occur frequently, often in conjugation with delusions of persecution. Patients are attacked by jealous enemies who seek to bar them from the throne. They are to be exalted; the angel of the Lord has visited them. Millions of dollars are kept secretly away from them. They embark for Washington; the President wishes their advice. Commonly most patients do not act on their delusions; rather they seem content to be comforted and sustained by them. Exceptions do occur, of course. One patient announced a plan for world happiness in a full-page newspaper ad; another sent a letter of advice to the Secretary of State.

Delusions of reference are intimately tied to delusions of persecution or of grandeur. Here patients believe that otherwise chance occurrences or random encounters have special meaning for them. What was done refers to them; it pertains to them. A busboy leaves a particle of food on the table; it is an intentional offense to the patient. The street lights blink on; it is a sign for the persecutors to close in for the final attack. The television newscaster speaks in code; the songs on the radio hold special meaning for the patient. There are no more coincidences in life, no accidental happenings. To the grandiose patient the events of creation are exalting; to the persecuted patient, walking the streets can provoke a terrifying self-consciousness. Everything is pregnant with meaning.

Some patients may develop some peculiarly bizarre beliefs about thinking itself, known as thought broadcasting, thought withdrawal, and thought insertion. In thought broadcasting patients experience thoughts as being broadcast from their heads, as if by electricity. "It is like radio broadcasting," explained one patient. These thoughts may then be picked up by others. Some patients compare it to telepathy; some feel they can receive others' thoughts. "There is mind reading going on," commented one patient. Sometimes the television may broadcast their thoughts back to them. In thought withdrawal the patients' thoughts are removed, taken from them. The mind is left blank. "There are no thoughts anymore," complained one patient. Magnetic devices may be used; the thoughts are never returned.

Patients who experience this symptom of thought withdrawal may concurrently, if they happen to be speaking their thoughts, display the sign known as "thought blocking." Here, patients in the middle of speaking abruptly cease

talking, and this happens precisely because they abruptly find themselves with no thoughts to express. In thought insertion, a phenomenon opposite to that of thought withdrawal occurs. Here patients experienced the insertion of thoughts into their minds. The thoughts are alien, not their own; they were placed there by some other agency. The thoughts are transmitted toward them electrically; they can feel a tingling as they enter their brain. They cannot rid themselves of them.

Allied to the foregoing three delusions are what are known as delusions of influence, or control. Patients experience their thoughts, emotions, or actions to be directly controlled by some outside force or agency. They are made to experience or do these things; they are like robots or automatons, without any independence of will. The influence may emanate from the television broadcast tower; a spell may be cast on them; a massive computer has merged its workings into them. They are not themselves anymore.

Other delusions may occur. In fact any imaginable belief may be held, no matter how fantastic. Angels live in the patient's nose; sulphur is cast on the body during sleep; parents have risen from their graves; all fluids have evaporated from the body. Another delusion is the delusion of doubles, also known as the "Capgras phenomenon," or the delusion of impostors. Here the patient believes that someone, or something, has occupied the body of another. Although the body looks the same and the voice is the same, indeed, for all intents and purposes, it is the same person, yet the patient knows without doubt that it is an impostor. The patient may see subtle signs of it elsewhere; it is part of the conspiracy. The senses cannot be trusted anymore; appearances must be doubted. Doubles may be used for one's spouse or children; no one is immune. The patient must be on guard at all times.

Disorganized speech is the next symptom to consider. Here, we are concerned not so much with the content of the patient's speech, that is to say with delusions, but rather with the form of speech. This "formal thought disorder" is most often characterized as "loosening of associations"; less frequently it is referred to as incoherence or "derailment." The patient's speech becomes illogical; ideas are juxtaposed that have no conceivable connection. A family member may say that the patient "doesn't make sense." At its extreme, loosening of associations may present as a veritable "word salad." An example of loosening of associations follows. A patient was asked to report the previous day's activities; the patient replied, in part, "The sun bestrides the mouse doctor. In the morning, if you wish. Twenty-five dollars is a lot of money! Large faces and eyes. Terrible smells. Rat in the socket. Can there be darkness? Oh, if you only knew!" Here any inner connection among the various ideas and concepts is lost; it is as if they came at random. Or to put it another way the thoughts are no longer "goal-directed"; they no longer cohere in pursuit of a common purpose. If patients are pressed to explain what they mean, they are unable to offer a satisfactory reply. The question may be responded to, but only with another incoherent utterance. Interestingly, also, these patients seem little concerned about their incoherence. They seem oblivious to it and make little if any effort to clarify what they say.

Allied to loosening of associations are neologisms. These are words that occur in the normal course of the patient's speech and that the patient treats as an integral part of it, but that convey no more meaning to the listener than if they were from a long-dead foreign language. To the patient, however, they have as much meaning and status as any other word, but

that meaning is private and inaccessible to the listener. When one patient was offered a cup of coffee, the reply was, "Yes, doctor, thank you. With bufkuf." When asked the meaning of "bufkuf," the patient replied "Oh, you know," and made no further effort to define or explain it.

Catatonic symptoms include negativism, certain peculiar disturbances of voluntary activity known as catalepsy, posturing, stereotypies and echolalia or echopraxia.

Negativism is characterized by a mulish, automatic, almost instinctual opposition to any course of action suggested, demanded, or merely expected. In some cases this negativism is passive: if food is placed in front of patients, they do not eat; if their clothes are set out for them, they do not dress; if a question is asked, they do not answer, and a bizarre scowl may mar the facial expression. In more extreme cases the negativism becomes active, and patients may do the exact opposite of what is expected: if shown to their room, they may enter another; if asked to open their mouths, they may clamp shut; if asked to walk from a burning room, they may walk back in. Such active negativism seems neither thought out nor done for a purpose; rather it appears instinctual, as if the patients themselves had no choice but to do the opposite. Remarkably, in some patients one may see the exact opposite of negativism in the symptom known as "automatic obedience." Here, patients do whatever they are told to do, regardless of what it is. In the nineteenth century, one way to test for this symptom was to tell a patient that you wished him to stick the tongue out so that it might be pierced with a needle. Patients would protrude their tongues and not flinch when pierced by the needle.

Catalepsy, or, as it is also known, waxy flexibility, is characterized by a state of continual and most unusual muscular tension. If one attempts to bend the patient's arm, it is as if one were bending a length of thick metal wire, like soldering wire. Definite resistance, though not great enough to hinder movement, is nevertheless present. The remarkable aspect here is that, as in bending the wire, the patient retains whatever position the limb, or for that matter, the body, is placed in. This happens regardless of whether the patient is instructed to maintain the position or not. In this way the most uncomfortable, grotesque, and strenuous positions may be maintained for hours. This symptom, rarely seen in modern times, was common before the advent of antipsychotic medicines in the middle of the twentieth century. The back wards of state hospitals housed many catatonic patients who held their bodies in positions throughout each nursing shift, day in and day out.

Posturing is said to occur when the patient, for no discernible reason, assumes and maintains a bizarre posture. One may keep the arms cocked; another stood bent at the waist to the side.

Stereotypies are constituted by bizarre, perseverated behaviors. A patient may march back and forth along the same line for hours; another may repeatedly dress and undress. Other persons may be approached again and again, each time being asked the same question. The same piece of paper may be folded and unfolded until it disintegrates. Most patients can offer no reason for their senseless activity. When asked, a patient replied, "it must be so."

Echolalia and echopraxia are said to occur when the patient's behavior mirrors that of the other person, and, importantly,

when this happens automatically, and in the absence of any request. If asked a question the echolalic patient will simply repeat it, sometimes over and over again. The echopraxic patient may clumsily mirror the gestures and posture of the interviewer and, as in echolalia, may continue to do this long after the other person has left, as if uncontrollably compelled to maintain the same activity. Here it is as if the ability to will something independent of the environment has been lost, and the patient is thus left enslaved in a mimicry of whatever is close at hand.

Bizarre behavior may manifest as mannerisms, bizarre affect or an overall disorganization and deterioration of behavior.

Mannerisms are bizarre or odd caricatures of gestures, speech, or behavior. In manneristic gesturing patients may offer their hands to shake with the fingers splayed out, or the fingers may writhe in a peculiar, contorted way. In manneristic speech, cadence, modulation, or volume are erratic and dysmodulated. One patient may speak in a sing-song voice, another in a telegraphic style, and yet another with pompous accenting of random syllables. Overall behavior may become manneristic. Rather than walking, some patients may march in bizarre, stiff-legged fashion.

Bizarre affect appears to represent a distortion of the normal connection between felt emotion and affective expression. Often, facial expression appears theatrical, wooden, or under a peculiar constraint. Patients may report feeling joy, yet the rapturous facial expression may appear brittle and tenuous. Conversely patients may report grief, and indeed tears may be present, yet the emotion lacks depth, as if patients were merely wearing a mask of grief that might disappear at any moment. Inappropriate affect may also be seen. Here the connection between the patient's ideas and affect seems completely severed. A young patient, grief stricken at a parent's funeral, was seen to snicker; another patient, relating the infernal tortures suffered just the night before, smiled beatifically.

Another, very important form of bizarre affect is unprovoked and mirthless laughter. For no apparent reason patients may break into bizarre and unrestrainable laughter. Though appearing neither happy nor amused, the laughter continues. Some patients report that they were unable to not laugh, that the laughter moved itself no matter how they felt.

The overall deterioration of behavior in schizophrenia is what often makes these patients "stand out" in public. Patients become untidy and may neglect to bathe or wash their clothes; the fingernails may become very long. Dress and grooming may become bizarre. Several layers of clothing are often worn, even during the summer. Bits of string or cloth may festoon the patient's hair or garments; makeup may be smeared on. Not uncommonly, paranoid patients shave their heads, and this often reliably predicts an oncoming exacerbation of illness, and also some form of self-mutilation. Patients may pluck out their eyelashes or cut deep gouges in their legs. Some seem to be almost completely analgesic: an eye may be plucked out; pieces of flesh may be bitten off; in extreme cases, self-evisceration may occur, "just to see" what the intestines look like. Although most often no purpose seems to drive this bizarre behavior, at times the patient may offer a reason. One patient wallpapered the walls, ceiling, and floors with aluminum foil "to keep the rays out"; another kept cotton in the ears "to keep the voices away."

Negative symptoms include flattening of affect, alogia (also commonly known as poverty of speech and thought), and avolition.

Flattening of affect, also known, when less severe, as "blunting" of affect, is characterized by a lifeless and wooden facial expression accompanied by an absence or diminution of all feelings. This is quite different from a depressed appearance. In depression patients appear drained or weighted down; there is a definite sense of something there. In flattening, however, patients seem to have nothing to express; they are simply devoid of emotion. They appear unmoved, wooden, and almost at times as if they were machines.

Poverty of speech is said to occur when patients, though perhaps talking a normal amount, seem to "say" very little. There is a dearth of meaningful content to what they say and speech is often composed of stock phrases and repetitions. Poverty of thought is characterized by a far-reaching impoverishment of the entire thinking of the patient. The patient may complain of having "no thoughts," that "the head is empty," that there are no "stirrings." Of its own accord nothing "comes to mind." If pressed by a question the patient may offer a sparse reply, then fail to say anything else.

Avolition, referred to by Kraepelin as "annihilation of the will," is said to be present when patients have lost the capacity to embark on almost any goal-directed activity. Bills are not paid; the house is not cleaned; infants are neither changed nor fed. This is not because patients feel inhibited, lack interest, or suffer from fatigue, but rather because the ability to will an action has become deficient.

Before leaving this discussion of the individual signs and symptoms of schizophrenia and proceeding to a discussion of subtypes, two other symptoms, neither of which fit neatly into the categories employed above, should be mentioned, namely ambivalence and "double bookkeeping."

Ambivalence may render patients incapable of almost any volitional activity. Here, patients experience two opposed courses of action at the same time, and for lack of ability to decide between them, do nothing. One patient stood at the washstand for hours unable to decide whether to shave or to use the toothbrush. This "paralysis of will," however, may at times be easily removed if another person gives directions. In this case an aide simply told the patient to brush his teeth and then put the toothbrush in the patient's hand. Immediately and with peculiar alacrity the patient then set to brushing his teeth. This kind of ambivalence found in schizophrenia is to be distinguished from the indecisiveness seen at times in depression and the "normal" ambivalence that anyone may experience. The depressed patient's inability to embark on decision-making stems more from a lack of energy and initiative; unlike the patient with schizophrenia, the depressed patient generally is not able to act when others make the decision. In normal circumstances competing desires may leave the patient unable to decide. With time, however, a normal person makes a decision because the capacity to do so is not lost. In schizophrenia, however, it is this very capacity that is no longer present.

"Double bookkeeping," a phenomenon first identified by Bleuler, refers to the patient's ability to, as it were, live in two worlds at the same time. On the one hand is the world of voices, visions, and delusions, and on the other hand, and

quite coincident with this psychotic world, is the world as perceived by others. To the patient both worlds seem quite real. For example, a patient may hear a voice as clearly as the voice of the physician and believe it just as real, yet at the same time acknowledge that the physician does not hear it. Or the grandiose patient who fully believed that a coronation was imminent may yet continue to work at a janitor's job and go on doing so, living in two worlds, and feeling little if any conflict between them. A variant of double bookkeeping, known as "double orientation," or "delusional disorientation," may at times mislead the interviewer into thinking that the patient is disoriented. For example, a grandiose patient believed that he was John F. Kennedy, and when asked what year it was replied 1962. Later on, however, when filling out a form, he put down the correct year.

Subtypes of schizophrenia are characterized by particular constellations of symptoms and include the following: paranoid, catatonic, hebephrenic (or "disorganized"), and simple (which has also been referred to as "simple deteriorative disorder"). Patients whose illness does not fall into any of these subtypes are said to have an "undifferentiated" subtype. Subtype diagnosing is not an academic exercise, for, as discussed under Course, the different subtypes may have different prognoses. Furthermore, knowing the subtype allows one to predict with better confidence how any given patient might react in any specific situation.

Paranoid schizophrenia, which tends to have a later onset than the other subtypes, is characterized primarily by hallucinations and delusions. Other symptoms, such as loosening of associations, bizarre behavior, or flattened or inappropriate affect, are either absent or relatively minor. The hallucinations are generally auditory and typically hostile or threatening. The delusions are generally persecutory and referential. Voices warn patients that their supervisors plot against them. They begin to suspect that their co-workers talk about them behind their backs and laugh quietly as they pass by. Newspaper headlines pertain to them; the CIA is involved; meal portions at the factory cafeteria are secretly poisoned, and patients may refuse to eat at work. At times these patients may appeal to the police for help, or they may suffer their slights in rigid silence. Their attitude becomes one of intense, constrained anger and suspiciousness. Occasionally they may move away to escape their persecutors, yet eventually they are "followed." At times they may turn on their supposed attackers, and violent outbursts may be seen.

In paranoid schizophrenia, more so than in the other subtypes, the delusions may be somewhat systematized, even plausible. In most cases, however, inconsistencies appear, which, however, have no impact on the patients. Often, along with persecutory delusions, one may also see some grandiose delusions. Patients believe themselves persecuted not for a trivial reason; others now know that the patient recently acquired a controlling interest in the company. Rarely, grandiose delusions may be more prominent than persecutory ones and may dominate the entire clinical picture. A patient may believe herself anointed with holy oil; trumpets blared forth her appearance as a prophet. She has a message that will save the world, and sets about spreading it.

Catatonic schizophrenia manifests in one of two forms: stuporous catatonia or excited catatonia. In the stuporous form one sees varying combinations of immobility,

negativism, mutism, posturing, and waxy flexibility. One patient curled into a rigid ball and lay on the bed, unspeaking, for days, moving neither for defecation nor urination, and catheterization was eventually required. Saliva drooled from the mouth, and as there was no chewing, food simply lay in the oral cavity and there was danger of aspiration. Another patient stood praying in a corner, mumbling very softly. A degree of waxy flexibility was present, and the patient's arm would, for a time, remain in any position it was placed, only eventually to slowly return to the position of prayer.

In the excited form of catatonia one may see purposeless, senseless, frenzied activity, multiple stereotypies, and at times extreme impulsivity. Patients may scream, howl, beat their sides repeatedly, jump up, hop about, or skitter back and forth. A patient leaped up and attacked a bystander for no reason, then immediately returned to a corner and restlessly marched in place, squeaking loudly. Often speech is extremely stereotyped and bizarre. Patients may shout, declaim, preach, and pontificate in an incoherent fashion. Words and phrases may be repeated hundreds of times. Typically, despite their extreme activity, these patients remain for the most part withdrawn. They often make little or no effort to interact with others; they keep their excitement to themselves, perhaps in a corner, perhaps under a bed. Rarely Stauder's lethal catatonia may occur. Here, as the excitation mounts over days or weeks, autonomic changes occur with hyperpyrexia, followed by coma and cardiovascular collapse.

Although some patients with catatonic schizophrenia may display only one of these two forms, in most cases they are seen to alternate in the same patient. In some cases a form may last days, weeks, or longer, before passing through to the other. In other cases, however, a rapid and unpredictable oscillation from one form to another may occur. A stuporous patient suddenly, without warning, jumped from his bed, screamed incoherently, and paced agitatedly from one wall of the room to another. Then, in less than an hour, the patient again rapidly fell into mute immobility.

Hebephrenic schizophrenia tends to have an earlier onset than the other subtypes and tends to develop very insidiously. Although delusions and hallucinations are present, they are relatively minor, and the clinical picture is dominated by bizarre behavior, loosened associations, and bizarre and inappropriate affect. Overall the behavior of these patients seems at times a caricature of childish silliness. Senselessly they may busy themselves first with this, then with that, generally to no purpose, and often with silly, shallow laughter. At other times they may be withdrawn and inaccessible. Delusions, when they occur, are unsystematized and often hypochondriacal in nature. Some may display very marked loosening of associations to the point of a fatuous, almost driveling incoherence.

Simple schizophrenia has perhaps the earliest age of onset, often first beginning in childhood, and shows very gradual and insidious progression over many years. Delusions, hallucinations, and loosening of associations are sparse, and indeed are for the most part absent. Rather the clinical picture is dominated by the annihilation of the will, impoverishment of thought, and flattening of affect. Gradually over the years these patients fall away from their former goals and often become cold and distant with their former acquaintances. They may appear shiftless, and some are accused of laziness. Few thoughts disturb their days, and they may seem quite content to lie in bed or sit in a darkened room all day. Occasionally some bizarre behavior or a fragmentary

delusion may be observed. For the most part, however, these patients do little to attract any attention; some continue to live with aged parents; others pass from one homeless mission to another.

Undifferentiated schizophrenia is said to be present when the clinical picture of any individual case does not fit well into one of the foregoing subtypes. This is not uncommonly the case, and it also appears that in some instances the clinical picture, which initially did “fit” a subtype description, may gradually change such that it no longer squares with one of the specific subtypes: this appears to be more common with the catatonic and hebephrenic subtypes than with paranoid or simple schizophrenia.

Before leaving this discussion of subtypes, it is appropriate to briefly discuss another proposal for subdividing schizophrenia, which is said by some to have more predictive and heuristic value than the classical subtyping just discussed. Two subdivisions are proposed: “good prognosis,” “reactive,” or “type I” schizophrenia, and “poor prognosis,” “process,” or “type II” schizophrenia. The contrasting characteristics of these two subdivisions are outlined in [Table 67-1](#). “Positive” symptoms are hallucinations, delusions and disorganization of speech, whereas “negative” symptoms consist of flattening of affect, poverty of thought and avolition.

Although this “good prognosis”/“poor prognosis” scheme is useful, many patients do not fit neatly into type I or type II but rather evidence a mixture of features of both types. Indeed, whether this typology represents an advance over the old “classical” subtypes is not yet clear. One might, for example, argue that the type I patient

TABLE 67-1 -- Type I and Type II Schizophrenia

	Type I	Type II
Premorbid personality	Normal	Poor adjustment
Age of onset	Late, often adult years	Early
Mode of onset	Acute	Gradual and insidious
Symptoms associated with onset	Confusion and depression	Few
Kind of symptoms	Positive	Negative
Ventriculomegaly on CT scan	Absent	Present
Course	More favorable	Unfavorable

has paranoid schizophrenia and the type II patient has simple schizophrenia. Further research is needed.

COURSE

Schizophrenia is a chronic disease, and, in most cases, exhibits one of two overall patterns. In one, the course of symptoms is waxing and waning, whereas in the other there is a more or less stable chronicity.

The waxing and waning course is marked by exacerbations and partial remissions. The pattern of these changes is often quite irregular, as are the durations of the exacerbations and partial remissions, ranging from weeks, to months, or even years. Some patients, during episodes of partial remission of the “positive” symptoms, may develop a sustained and pervasive depressed mood accompanied by typical vegetative symptoms. This condition, often referred to as a “postpsychotic depression,” increases the risk of suicide. Importantly, such a postpsychotic depression should not be confused with the frequent, transient, and isolated depressive symptoms seen during an exacerbation of the other symptoms of the illness.

At times, exacerbations may be precipitated by life stresses; however, at other times they simply happen. Among the stresses that can precipitate exacerbations, living in a family with high “expressed emotion” is important. Such family members tend to be intrusive, critical, and over-involved, and patients exposed to such an onslaught, even when provided with optimum medical treatment, are likely to relapse. Some patients experience this fluctuating course for their entire lives; in many others, however, after 5 to 20 years, this pattern gives way to one of stable chronicity.

The stable chronicity seen in some patients may appear in some cases after the initial onslaught of symptoms seen at the onset of the disease has dampened, and in others, as for example those with simple schizophrenia, it may be apparent from the onset itself. Over long periods of time, patients with this course may show very slow progression until the disease eventually “burns out” leaving them in a deteriorated state.

The classical subtype diagnosis may allow for some prediction as to course. Those with paranoid or catatonic schizophrenia tend to pursue a fluctuating course, and of the two the eventual outcome appears to be worse for the catatonic subtype. The hebephrenic and simple subtypes tend to pursue either a stable or progressively deteriorating chronicity, and of the two the simple subtype seems to often undergo the greatest deterioration.

As noted earlier one may also make predictions as to course by subdividing cases into Type I and Type II, with the Type I cases showing a waxing and waning course and the Type II cases undergoing a more or less chronic deterioration.

Before leaving this discussion of the course of the disease, it is appropriate to consider whether or not schizophrenia, in the natural course of events, and in the absence of antipsychotic treatment, ever undergoes a full and complete remission. Certainly, far-reaching remissions have been documented; indeed, in many cases patients may appear at first glance to be recovered, and if one’s definition of “recovery” or “remission” is broad enough, as is the case in many published studies, one might say that a remission did occur. However, on closer inspection one may generally find lingering residual symptoms in these “recovered” patients, such as fleeting hallucinations, odd thoughts, mannerisms or a certain poverty of thought. Thus, although “social” recoveries in the absence of treatment, although rare, do occur, it is very unlikely that, in the natural course of the disease, there is ever a *restitutio ad integrum*.

COMPLICATIONS

Academic and business failure are common; most patients are incapable of sustaining intimate relationships. About half attempt suicide, and about 10% succeed. Most suicides occur early in the course of the illness; depressive symptoms, as are seen in postpsychotic depression, male sex and unemployment increase the risk.

A not uncommon, but often overlooked, complication is hyponatremia. Some patients become “compulsive water drinkers”; however, the hyponatremia appears not to be caused solely by excessive intake of water. The renal tubule cells appear to be hypersensitive to ADH, leading to a urine osmolality that is less than maximally dilute relative to the degree of hyponatremia. Symptoms are as described in the chapter on hyponatremia.

ETIOLOGY

CT and MRI scans have conclusively demonstrated ventricular dilation and cortical atrophy in schizophrenia; furthermore there is a good correlation between the degree of atrophy of the posterior portion of the left superior temporal gyrus and the severity of auditory hallucinations and speech disorganization. Some studies have also demonstrated atrophy of the thalamus; however, these findings are not as robust. Enlargement of the basal ganglia, demonstrated in earlier studies, now appears to be an artifact of antipsychotic treatment. Interestingly, the ventricular dilation and cortical atrophy are present at the onset of the disease, and some studies have also suggested that they may progressively worsen over time.

Neuropathologic findings in schizophrenia have been notoriously difficult to replicate; however, certain findings appear to be standing the test of replication. First, it appears that there is neuronal loss in the mediodorsal nucleus of the thalamus. Second, there is, in the subcortical white matter in the frontal and temporal lobes, an increased number of residual neurons, neurons which, in the normal course of development, either undergo apoptotic death or migrate on through the white matter to settle in the overlying cortex.

Inheritance plays a very large part in schizophrenia. The lifetime prevalence of schizophrenia, as noted earlier, is about 1%; in first-degree relatives of patients, however, it is about 5%. Furthermore, whereas among dizygotic twins the concordance rate is from 10 to 15%, the concordance in monozygotic twins is roughly 50%. These findings, of course, could also be explained on the basis of environmental influence; however, adoption studies have clearly demonstrated that the influence here is genetic. Despite this evidence for inheritance; however, it has been extraordinarily difficult to conclusively identify any specific genes or establish linkage for schizophrenia. This being said, however, there is some evidence for linkage to loci on chromosomes 6, 8 and 22.

Taking these findings together, it is not unreasonable to consider that schizophrenia is a neurodevelopmental disorder characterized by defective neuronal migration, leading to thalamic and cortical atrophy, and that this defect is, at least in part, determined genetically. Environmental factors, however, are clearly at work, given that the monozygotic concordance rate is only 50%.

Of the multiple environmental factors investigated, there is reasonably good evidence for two. First, it appears clear that patients with schizophrenia are more likely to have had a difficult birth or to have suffered obstetrical trauma, and such events are capable of disrupting neuronal migration, which continues long after birth. Second, it also appears that there is an excess of winter births in patients with schizophrenia. Clearly, many factors could account for this, but one that has stood out has been the possibility of a seasonal viral infection that could have affected patients in utero. Fetal viral infections can clearly distort neuronal migration, and it has been speculated that what is inherited in schizophrenia is a vulnerability of neurons to viruses which, in normal circumstances, are not neurotropic.

This “neurodevelopmental” theory of the etiology of schizophrenia, though reasonable in light of the evidence, is not without controversy, and the reader is encouraged to watch the literature closely.

DIFFERENTIAL DIAGNOSIS

Given the broad range of symptoms that may occur in schizophrenia, it is not surprising that the differential diagnosis is quite large.

A manic episode of a bipolar disorder may “cross-sectionally” appear similar to hebephrenia, excited catatonia, or paranoid schizophrenia. If, however, one has an accurate history, the diagnosis is relatively straightforward. In schizophrenia, which is a chronic illness, psychotic symptoms almost always precede the excitement; in mania, which occurs as an episodic illness, however, affective symptoms appear first, and psychotic ones only appear as the patient progresses into the acute stage of mania and on up to the height of a manic episode, delirious mania. When a history is lacking, certain symptomatic differences may allow for a differential diagnosis. The mood and affect of a patient with mania are typically “infectious” and well developed. By contrast, the mood of an excited hebephrenic is one of silly, shallow hilarity, which, rather than provoking laughter, might leave the interviewer with a sense of puzzlement. Furthermore the activity of a manic patient is outgoing and extroverted; this is in striking contrast to an excited catatonic who, though hyperactive, remains withdrawn and may actually avoid contact with others. Finally, the irritable manic is “on the attack,” whereas the agitated patient with paranoid schizophrenia is “on guard.” Both are dangerous, the manic recklessly so, the schizophrenic only if approached in what appears to the patient to be a hostile manner.

During depressive episodes, occurring either as part of a major depression or bipolar disorder, one may see delusions and hallucinations. Here, however, the psychotic symptoms are preceded by the depressive ones and only occur when the depressive symptoms are severe. By contrast, whereas depressive symptoms may occur in schizophrenia, no invariable relationship exists between them and the psychotic symptoms. In schizophrenia one sees psychotic symptoms both when the patient is depressed and also when free of depressive symptoms. Should this history regarding the course of the depression be unavailable, certain “cross-sectional” features may assist in the differential diagnosis. Delusions, when they appear in a depressive episode, tend to be “mood congruent”; that is, they make sense given the way the patient is feeling. Conversely, in schizophrenia the

delusions tend to be bizarre and generally unrelated to the mood.

The differential diagnosis between a catatonic stupor and a psychomotorically retarded depression may be facilitated if the patient is closely observed for movement over an extended period of time. In stupor one may occasionally see rapid movements as the negativism briefly remits; by contrast, in a psychomotorically retarded depression all movements are always slowed down.

The differential diagnosis between schizoaffective disorder and schizophrenia rests on a thorough and accurate history of the course of the illness. Both illnesses are characterized by chronic psychotic symptoms, such as hallucinations and delusions; however, in schizoaffective disorder one also sees the occurrence of full and sustained affective episodes (depressive, manic or mixed manic) during which, importantly, one also sees an exacerbation of the pre-existing psychotic symptoms. Although schizophrenia may also be marked by mood disturbances, these tend to be transient and not severe. One exception to this is the post-psychotic depression, described earlier under "Course," which is sustained and may be quite severe. Here, however, there is not an exacerbation of psychotic symptoms and it is this which distinguishes the depression of post-psychotic depression in schizophrenia from the depression seen in schizoaffective disorder.

As alcoholism and schizophrenia not uncommonly occur in the same patient, the differential diagnosis between alcohol hallucinosis or alcoholic paranoia and schizophrenia may be difficult. Certainly, if the psychotic symptoms began before the patient started to drink or relatively early on in the drinking career, then the diagnosis of schizophrenia would be favored. When, however, psychotic symptoms begin after many years of alcoholism and repeated episodes of delirium tremens, the differential between paranoid schizophrenia and alcohol hallucinosis or alcoholic paranoia may be difficult. The presence of mannerisms, stereotypies, or loosened associations favor schizophrenia; a remission of symptoms after 6 months or more of abstinence would favor alcohol hallucinosis or alcoholic paranoia.

Delusional disorder, or paranoia, is distinguished from paranoid schizophrenia by the systematization and "plausibility" of the delusions in paranoia and by the absence of symptoms typical of schizophrenia, such as loosening of associations, mannerisms, and stereotypies. Hallucinations, though they may appear in paranoia, play only a minor role in contrast with paranoid schizophrenia, where they are often abundant.

Paranoid personality disorder may be very difficult to distinguish from paranoid schizophrenia. Certainly the presence of delusions or hallucinations would favor a diagnosis of schizophrenia; however, in both disorders patients may be very guarded and secretive, and the interviewer may not be able to reliably determine if psychotic symptoms are present. In such instances the overall demeanor and behavior of the patient may help. The patient with paranoid personality disorder presents a fully integrated and internally consistent behavioral repertoire; indeed one may get the sense of a seamless fabric of anger and resentment. By contrast, the patient with paranoid schizophrenia often displays some fragmentation: affect may be somewhat

dysmodulated or inappropriate; associations may be somewhat loosened; a mannerism may be seen.

Schizotypal personality disorder is distinguished from most of the subtypes of schizophrenia by the absence of psychotic symptoms. Differentiation from simple schizophrenia may not be possible on the basis of "cross-sectional" data. The course of the illness, however, enables a differential diagnosis: the patient with schizotypal personality disorder presents a stable clinical picture over time, whereas the patient with simple schizophrenia presents a clinical picture marked by progressive deterioration.

Patients with borderline personality disorder when under great stress may occasionally experience hallucinations and delusions. By contrast, in schizophrenia these symptoms, though exacerbated by stress, are present also in calm times.

Obsessions and compulsions may occasionally be seen in the prodrome to schizophrenia; the eventual appearance of unrelated psychotic symptoms, however, clarifies their differential import.

Autism may at times be difficult to distinguish from schizophrenia of childhood onset. Certainly, if symptoms appear before the age of 3 years, autism is the more likely diagnosis, as the earliest noted age of onset of schizophrenia is 5 years of age. The presence of hallucinations and delusions indicates schizophrenia; their absence, however, does not rule against schizophrenia, as young children may not be able to report such symptoms. Conversely the presence of typical autistic symptoms, such as gaze avoidance or a "flapping" tremor, argues strongly for a diagnosis of autism.

Mental retardation and schizophrenia are two not uncommon illnesses, and their coincidence in the same patient is not rare. Such "engrafted" schizophrenia may be heralded by a deterioration in a previously stable condition or by the appearance of delusions, hallucinations, or loosening of associations, features that are not seen in straightforward mental retardation. However, in patients with severe or profound mental retardation, such symptoms may not be ascertainable at all. In such instances close examination should be made for signs such as bizarre or flattened affect, echopraxia, and waxy flexibility.

Intoxication with phencyclidine, stimulants, or cocaine may produce psychotic symptoms; the prior history of substance use, a compatible urine or serum toxicology, and the remission of symptoms with enforced abstinence make the diagnosis.

Folie à deux, as described in that chapter, is distinguished by the presence of a "dominant" partner who does have schizophrenia, and by recovery with forced separation of the patient from this dominant partner. Malingering or factitious illness may at times cause diagnostic difficulty. Certainly the presence of mannerisms and similar symptoms would argue for schizophrenia because these symptoms are generally not known to the public at large and in any case are very difficult to fake.

Psychosis may also occur secondary to a large number of neurologic disorders, as discussed in the chapter on Secondary Psychosis. Of these, the most likely to be

confused with schizophrenia are the chronic interictal psychosis, Huntington's disease, Wilson's disease and metachromatic leukodystrophy.

Before leaving this section on differential diagnosis, a word is in order regarding the putative entities known as "brief psychotic disorder" and "schizophreniform disorder," each of which are discussed in more detail in their own chapters. Both these illnesses are characterized by symptoms essentially identical to those which may be seen in schizophrenia: where they differ is in their supposed course. Patients who experience a full and complete remission of their psychosis in less than one month are said to have brief psychotic disorder and those whose psychosis persists past one month but fully remits before six months are said to have schizophreniform disorder. There is debate as to whether either disorder actually exists. Certainly there are patients with psychosis who remit fully with antipsychotic treatment, but whether there are patients who remit fully and completely, without a lingering trace of psychosis, without treatment, has not been demonstrated conclusively. Although by convention a diagnosis of schizophrenia is withheld until the patient has been ill for at least six months, one should always be prepared to revise the diagnosis of brief psychotic disorder and schizophreniform disorder as the months go by and the patient, as is almost always the case, remains ill.

TREATMENT

The treatment of schizophrenia almost always involves the use of an antipsychotic drug. Patients may also be seen in supportive psychotherapy, either on an individual basis or in a group, and in social skills training groups. A "token economy" approach may be required for severely debilitated patients. Families may also be seen, not only for educational purposes, but also to enable them to lessen the kinds of family interactions that tend to be followed by relapse. Assistance may be required to enable the patient to secure housing and employment.

The antipsychotics may be broadly divided into two groups, namely "first generation," or "typical" drugs, and "second generation," or "atypical" drugs. All of these agents are covered in detail in their respective chapters in the Section on Psychopharmacology, and discussion here will be limited to only a few. Commonly used first generation antipsychotics include haloperidol, fluphenazine and chlorpromazine. There is an ever growing number of second generation drugs, which now includes clozapine, olanzapine, risperidone, quetiapine, ziprasidone and aripiprazole. Clozapine, olanzapine and risperidone are probably all therapeutically superior to the first generation agents (especially with regard to negative symptoms), and, in the cases of olanzapine and risperidone, are generally better tolerated. Although quetiapine, ziprasidone and aripiprazole are also in general better tolerated than the first generation agents, it is not as yet clear that they are therapeutically superior.

All other things being equal, it is probably best to begin treatment with a second generation agent, such as olanzapine or risperidone; clozapine, although therapeutically superior to either of these, has such severe side-effects that it is generally held in reserve for treatment-resistant patients, as discussed below. The other second generation agents (quetiapine, ziprasidone and aripiprazole) cannot be as strongly recommended: although they are in general better-tolerated than the first generation drugs, there is not yet good evidence

for their therapeutic superiority over the first generation agents. The choice between olanzapine and risperidone is not easy, as it is not as yet clear whether one is therapeutically superior to the other. In terms of side effects, olanzapine carries the risks of weight gain, diabetes and hyperlipidemia, whereas risperidone is more likely than olanzapine to cause extrapyramidal side effects such as akathisia or parkinsonism. Olanzapine may be used in doses ranging from 10 to 30 mg daily, and in the case of risperidone a dose of 4 mg daily appears optimal.

In some cases, it may be appropriate to use a first generation agent. Cost is an issue for many patients: the oral preparations of the first generation agents, unlike the second generation ones, are all available in generic form, and the cost differences can be very large. Another issue is a history of a good response: for patients who have done perfectly well on a first generation agent, there may be little reason to change. Finally, there is the availability of two of the first generation agents, haloperidol and fluphenazine, in long-acting injectable decanoate preparations: noncompliance with oral medications is very common in schizophrenia, and in some cases the use of a long-acting injectable is the only way to maintain the patient in the community. Although a long-acting injectable form of risperidone has been developed, it has not, as of this writing, been released in the United States; if it is released, then this reason for using a first generation agent may well disappear. Choosing among the first generation agents is simplified, as discussed in that chapter, by dividing them into "low potency" drugs, such as chlorpromazine, and "high potency" drugs, such as haloperidol or fluphenazine. Low potency agents tend to cause sedation, hypotension and anticholinergic effects (e.g., dry mouth, blurry vision, constipation, urinary hesitancy), but have a lower tendency to cause extrapyramidal side effects (e.g., parkinsonism, dystonia, akathisia); high potency drugs, by contrast, exhibit a high potential for extrapyramidal side effects, but are relatively benign otherwise. Sometimes the choice between low and high potency drugs may be made on the basis of side effects: for example, a patient with postural dizziness probably should not be given a low potency agent that might exacerbate postural hypotension; on the other hand a patient in traction might not tolerate a dystonia very well at all and might be better served by a low potency agent. In cases where side effects are not a compelling issue, then using either haloperidol or fluphenazine is probably best, as this would facilitate transition to a decanoate form should that become necessary.

Once an antipsychotic has been chosen, it should be given at an adequate trial, not only in terms of duration but also dose. In general, presuming the dose is adequate, two weeks is long enough to see an initial response. Adequate doses for risperidone and olanzapine were discussed earlier; doses for the other atypicals are discussed in the respective chapters. Adequate oral doses for haloperidol and fluphenazine are 5 to 15 mg/d, and for chlorpromazine 100–300 mg. Obviously, lower doses are indicated for the elderly and frail and for patients with significant hepatic dysfunction or for those with significant general medical illnesses. In some cases, in particular with agitated or assaultive patients, one may have to use adjunctive treatments at the start, and continue them until the antipsychotic has had a chance to take effect. Divalproex, given in a loading dose of 15 to 20 mg/kg/d for otherwise healthy patients, is effective, as is use of as needed doses of a benzodiazepine, such as lorazepam at 2 mg orally roughly every four hours. In some cases one may also simply use much higher doses of the antipsychotic; however, this always incurs the risk of worse side effects. Although

experience with high dose risperidone and olanzapine is limited, haloperidol has been given in doses of 60 mg daily and chlorpromazine in doses of up to 3000 mg daily. These issues are more thoroughly discussed in the chapter on Rapid Pharmacologic Treatment of Agitation.

If the patient gets an initial good response, then the agent may be continued as maintenance treatment, as discussed below. If the response is only partial, but otherwise promising, one may continue treatment for an additional four weeks. At that point, if the response is good one may move to maintenance treatment. If the response is less than adequate, then one should first review the case, and make sure the diagnosis is correct. Assuming the diagnosis is correct, then one should consider significantly increasing the dose, and observing the patient for another couple of weeks. If the response is still inadequate or if side effects are unacceptable, then one may consider switching to another agent. Certainly, if the patient had not been given a trial of risperidone or olanzapine, one of these should be considered, and if one of these two had been used and found wanting, then the other should be given a trial. A good response is followed by maintenance treatment; an inadequate response should prompt consideration of clozapine.

Clozapine is superior to every other antipsychotic, and may succeed where all the others have failed. Enthusiasm for its use, however, is tempered by its many side effects, most notably the risk of agranulocytosis and the necessity for routine CBCs. Details regarding clozapine are covered in the respective chapter.

Maintenance treatment is appropriate for almost all patients. Initially, patients should be maintained on a dose similar, if not identical, to that which initially provided relief. Once patients are stable in the community, cautious dose adjustments may be considered once every three or four months. As noted earlier, in many cases the course of schizophrenia is characterized by a waxing and waning of symptoms, and in these cases, it is appropriate to attempt to "titrate" the dose to the underlying severity of the disease. Furthermore, some patients may become so distressed at side effects that they find a mild increase in the symptoms of the disease a reasonable price to pay for a reduction in the intensity of side effects. Should patients become almost symptom free, some psychiatrists may elect to decrease the dose in a step-wise fashion every 3 months until either symptoms reappear or drug discontinuation is achieved, with the patient being left with only mild, residual symptoms. Unfortunately, however, even when patients and family members are instructed regarding the "early warning signs" of relapse, troublesome symptom recurrence is common; therefore, chronic maintenance treatment, albeit with low doses, may be better than intermittently attempting trials at drug discontinuation. In general, over long term follow-up it is appropriate to keep the dose overall as low as possible to reduce the risk of tardive dyskinesia. This side effect, discussed in its own chapter, occurs in a significant minority of patients who take antipsychotics over the long haul, and hence the physician must always be alert to the emergence of any abnormal involuntary movements.

Should a post-psychotic depression occur, it is appropriate to give an antidepressant, such as an SSRI, and to treat the patient in the same fashion as one would acutely treat a depressive episode that occurred in a major depression, as described in the chapter. One must always be careful, however, to distinguish between a depression and a

antipsychotic-induced bradykinesia (or akinesia), as may be seen especially when high potency first generation agents are used. Bradykinesia, as discussed in the chapter on first generation neuroleptics, when occurring in isolation, may appear similar to a psychomotorically-retarded depression. ECT may also be helpful in post-psychotic depression. Interestingly, ECT is also at times effective in catatonic schizophrenia, whether excited or stuporous, regardless of whether depressive symptoms are present.

Before leaving the subject of antipsychotic treatment, a word is in order regarding akathisia. This extrapyramidal side-effect, also discussed in more detail in the chapter on first generation antipsychotics, may "masquerade" as an exacerbation of psychosis, and if this diagnosis is missed then the clinician, mistakenly believing that the exacerbation of psychotic symptoms is resulting from an exacerbation of the underlying illness, might go ahead and increase the dose of the antipsychotic, thus increasing the akathisia and initiating a downwardly spirally therapeutic misadventure.

After antipsychotics have brought more florid symptoms under control, patients may profit from cognitive-behavioral therapy and, if still in contact with family, family therapy. Insight or psychoanalytically oriented psychotherapy is contraindicated. Not only does it not help, but also indeed some patients may worsen while being thus treated.

When families are involved, psychoeducationally oriented multiple-family groups are very helpful. Parents should be clearly told that they did not "cause" the illness and that no connection exists between child-rearing or early childhood events and the appearance of schizophrenia. When family members are critical, intrusive, and over-involved, behavioral family therapy aimed at reducing these behaviors is very helpful and reduces the number of hospital stays required.

Hospitalization is required for most patients at some point in their illness, and in some cases, repeated admissions occur. Involuntary admission may be required and may be lifesaving. Partial hospitalization services are available in many areas and have enabled many former "back ward" patients to survive and maintain themselves in the community.

BIBLIOGRAPHY

- Andreasen NC. Negative symptoms in schizophrenia: definition and reliability. *Archives of General Psychiatry* 1982;39:784–788.
- Barta PE, Pearlson GD, Powers RE, et al. Auditory hallucinations and smaller superior temporal gyrus volume in schizophrenia. *The American Journal of Psychiatry* 1990;147:1457–1462.
- Black DW, Boffeli TJ. Simple schizophrenia: past, present and future. *The American Journal of Psychiatry* 1989;146:1267–1273.
- Byne W, Buchsbaum MS, Mattiace LA, et al. Postmortem assessment of thalamic nuclear volume in subjects with schizophrenia. *The American Journal of Psychiatry* 2002;159:59–65.

- Cahn W, Pol HE, Lems EB, et al. Brain volume changes in first-episode schizophrenia: a 1-year follow-up study. *Archives of General Psychiatry* 2002;59:1002–1010.
- Csernansky JG, Mahmoud R, Brenner R, et al. A comparison of risperidone and haloperidol for the prevention of relapse in patients with schizophrenia. *The New England Journal of Medicine* 2002;346:16–22.
- Fenton WS, McGlashan TH. Natural history of schizophrenia subtypes. I. Longitudinal study of paranoid, hebephrenic, and undifferentiated schizophrenia. *Archives of General Psychiatry* 1991;48:969–977.
- Kane JM, Davis JM, Schooler N, et al. A multidose study of haloperidol decanoate in the maintenance treatment of schizophrenia. *The American Journal of Psychiatry* 2002;159:554–560.
- Kasai K, Shenton ME, Salisbury DF, et al. Progressive decrease of left superior temporal gyrus gray matter volume in patients with first-episode schizophrenia. *The American Journal of Psychiatry* 2003;160:156–164.
- Kelleher JP, Centorrino F, Albert MJ, et al. Advances in atypical antipsychotics for the treatment of schizophrenia: new formulations and new agents. *CNS Drugs* 2002;16:249–261.
- Marder SR. Integrating pharmacological and psychosocial treatments for schizophrenia. *Acta Psychiatrica Scandinavica* 2000;102(Suppl):87–90.
- Pilling S, Bebbington P, Kuipers E, et al. Psychological treatments in schizophrenia: I. Meta-analysis of family intervention and cognitive behavior therapy. *Psychological Medicine* 2002;32:763–782.
- Pilling S, Bebbington P, Kuipers E, et al. Psychological treatments in schizophrenia: II. Meta-analyses of randomized controlled trials of social skills training and cognitive remediation. *Psychological Medicine* 2002;32:783–791.
- Rioux L, Nissano J, Lauber K, et al. Distribution of microtubule-associated protein MAP2-immunoreactive interstitial neurons in the parahippocampal white matter in subjects with schizophrenia. *The American Journal of Psychiatry* 2003;160:149–155.
- Sawa A, Snyder SH. Schizophrenia: diverse approaches to a complex disease. *Science* 2002;296:692–695.
- Shenton ME, Kikinis R, Jolesz FA, et al. Abnormalities of the left temporal lobe and thought disorder in schizophrenia: a quantitative magnetic resonance imaging study. *The New England Journal of Medicine* 1992; 327:604–612.
- Thakar GK, Carpenter WT. Advances in schizophrenia. *Nature Medicine* 2001;7:667–671.
- Volavka J, Czobor P, Sheitman B, et al. Clozapine, olanzapine, risperidone, and haloperidol in the treatment of patients with chronic schizophrenia and schizoaffective disorder. *The American Journal of Psychiatry* 2002;159:255–262.