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Schizophrenia

WHAT IS SCHIZOPHRENIA?

Schizophrenia is now known to be a disease of the brain, just like Alzheimer's and Parkinson's diseases. The term schizophrenia was first used in 1911 by Eugen Bleuler, a Swiss psychiatrist, to categorize patients whose thought processes and emotional responses seemed disconnected. The term schizophrenia literally means split mind, and many people still believe incorrectly that the condition causes a split personality (which is an uncommon problem involving dissociation).

Schizophrenia is characterized by a cluster of symptoms that typically includes the following:

- Delusions.
- Hallucinations.
- Disordered thinking.
- Emotional unresponsiveness.

Because symptoms of schizophrenia arise from various physical processes and respond differently to treatments, some experts recommend classifying the disease based on the presence of the following symptom groups:

- Negative symptoms (including apathy and social withdrawal).
- Psychotic symptoms.
- Disordered thinking. Some experts group psychotic and disordered thinking into a single category called positive symptoms.

The disease is complicated by the fact that although a schizophrenic patient may have more than one symptom, he or she rarely has all of them. Symptoms also often go into remission. As the mechanisms in the brain that lead to schizophrenia are being discovered, researchers are attempting to define more accurate ways of describing the disease as it relates to the biologic processes that cause them.

Negative Symptoms

Negative symptoms reflect the following states:

- Diminishment of the self.
- Lack of emotions.
- Colorless speaking tones.
- A general loss of interest in life and the ability to experience pleasure. One study reported that patients were able to experience unpleasant odors in a normal way, but not pleasant ones.
- Inappropriate affect (a condition in which the patient displays inappropriate reactions to an event, such as laughing hysterically over a loss).

Often certain negative symptoms (e.g., lack of responsiveness and poor sociability) appear in childhood as the first indications of schizophrenia. Certain imaging techniques suggest that these findings are based on biologic changes in specific parts of the brain. In many patients, however, negative symptoms do not appear until after

positive symptoms develop. Negative symptoms tend to be more common than positive symptoms in older patients and typically persist after positive symptoms have been treated.

Psychotic Symptoms

Psychotic symptoms, particularly delusions and hallucinations, are the most widely recognized manifestations of schizophrenia.

- *Hallucinations*. Hallucinations are the experiences of seeing, hearing, tasting, smelling, or feeling things that don't exist. Auditory hallucinations are false senses of sound, such as hearing voices that go unheard by others. They are the most common psychotic symptoms, affecting about 70% of patients. One study even reported that schizophrenic patients who had been profoundly deaf since birth were able to describe convincing experiences of hearing voices. Patients describe the voices as occurring all about them and that they are impossible to filter out or ignore.
- *Delusions*. Delusions are fixed, false beliefs. They can be *bizarre* (e.g., invisible aliens have entered the room through an electric socket) or *nonbizarre* (e.g., unwarranted jealousy, or the paranoid belief in being persecuted or watched).

After the initial event, psychotic symptoms usually occur episodically and are interspersed with periods of remission. They typically occur in men between the ages of 17 and 30 and in women between the ages of 20 and 40.

Cognitive Impairment (Disordered Thinking)

The symptoms of cognitive impairment and disordered thinking include the following and may occur before other symptoms of schizophrenia:

- A lack of attention.
- Impaired information processing and an aberrant association between words and ideas. Sometimes this condition is so extreme that speech becomes incoherent and is referred to as "word salad." Patients may connect words because of similarity of sound, rather than by meaning, a condition known as "clang associations."
- Memory impairment. In keeping with other aspects of disordered thinking, memory impairment in schizophrenia is likely to involve the inability to connect an event with its source into a complete and whole memory. For instance, a patient may recall and even feel a familiarity with a specific event but be unable to remember where, when, or how it took place.
- Backward masking dysfunction. This is a trait in which a distraction causes a person to forget a preceding event. It might be an important symptom and a marker of schizophrenia even in people with normal working memories. As an example of a test used to diagnose this trait, the patient is given an item to look at, such as four letters on a computer screen. The screen goes blank and another image (called a masking stimulus) appears, such as four broken letter fragments. The patient is then asked to type in the original letters. Both symptomatic and presymptomatic patients commonly have problems with this particular exercise.

In summary, people with schizophrenia do poorly on mental tasks requiring conscious awareness, such as verbal fluency, short-term and working memory, and processing speed. However, they are no worse than the general population in underlying (implicit) learning, such as grammar skills, vocabulary, and spatial skills (e.g., map reading). Some experts believe that impaired verbal memory in schizophrenia is a consequence of depression and slowness, but not a result of the disease process.

Other Symptoms

People with schizophrenia may experience other symptoms, such as intolerance of heat (which is associated with antipsychotic medications) and a reduced sense of smell.

WHAT CAUSES SCHIZOPHRENIA?

No single cause can account for all cases of schizophrenia. Rather, it appears to be the result of multiple "hits" from genetic factors, environmental and psychological assaults, and possible hormonal changes that alter the brain's chemistry and trigger this devastating disease.

Abnormalities in Brain Structure, Circuitry, and Chemicals

Brain scans using magnetic resonance imaging (MRI) have now detected a number of abnormalities in the brain's structure that have been associated with schizophrenia. Such abnormalities can cause nerve damage and disconnections in the pathways that carry brain chemicals.

Abnormalities of Brain Volume and Activity. Imaging techniques have revealed reduced volume and actual loss of tissue in the brains of people with schizophrenia. Of particular importance are volume losses and abnormal activity in the *prefrontal cortex*, which contains the white matter of the brain, and the *temporal lobes*, which contain the limbic system.

- Reductions in volume of the prefrontal cortex have been observed in many patients with schizophrenia. Deterioration here can damage nerve cells and impair the connections that are required for verbal memory, attention, decision-making, reasoning, aggression, and meaningful speech. Impairment in the left side of the cortex is also associated with auditory hallucinations (e.g., hearing voices). (Not all patients have this deficit. For example, patients with paranoid schizophrenia tend to have normal left prefrontal volumes.)
- Loss of volume in the limbic areas (located deep in the brain), which contain the hypothalamus, amygdala, and, importantly, the hippocampus. A number of studies have specifically noted smaller left hippocampi in people with schizophrenia, which is associated with problems in verbal memory. Activity in the limbic area in general is related to emotions and memory, and abnormalities there are also associated with positive symptoms, including delusions and hallucinations, and also with disordered thinking.
- Because such abnormalities tend to show up on brain scans of people with chronic schizophrenia rather than in newly diagnosed patients, some experts believe they may be a result of the disease and its treatments rather than a cause. (Medications used for schizophrenia can also cause brain volume loss over time.) Nevertheless, there is now strong evidence to suggest that small hippocampi coupled with environmental conditions (notably low oxygen levels at the time of delivery) are important contributory factors in many cases of schizophrenia.

Abnormal Brain Chemicals. Schizophrenia is associated with an unusual imbalance of neurotransmitters (chemical messengers between nerve cells) and other factors.

- *Abnormalities in dopamine receptors.* Imbalances in the neurotransmitter dopamine are important research targets in schizophrenia. Dopamine overactivity is now known to be closely linked to *reduced* prefrontal cortex activity. Over-activity, particularly on the left side, is associated with psychotic symptoms and appears to be due to an increase in specific chemical receptors, particularly those called C1 and D1. (These receptors attract and lock dopamine.)
- *Abnormalities in glutamate receptors.* Glutamate, an amino acid known to affect dopamine and excite nerve activity, is also under scrutiny. For example, glutamate binds to N-methyl-D-aspartate (NMDA) receptors, which play a critical role in healthy nerve development and may be abnormal in schizophrenia. Abnormalities in NMDA and other molecules in the glutamate pathway appear to play significant roles in impairment of mental function and development of negative symptoms.
- *Loss of reelin.* A protein called reelin, which is involved in the nerve cell architecture, is also being investigated. Studies have observed abnormally low levels of reelin in the prefrontal cortex region of patients with both schizophrenia and bipolar psychosis, perhaps contributing to psychosis and to impaired information processing.

Abnormal Circuitry. Abnormalities in brain structure are also reflected in the disrupted connections between nerve cells that are observed in schizophrenia. Such miswiring could impair information processing and coordination of mental functions. For example, auditory hallucinations may be due to miswiring in the circuits

that govern speech processing. Strong evidence suggests that schizophrenia involves decreased communication between the left and right sides of the brain.

Genetic Factors

Schizophrenia undoubtedly has a genetic component. The risk for inheriting schizophrenia is 10% in those who have one immediate family member with the disease and about 40% if the disease affects both parents or an identical twin. Family members of patients also appear to have higher risks for the specific symptoms (i.e., negative or positive) of the relative with schizophrenia.

Researchers are seeking the specific genetic factors that may be responsible for schizophrenia in such cases, although current evidence suggests that there are a multitude of genetic abnormalities involved in schizophrenia, possibly originating from one or two changes in genetic expression.

Of particular interest are mutations in two genes (PRODH2 and DGCR6) that regulate enzymes involved in production of glutamate and in related functions that may play an important role in cases of early-onset schizophrenia.

Other research targets are genes that affect brain structure. For example, mutations in the COMT gene may make people susceptible to deficits in the prefrontal cortex of the brain, where schizophrenia develops.

It should be noted that heredity does not explain all cases of the disease. About 60% of people with schizophrenia have no close relatives with the illness.

Infectious Agents

Viruses. The case for viruses as a cause of this disease rests mainly on circumstantial evidence, such as living in crowded conditions. The following are some studies suggesting an association:

- Winter and Spring Births. The risk for schizophrenia worldwide is 5% to 8% higher for those born during winter and spring, when colds and viruses are more prevalent.
- The risk is higher for people who are born in cities than in the country. The longer one lives in the city, the higher the risk.
- Large Families. The risk for schizophrenia is also greater in large families in which there are short intervals between siblings (two or fewer years). Such observations suggest that exposure to infectious agents early in infancy may help set the stage for later development of the disease.
- Pregnant Mother's Exposure to Viruses. The *mother's* exposure to viral infections such as rubella, measles, chicken pox, or others while the infant is in the womb has also been associated with a higher risk for schizophrenia in her child.
- Researchers are trying to identify specific viruses that may be responsible for some cases. Of particular interest is research finding evidence of a virus that belongs to the HERV-W retrovirus family in 30% of people with acute schizophrenia.

Toxoplasmosis. Some researchers have found an association between some cases of schizophrenia and *toxoplasmosis* (a parasite carried by cats and other domestic animals), which can lie dormant in the nervous system and migrate to the brain over many years. Schizophrenic patients who are exposed to the parasite respond poorly to clozapine treatment. There is no evidence, however, that exposure to toxoplasmosis causes schizophrenia.

Loss of Oxygen around the Time of Birth

Many studies have reported an association between schizophrenia and problems surrounding birth, particularly those that cause oxygen deprivation, which could affect the nerve growth or structure in the developing brain. Specific complications that have been associated with such a higher risk include the following:

- Prolonged labor.
- Bleeding during pregnancy.
- A short gestation period and low birth weight.

Psychologic Factors

Although parental influence is no longer believed to play a major role in the development of schizophrenia, it would be irresponsible to ignore outside pressures and influences that may exacerbate or trigger symptoms. The prefrontal lobes of the brain, which are the brain areas often thought to lead to this disease, are extremely responsive to environmental stress. Given the fact that schizophrenic symptoms naturally elicit negative responses from the sufferer's circle of family and acquaintances, it is safe to assume that negative feedback can intensify deficits in a vulnerable brain and perhaps even trigger and exacerbate existing symptoms.

One study to support this indicated that early parental loss, either from death or separation, increases the risk for psychiatric disorders, including schizophrenia. In another interesting 2000 study, criticism by family members was significantly correlated with the onset of disorganized thinking in patients with impaired working memory. (This effect of criticism was not observed in patients with functioning working memories.)

WHO DEVELOPS SCHIZOPHRENIA?

Schizophrenia is the most common psychotic condition. It affects about 1% of the earth's population, including more than 2.7 million people in the US.

Age

Schizophrenia can occur at any age, but it tends to first develop (or at least become evident) between adolescence and young adulthood. Schizophrenia that is recognized in children is likely to be severe. Although the risk of schizophrenia declines with age, there is a lesser peak incidence at around 45 years and another, mostly in women, in the mid-60s. Late-onset schizophrenia that develops in the 40s is most likely to be the paranoid subtype with fewer negative symptoms or learning impairment. Such patients usually have functioned at a near-normal level until structural deficits in the brain break down.

Gender

Although schizophrenia affects both genders, there are some differences:

- Men tend to develop schizophrenia between the ages of 15 and 24. Paranoid schizophrenia, in particular, may be more common in men, and symptoms tend to be more severe.
- The onset in women is usually slightly later, between 25 and 34, and the symptoms tend to be less severe. The earlier a girl starts menstruation, the longer she is protected against schizophrenia. And, in women with schizophrenia, the disease is more severe during the time in their menstrual cycle when estrogen levels are low. Such findings and other evidence suggest that estrogen may have nerve-protecting properties. For example, the higher the estrogen levels in female patients with schizophrenia, the better their mental functions.

Intelligence

Genius is not spared; schizophrenia's victims span the full range of intelligence. In fact, one study reported that a higher than expected number of people who develop schizophrenia had been intellectually gifted children. Research suggests, however, that a decline in IQ scores during childhood may be a harbinger of psychotic symptoms in adults.

Cultural and Geographic Factors

No cultural or geographic group is immune, although the course of the disease seems to be more severe in developed than in developing countries. Also, interestingly, the content of delusions may vary depending on a person's culture. According to one study, for example, European patients were more apt to have delusions of poisoning or religious guilt while in Japan the delusions were most often related to being slandered.

Socioeconomic Factors

The disease occurs twice as often in unmarried and divorced people as in married or widowed individuals. Furthermore, people with schizophrenia are eight times more likely to be in the lowest socioeconomic groups. According to a 2001 study, however, these findings are likely to be a result of schizophrenia rather than a cause. Nevertheless, low income and poverty increases the risk for delayed diagnosis and treatment, and such delays could lead to more severe disease in patients with fewer resources. Poverty may also increase exposure to biologic factors (e.g., infections or toxins) or social stressors that could trigger the illness in susceptible people.

Other Factors Associated with Schizophrenia

Non-Right Handedness. The prevalence of mixed- and left-handedness is significantly higher in patients with schizophrenia than in the general population, suggesting some neurologic pattern that may be responsible for each. (A large minority of the population is non-right handed and very few of these people develop schizophrenia.)

Abnormal Olfactory Bulbs. Studies are reporting impairment in the sense of smell in patients with schizophrenia. One study reported abnormally small olfactory bulbs in patients with schizophrenia. Olfactory bulbs are nerve centers in the brain that regulate the sense of smell.

Obsessive-Compulsive Disorder. Obsessive compulsive disorder (OCD) affects a significant number of schizophrenic patients. OCD is an anxiety disorder marked by obsessions (recurrent or persistent mental images, thoughts, or ideas) that may result in compulsive behaviors, repetitive, rigid, and self-prescribed routines that are intended to prevent the manifestation of the obsession. Some experts believe the behaviors exhibited in the disorder may actually be protective in people with schizophrenia in early stages.

Behavioral and Motor Problems in Childhood. Children who later develop schizophrenia often suffer from the following certain problems, including excessive shyness or minor early physical and motor-control problems. Such problems are so common, however, that their presence without any other risk factors is no cause for concern.

Malnutrition in the Pregnant Mother. Malnutrition in the mother during the first trimester of pregnancy (less than 1,000 calories a day) has been associated with later schizophrenia in the child. Nutritional deficiencies during that time are believed to impair fetal brain growth.

Father's Age. According to some studies, the older a father is when a child is born, the greater the risk is for schizophrenia in his offspring, perhaps because of a greater chance of genetic mutations in the sperm that can be passed on. In one study, children of fathers who were 50 years old or more or faced a three-fold risk for schizophrenia compared to children of fathers who were 25 or younger.

WHAT ARE THE SIGNS OF SCHIZOPHRENIA AND HOW DOES IT PROGRESS?

Research indicates that symptoms in childhood strongly predict disease in adulthood. In one long-term study, over 40% of schizophrenics who developed the disease in young adulthood had reported psychotic symptoms at age 11. For children with a family history of schizophrenia, the following inherited traits may be warning signs:

- Deficits in working (short-term) and verbal memory.
- Impairments in gross motor skills (the child's ability to control different parts of the body).
- Attention deficits.

- Mixed-handedness (the use of different hands for different tasks), particularly in females.
- Hallucinations or delusions. (This does not include normal childhood fantasies and stories, in which the child is aware that they are inventions.)
- A decline in verbal memory, IQ, and other mental functions.

Some experts suggest that screening young high-risk individuals using brain imaging techniques possibly followed by treatment may help prevent nerve damage and improve the outcome for this difficult disease.

Most often, early warning signs go unnoticed and schizophrenia usually becomes evident for the first time in late adolescence or early adulthood. Schizophrenia that starts in childhood or adolescence tends to be severe. It should be strongly noted that the traits discussed above, even combinations of them, can be present without schizophrenia.

Symptoms of Progression to Full-Blown Schizophrenia

The course of the disease varies from one patient to the next. Symptoms of psychosis can become evident either gradually or suddenly.

- In up to a third of patients, the disease is unrelenting and progresses from the first episode onward.
- In others, schizophrenia follows a fluctuating course with psychotic flare-ups, followed by remissions.
- In one study, 31% experienced a complete remission of symptoms within three years after one or more episodes. Women are more likely to go into remission, possibly because of some protective effect of estrogen on the brain.

Typically, patients develop considerable cognitive dysfunction (disordered thinking) within the first four or five years of the onset of psychotic symptoms. There is some evidence that the physical disease process in schizophrenia is progressive, as with Alzheimer's and Parkinson's. However, schizophrenia does not progress in the same way as those two diseases. In one study, men with schizophrenia showed an annual decline of 3% in areas in the front of the brain compared to slightly less than 1% in men without schizophrenia. Unlike Parkinson's and Alzheimer's, however, eventually cognitive function usually stabilizes. Psychosis, disorganized thought, and negative symptoms often improve over time, although, even in such cases, deficits in verbal memory usually persist. (Thought disorder often improves in concert with improvements in negative symptoms.)

WHAT ARE THE CONSEQUENCES OF SCHIZOPHRENIA?

The disease has a devastating effect on all aspects of human thought, emotion, and expression. Only about 20% reach full recovery after a first episode, but new drugs are offering significant hope for improving the patient's life. Even with care and adequate treatment, however, people with schizophrenia suffer.

Medical Illnesses

Studies in 2002 reported that people with severe mental illnesses suffered more from serious health problems than those without mental disorders and they are less likely to receive medical help. Substance abuse is a significant factor in this higher risk.

Depression

Depression is common later in adulthood. Although such a mood disorder can certainly be a result of the negative social impact of schizophrenia, some experts believe that depression is part of the disease process itself.

Effect on Social Status

Studies indicate that after 20 to 30 years, half of schizophrenic patients are able to care for themselves, work,

and participate socially. Support services and appropriate housing improve this outcome. Unsurprisingly, the decline in status, including the inability to earn a living, is less steep when there are more financial resources and fewer emotional disorders at the outset of symptoms. Also, on average, the later the onset of the disease, the milder the social impact. The long-term effects on work and relationships, however, are usually severe and difficult to repair, even if symptoms improve.

Effect on Intelligence

In one study, about half of patients experienced some decline in IQ (10 points or more), but intelligence scores remained the same in the other half. Experts believe that a decline in IQ reflects early nerve damage but that it is not an inevitable consequence of the disease process.

Suicide and Self-Destructive Behaviors

In spite of their sometimes frightening behavior, people with schizophrenia are no more likely to behave violently than are those in the general population. In fact, these patients are more apt to withdraw from others or to harm themselves.

Suicide. Between 20% and 50% of patients with schizophrenia attempt suicide and an estimated 9% to 13% of schizophrenics succeed.

The general risk for suicide is higher at certain times in the course of the disease:

- Within the first five years of onset of the disease.
- During the first six months after hospitalization.
- Following an acute psychotic episode.

The widespread use of antipsychotic drugs over the past decade does not appear to have had much effect on suicide rates. In fact, evidence suggests that the use of these agents as a way of reducing hospitalization time is increasing the incidence of suicide. Hopelessness, not delusions, appears to be the most important motive for suicide in these patients. In one study of patients who had attempted suicide, the most frequent reason given for an attempt was depression, and the second was the loss of an intimate partner. Cognitive impairment, which reduces the patient's ability to hold jobs and function normally, also seems to be a major factor in suicidal motivation.

Smoking and Other Addictions. A large majority of people with schizophrenia abuse nicotine, alcohol, and other substances. Substance abuse, in addition to its other adverse effects, increases non-compliance with antipsychotic drugs in the schizophrenic patient and may exacerbate symptoms.

Smoking is of special interest. According to a 2000 study, up to 88% of schizophrenic patients are nicotine dependent. Biologic and genetic factors may be partially responsible for the addiction in this particular group. Nicotine helps reduce psychotic symptoms and impulsivity, perhaps by inhibiting the activity of a protein called monoamine oxidase B (MAO-B), which is linked to improved mood and possibly to nerve protection. Smoking for schizophrenics, then, may be a form of self-medication.

Note: Although attempts to help schizophrenic patients quit smoking usually fail, those taking atypical medications have a better chance of quitting successfully than those taking typical medications. The use of bupropion and therapeutic administration of nicotine may also help. (For further information, see the *Well-Connected* report, *Smoking*).

Effect on Family Members

Family members suffer from grief, long-term guilt, and many emotional issues when faced with a schizophrenic loved one. If such patients commit suicide, which is not uncommon, the effects can be devastating.

Lack of Social and Government Support

In the 1970s, tens of thousands of patients were put on antipsychotic agents and released from institutions into the community, a concept called deinstitutionalization. In spite of these attempts to reduce mental hospital costs, schizophrenia still accounts for 40% of all long-term hospitalization days. More than half of patients with schizophrenia require public assistance within a year of their reentry into the community. And using drugs alone has done nothing to reduce the high suicide rates among this patient group.

WHAT WILL CONFIRM A DIAGNOSIS OF SCHIZOPHRENIA?

The physician will use one or more verbal screening tests to help determine whether a patient's symptoms meet the criteria for schizophrenia. Because no single symptom is specific to schizophrenia, a diagnosis may be made when one or more of the following conditions is present:

- If a patient has at least one active flare-up lasting a month or less. The flare-up consists of at least two characteristic symptoms (e.g., hallucinations, delusions, evidence of disorganized thinking, and emotional unresponsiveness with a flat speaking tone).
- If the patient has particularly bizarre delusions or hallucinations even in the absence of other characteristic symptoms.
- If certain symptoms are present for at least six months even in the absence of active flare-ups. Such symptoms include marked social withdrawal, peculiar behavior (talking to oneself, severe superstitiousness), vague and incoherent speech, or other indications of disturbed thinking. The patient's social and personal relationships would also have deteriorated since the onset of symptoms.

Possible Markers of Schizophrenia

Experts are investigating tests of specific phenomenon that might suggest a higher risk for or even the presence of schizophrenia.

· *Eye Tracking Dysfunction.* A dysfunction in eye tracking is a genetic trait that is strongly associated with schizophrenia and may reflect abnormalities in the frontal regions of the brain. (Some experts believe that this is such a powerful marker in patients with close relatives with schizophrenia that it can be used as a predictor. This trait can only be detected by a health professional using special equipment.)

· *Impaired Prepulse Inhibition.* Prepulse inhibition (PPI) is a phenomenon in which a weak stimulus (such as a low sound) that occurs before a strong stimulus (i.e., a loud sound) reduces the startle response to it. PPI is impaired in schizophrenia.

Ruling Out Other Conditions

The common hallmarks of schizophrenia are also symptoms that can occur in dozens of other psychologic and medical conditions, as well as with certain medications. Shared symptoms include delusions, hallucinations, disorganized and incoherent speech, a flat tone of voice, and bizarrely disorganized or catatonic behavior (such as lack of speech, muscular rigidity, and unresponsiveness).

Among the conditions that may resemble schizophrenia are the following:

- *Depression.* Delusions that focus on a physical abnormality or disease that isn't real, known as somatic delusions, sometimes occur in people with depression.
- *Bipolar Disorder.* Paranoia and delusions of grandeur (the belief that one has a special power or mission) can occur in people with bipolar disorder during the manic phase. In fact, sometimes it is difficult even for experts to differentiate between these two disorders. Evidence suggests that they may share certain genetic factors that make some families vulnerable to either one.
- *Schizophrenia-Like Psychoses.* There are a number of conditions that exhibit schizophrenia-like psychoses but do not meet the diagnostic criteria for schizophrenia. Such conditions may be variations of

entirely different diseases and are classified at this time as schizoaffective disorder, schizophreniform psychosis, and atypical and brief reactive schizophrenia.

- *Alcohol and Drug Abuse.* Either substance abuse itself or withdrawal from drugs or alcohol can also trigger psychosis. Because of the high risk for substance abuse among people with schizophrenia, it is important that the health professional distinguish psychosis triggered by drugs or alcohol from a schizophrenic episode. Usually, the diagnosis is confirmed if the psychosis ends after withdrawal from drugs or alcohol, and returns if the patient returns to alcohol or substance abuse.
- *Medical Illnesses.* Other causes of psychotic symptoms include cancer in the central nervous system, encephalitis, neurosyphilis, thyroid disorders, Alzheimer's disease, epilepsy, Huntington's disease, multiple sclerosis, stroke, Wilson's disease, some vitamin B deficiencies, and systemic lupus erythematosus.
- *Medication Reactions.* Many medications may induce psychosis as a side effect, and some can precipitate delusions and severe confusion. Such medication-induced symptoms are most often observed in elderly patients.

Imaging Techniques

A number of brain imaging techniques are becoming useful in detecting changes in the brain structure that relate to specific sets of symptoms in schizophrenia. At this time such techniques are used only as research tools, although some experts believe they may be useful for identifying candidates for early treatment among high-risk young people with early warning signs of schizophrenia and brain damage.

Magnetic Resonance Imaging. Magnetic resonance imaging (MRI) has become a particularly valuable tool for revealing parts of the brain inaccessible to other scanning methods. MRI does not use radiation, and it can show the brain from a number of different perspectives.

Other Imaging Techniques. Other imaging techniques are single photon emission computed tomography (SPECT) and positron emission tomography (PET), which can provide information on blood flow and metabolism in the brain.

Investigative Tests

Research is ongoing to find simple tests that will detect schizophrenia accurately and early enough to initiate preventive measures. Some examples include the following:

- One investigative test uses computers to analyze brain scans and identify changes in blood flow indicative of schizophrenia, even before symptoms occur. It appears to be highly reliable, and more research is warranted.
- A blood test that detects genetic evidence of high levels of D3 dopamine receptor may prove to be useful. People with schizophrenia have over three times the normal amount of this substance.

Measurements of certain esters (phosphomonoesters and phosphodiesterases) may detect high-risk individuals.

WHAT ARE THE GENERAL GUIDELINES FOR TREATING SCHIZOPHRENIA?

Integrated Approach. Schizophrenia is now officially categorized as a brain disease, not a psychologic disorder, and drug treatment is the primary therapy. Studies indicate, however, that an integrated approach is superior in preventing relapses compared to routine care (drugs plus monitoring and access to rehabilitation programs). In one study, this approach involved the following:

- Motivational interviewing to encourage the patients' commitment to change.
- Use of antipsychotic medications (generally atypical or novel antipsychotics) with monitoring.
- Community-based rehabilitation.
- Cognitive-behavioral therapy, which aims to reduce delusions and hallucinations.

- Family interventions.

In the study, relapse rates were 33% in the integrated group and 67% in the group who received routine care. Unfortunately, such treatment is expensive. Research shows that more than half of individuals with schizophrenia do not even receive routine care. Increased cost cutting in mental health services is making the situation worse. African-Americans, in particular, are less likely to receive effective treatment.

Early Treatment. The earlier schizophrenia is detected and treated, the better the outcome. Patients who receive antipsychotic drugs and other treatments during their first episode are hospitalized less frequently during the following five years and may require less time to control the symptoms than those who do not seek help as quickly. In spite of strong evidence for the positive effects of early treatment, patients usually endure an average of 10 months of serious symptoms before they receive treatment.

Researchers are also trying to determine if intensive early treatment with an atypical agent can prevent progression in people who are at very high risk for a first psychotic episode. In one study, risperidone delayed psychosis by six months, but did not prevent its occurrence. Even a delay in progression to full-blown schizophrenia, however, warrants more research.

Classes of Drugs Used for Schizophrenia

Most drugs that treat schizophrenia work by blocking receptors of the neurotransmitter dopamine, which is thought to play a major role in psychotic symptoms. Although they all have important benefits for schizophrenia, most drugs used for schizophrenia also pose a risk for side effects associated with reduced dopamine. The most disturbing and common side effects are those known as *extrapyramidal* symptoms, which involve the nerves and muscles controlling movement and coordination. [See Box Extrapyramidal Symptoms.]

The following drug classes are generally used for schizophrenia:

- Until recently, the mainstay treatments for schizophrenia have been *antipsychotic agents*--also called *neuroleptic drugs*. They include haloperidol (Haldol). Others include chlorpromazine (Thorazine), perphenazine (Trilafon), thioridazine (Mellaril), mesoridazine (Serentil), trifluoperazine (Stelazine), and fluphenazine (Prolixin). These agents have significant side effects, however, particularly extrapyramidal symptoms, which occur in up to 70% of patients taking these medications.
- The *atypical*, or *novel*, antipsychotics are proving to be better tolerated than the older antipsychotics and have significantly fewer severe extrapyramidal side effects. They include clozapine (Clozaril) (the first atypical antipsychotic), risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), and ziprasidone (Geodon). There is considerable difference among these agents and comparison studies are needed. [See Box Comparing Atypical Agents]
- Even newer agents called dopamine system stabilizers are under investigation. These agents are very selective and block certain dopamine receptors but not others. Such an effect reduces the risk for severe side effects associated with dopamine blockade. They include aripiprazole.

[For more details see What Are the Specific Drug Treatments for Schizophrenia?]

Choosing Between Atypical and Standard Antipsychotic Agents. Experts are debating whether older antipsychotics or the new atypicals should be used at the onset of symptoms. The debate includes some of the following issues:

- The atypicals are considerably more expensive than the conventional antipsychotics.
- The atypicals may be more effective than the older drugs, but the additional benefits may be modest for most patients. For example, a 2001 review of 52 trials reported that patients taking the conventional antipsychotics did worse overall than those on the atypicals. When the results were examined closely, however, patients who took *low* doses of the standard antipsychotics (haloperidol and chlorpromazine) did as well as those on the atypicals.
- Studies are increasingly reporting more rapid action and fewer dropouts from side effects with the new atypicals compared to the older antipsychotics.

- Some atypicals, such as risperidone, may be more effective in preventing relapse than the antipsychotics.
 - The older drugs may have a higher than normal risk for sudden death from a cardiac (heart-related) event. The newer atypicals were not compared in this study, however, and most of these pose a higher risk for weight gain, diabetes, and heart disease.

Some experts recommend the following approach:

- Use older antipsychotics at low doses as first-line agents for most patients.
- If the patients either do not respond to the conventional antipsychotics or have severe extrapyramidal effects, they should switch to atypicals.

Treating an Acute or Initial Phase

For the severe, active phase of schizophrenia, injections of an antipsychotic drug are typically given every few hours until the patient is calm. Anti-anxiety agents are also often administered at the same time. Some of the newer atypical agents, such as olanzapine or risperidone, may prove to be as effective as the older antipsychotics with significantly fewer severe side effects. In patients who are being treated for the first time, improvement in psychotic symptoms may be evident within one or two days of treatment, although the full benefit of the drug usually becomes manifested over about six to eight weeks. Thought disturbances tend to abate more gradually.

Maintenance

To reduce the risk of relapse, many physicians recommend that drugs be given daily for at least one year. Atypical agents are increasingly being used as maintenance for those with new-onset psychosis, although the choice of the drug depends on many factors. Side effects and effectiveness vary from individual to individual, and some trial and error adjustments may be necessary when prescribing dosage amounts so that the benefits of treatment outweigh the side effects of the therapy. The physician must monitor the drug effects carefully.

Keeping patients on maintenance therapy, however, is very difficult and many patients stop their medication. Two 2000 studies suggested factors that might affect either positive or negative medication compliance. In one, patients *least* likely to adhere to their medication regimens had the following:

- Lower occupational status.
- A history of alcohol or drugs abuse.
- Delusions of persecution.
- A history of stopping their medications within the first six months after diagnosis.

In the other 2000 study, patients were *more* likely to take their medications if they perceived their illness as severe and believed that the drugs would prevent future hospitalizations. It should be noted that neither of these studies indicated whether the medications used were standard antipsychotics or atypical agents. Adding psychotherapy, such as cognitive therapy, to the regimen may help reduce this rate.

Stopping Medications

According to a 2001 study, nearly all patients experience some relapse or worsening of symptoms within two years of stopping maintenance medication. However, in the same study they were closely monitored and medications were reinstated early enough so that only 13% required hospitalization.

Supportive Agents

Antidepressants and anti-anxiety agents may also play an important role in treating the patient with schizophrenia, particularly given the role of depression in the high rates of suicide among these patients.

General Guidelines for Psychologic Treatments

Experts generally agree that current treatment should offer both medical and psychological treatment to the patient. Cognitive-behavioral approaches are showing promise. Support to the family or other caregiver is also important for the long-term improvement of people with schizophrenia.

WHAT ARE THE SPECIFIC DRUG TREATMENTS FOR SCHIZOPHRENIA?

Atypical Drugs

A number of atypicals are either available or under investigation. Clozapine (Clozaril) was the first atypical antipsychotic. Newer agents include risperidone (Risperdal), olanzapine (Zyprexa), quetiapine (Seroquel), and others. They appear to have fewer side effects than clozapine. Not all are available in the U.S. It may take up to six months before they have an effect.

Benefits of Atypicals. Atypical agents have the following benefits:

- They simultaneously affect both dopamine receptors and other neurotransmitters responsible for psychotic symptoms.
- They improve negative as well as positive symptoms.
- Some may even improve working memory and mental functioning.
- They may reduce depression and hostility
- They may reduce the risk for suicide. (Clozapine is specifically approved for the prevention of suicide and may be more effective than other drugs in this important area.)
- These drugs, particularly the newer atypicals, have fewer extrapyramidal side effects than the typical neuroleptics. [*For description, see Box Extrapyramidal Symptoms*]

It is important to note, however, that they have some significant limitations and complications, and their benefits compared to each other and to the antipsychotics are not always clear-cut. In-depth comparative studies are underway to determine which specific agents are more effective and have fewer side effects than others. For example, in one 2002 study clozapine and olanzapine were more effective than risperidone, but the differences were modest. However, clozapine and olanzapine may have some heart risks that are not as great as with other atypicals. Studies to date do not report much effect on information processing and concentration, and in fact high doses can dull the mind to the same extent as the older drugs. [*See Table Comparing Atypical Agents.*]

Side Effects. The following are side effects of most atypicals:

- Nasal congestion or runny nose.
- Drooling.
- Dizziness.
- Headache.
- Drowsiness. (In some cases, however, drugs may also cause restlessness and insomnia.)
- Constipation.
- Rapid heart beat.
- Difficulty urinating.
- Skin rash.
- Increased body temperature because of reduced sweating. (On the other hand, some may also cause profuse sweating.)
- Mental effects (confusion, short-term memory problems, disorientation, and impaired attention).

The following are some severe side effects or complications that may occur in with most of these agents:

- Seizures. (Five-percent risk per year with clozapine. Others pose less of a risk.)
- A drop in blood pressure (associated with a few reports of sudden cardiac death with initial usage of the

- clozapine).
- A higher risk of heat stroke.
- Drop in white blood cells (neutropenia). The risk is highest with clozapine, which requires monitoring, but it may occur with other atypical agents as well.
- Extrapyramidal side effects. It should be noted that risks for these are lower than with standard antipsychotics. (They still occur in about 20% of patients taking most atypicals.) [See Box Extrapyramidal Symptoms]
- An increase in risk for cataracts and worsening of any existing glaucoma.
- An increase in prolactin levels. Prolactin is a hormone that can cause fluid secretions from breasts in women or impotence in men.

Comparing Atypical Agents

Agent	Comparative Studies on Effectiveness	Adverse Effects that May Differ from Other Atypicals
Clozapine (Clozaril)	<p>Superior to risperidone for severe, chronic schizophrenia (2001 study).</p> <p>Superior to olanzapine in reducing the risk for suicide (2003 study)</p> <p>May be slightly better than others for improving negative symptoms (2002 study).</p>	<p>Agranulocytosis (1.3% risk). Potentially life-threatening reduction in white blood cells. Occurs within three months of taking clozapine. Higher risk in older women. Unlikely to develop after six months. Can be reversed if clozapine is withdrawn at once.</p> <p>Reports of inflammation of the heart, which in rare cases can be fatal.</p> <p>Highest risk for weight gain of all atypicals. Also has higher risk for diabetes and elevated triglycerides than most others (except olanzapine).</p>
Risperidone (Risperdal)	<p>Not as effective as clozapine or olanzapine for chronic, severe schizophrenia, but differences are modest (2001 and 2002 studies).</p> <p>More and longer hospitalizations compared to olanzapine (2001 study).</p> <p>Monthly injection is available that may cause less symptom fluctuation than the oral form.</p>	<p>Less risk for weight gain and unhealthy cholesterol levels than clozapine and possibly some other atypicals, notably olanzapine. (There is still some risk for weight gain, however. In one study 12% gained weight.)</p>
Olanzapine (Zyprexa)	<p>Slightly more effective than risperidone in reducing symptoms (2001 and 2002 studies). May also improve concentration and thinking compared to risperidone (2000 study).</p>	<p>May have higher risk for unhealthy cholesterol levels, weight gain (27% in one study) and diabetes than other atypicals (except for clozapine).</p>
Quetiapine (Seroquel)	<p>Similar to older antipsychotics in treating positive and negative symptoms. May improve mental performance. May have benefits for elderly patients.</p>	<p>Can cause weight gain, but not as much as clozapine or olanzapine.</p> <p>Also appears to be free of extrapyramidal side effects and increases in prolactin.</p>
Ziprasidone (Geodon)	<p>May improve negative as well as positive symptoms. May also reduce anxiety.</p>	<p>Appears to have no significant risk for weight gain, high cholesterol levels, or diabetes. May, however, have some adverse effect on heart rate compared to other atypicals.</p>
Zotepine (Zoleptil)	<p>No clear difference from other atypicals.</p>	<p>Can cause weight gain, but not as much as clozapine or olanzapine. May have less risk for extrapyramidal side effects than some atypicals.</p>
Amisulpride	<p>Sometimes referred to as a</p>	<p>May have less risk for extrapyramidal and other side</p>

(Solian). *	dopamine system stabilizer. Reduces positive and negative symptoms. May also improve cognitive functioning. Faster response and better improvement than risperidone (2002 study).	effects than some atypicals. Low risk for weight gain.
*Other new dopamine stabilizers under investigation include aripiprazole (Abilitat) and iloperidone (Zomaril)		

Typical Antipsychotic (or Neuroleptic) Drugs

The standard neuroleptic drug used for schizophrenia is haloperidol (Haldol). Others include chlorpromazine (Thorazine), perphenazine (Trilafon), thioridazine (Mellaril), mesoridazine (Serentil), trifluoperazine (Stelazine), and fluphenazine (Prolixin). Studies have not shown any significant difference in benefits among these drugs.

The beneficial impact of these drugs is greatest on psychotic symptoms, particularly hallucinations and delusions in the early and midterm stages of the disorder. They are not very successful in reducing negative symptoms. Because of their significant side effects, compliance is often very low. Depot therapy (long-lasting monthly injections, usually of haloperidol or fluphenazine) has been used with success in people who have difficulty complying with a daily regimen of these agents. Researchers are studying low-dose regimens to discover if they can be effective and cause fewer side effects.

Side Effects of Neuroleptics. Neuroleptics can have adverse side effects related to many organs and systems in the body. The very name *neuroleptic* derives from the neurologic side effects that these drugs cause, which can be very severe. Side effects include the following:

- *Extrapyramidal symptoms.* These are the most disturbing and common side effects and involve disruption in the nerves and muscles controlling movement and coordination. They are a major reason for noncompliance. [*For a description, see Box Extrapyramidal Side Effects.*]
- Sleepiness and lethargy. This commonly occurs in the beginning of therapy but usually decreases over time. (It should be noted that the drugs can also cause insomnia and agitation.)
- Dulling of the mind (but they can also improve thinking and concentration)
- Gastrointestinal side effects (nausea, vomiting, diarrhea, constipation, heartburn).
- Dry mouth and blurred vision.
- Allergic reactions.
- Sexual dysfunction. This side effect is a common reason for noncompliance, although the drug amantadine may help offset this side effect.
- *Neuroleptic malignant syndrome.* This is a rare side effect, in which dangerously high body temperatures can occur. Without prompt and expert treatment, this condition can be fatal in up to 20% of those who develop it.
- Hyperprolactinemia (high levels of the hormone prolactin). This is common with the use of antipsychotics. This effect can cause menstrual abnormalities and may increase the risk for osteoporosis and possibly breast cancer. This risk is of special concern for adolescents, whose hormonal systems are still developing.
- A sudden drop in blood pressure (hypotension).
- An increased risk of sudden cardiac death.
- Higher potency drugs (e.g., haloperidol and fluphenazine) cause less drowsiness and drops in blood pressure but pose a higher risk for extrapyramidal side effects. Low-potency drugs (e.g., chlorpromazine, thioridazine) are more sedating and have side effects that are not as acute.

Extrapyramidal Symptoms

Nearly every agent used to date for schizophrenia can cause extrapyramidal side effects to some degree. These side effects involve the nerves and muscles controlling movement and coordination.

Description of Extrapyramidal Side Effects. These effects resemble some of the symptoms of Parkinson's disease and include the following conditions:

- *Tardive dyskinesia* is the most serious extrapyramidal side effect. It often manifests itself by repetitive and involuntary movements, or tics, most often of the mouth, lips, or of the legs, arms, or trunk. Symptoms range from mild to severe, and sometimes interfere with eating and walking. They may appear months or even years after taking the drugs. After the drug is withdrawn, symptoms can sometimes persist for weeks or months and may be permanent. Some people are more likely to develop these symptoms, including older patients, women, smokers, people with diabetes, and patients with movement disorders.
- *Acute dystonia* typically develops shortly after taking an antipsychotic drug. This syndrome includes abnormal muscle spasms, particularly sustained contortions of the neck, jaw, trunk, and eye muscles.
- *Other extrapyramidal symptoms.* Other effects are agitation, slow speech, tremor, and retarded movement. It should be noted that sometimes these symptoms mimic schizophrenia itself. In response, the physician may be tempted erroneously to increase the dosage.

Treatment of Extrapyramidal Side Effects. In general, if extrapyramidal side effects occur from neuroleptic drugs, the physician may first try to reduce the dosage or switch to an atypical drug. Other approaches to reduce these symptoms include the following:

- Ondansetron (Zofran), an anti-nausea medication, is now under investigation for treating tardive dyskinesia.
- Anti-parkinsonism drugs known as anticholinergics increase dopamine levels and help to restore balance. Among the anticholinergics sometimes used are trihexyphenidyl (Artane, Trihexy) and benztropine (Cogentin). They have no beneficial effect on tardive dyskinesia, however. Some of these drugs may also be helpful in managing negative symptoms of schizophrenia. The use of these agents, however, adds to the cost, complicates management, and they have their own, sometimes serious, side effects. Most experts recommend them only for patients who cannot be monitored regularly and for those who need very high doses of powerful antipsychotic drugs and are at risk for severe side effects. They should be withdrawn after three or four months if possible. If symptoms recur, the drugs can be reinstated. It should be noted that withdrawal from anticholinergics can cause depression that can exacerbate schizophrenia.
- Benzodiazepines may also alleviate these symptoms.
- Small studies have suggested that certain alternative agents, including vitamin B6 and melatonin, may help reduce these symptoms.

Supportive Add-On Agents

Antidepressants. Antidepressants are recommended along with antipsychotics to alleviate the depression that is so common in people with schizophrenia. One study indicated that taking antidepressants may even help prevent relapse. In spite of their benefits, less than half of all patients are given these medications.

Anti-Anxiety Drugs. Benzodiazepines are drugs normally used to treat anxiety. They also have some modest effect on psychotic symptoms. They may be useful in the early stages of a psychotic relapse for preventing a full attack. They also are sometimes used to treat the restlessness and agitation that can occur with the use of neuroleptics. Severe side effects, including respiratory arrest, very low blood pressure, and loss of consciousness, have been reported in a few people taking anti-anxiety medication and clozapine but there is no evidence yet of a clear danger associated with the use of these two drugs. In any case, prolonged use of anti-anxiety drugs is generally not recommended in schizophrenia; withdrawal from these agents should be achieved gradually.

Lithium. Lithium, ordinarily used for bipolar disorder, is useful for some schizophrenic patients. It appears to help those with fewer negative symptoms and without a family history of schizophrenia. However, there are no reliable criteria to predict who will benefit.

Antiepileptic Drugs. Drugs ordinarily prescribed for epilepsy, such as carbamazepine (Tegretol), gabapentin (Neurontin), lamotrigine (Lamictal), or others, are occasionally used in combination with neuroleptics or atypical agents for patients who do not respond to standard drugs.

Omega-3 Fatty Acids. Studies suggest that omega-3 fatty acids found in fish oils have been associated with improvement in patients with schizophrenia. Docosahexaenoic acid and eicosapentanoic acid (EPA) are the important compounds in these fatty acids. EPA is particularly promising. In a 2002 study, patients taking EPA in addition to their usual medicine reported improvements in treatment-related dyskinesia (involuntary movements) and in schizophrenia symptoms as well.

Stimulants and Other Agents to Promote Wakefulness. The drugs used for schizophrenia can cause severe and persistent sleepiness. This is a difficult side effect to treat because stimulants may trigger psychosis. Modafinil (Provigil), a drug used for narcolepsy, is being investigated because it has different activities and experts hope it might be safer. Unfortunately, a 2002 case report suggested that this agent, too, may pose a risk for triggering psychosis.

Estrogen Replacement in Women. Estrogen may be nerve-protective. Some investigators are studying whether estrogen therapy will improve symptoms. In a 2002 study, women who wore an estrogen patch plus their regular medication experienced improved symptoms compared to those who had a dummy patch.

COX-2 Inhibitors. COX-2 inhibitors, which include celecoxib (Celebrex), rofecoxib (Vioxx), and valdecoxib (Bextra), are recent agents that have similar properties to the common nonsteroidal anti-inflammatory drugs (NSAIDs) (such as aspirin and ibuprofen). COX-2 inhibitors suppress certain immune factors and have other effects that might benefit patients with schizophrenia. In support of this, a 2002 study reported that patients who took celecoxib with an atypical experienced improved symptoms. More research is warranted.

Agents Used to Reduce Weight Gain and Prevent Diabetes. A number of agents, such as orlistat and metformin, are under investigation to prevent weight gain and diabetes--important side effects of some of the atypicals.

Agents Used for Alzheimer's Disease. Agents used for Alzheimer's patients, such as rivastigmine or donepezil, are also being tested for patients with schizophrenia to see if they have any benefits on memory, attention, and planning skills and for reducing medication side effects. To date, studies have reported few or no benefits.

Investigative Therapies for Improving Cognitive Function

Experts are investigating agents to be used along with antipsychotics or atypicals for improving mental function. Developing such agents would be an important advance in this disease, particularly as some research suggests that cognitive disturbances play a major role in suicide motivation.

For example ampakines are agents that target specific glutamate receptors and some early evidence suggests that they may improve symptoms when used as add-ons to antipsychotic or atypical agents.

Other investigators are studying the effects of glycine, a common amino acid, which stimulates receptors in the brain that are impaired in schizophrenia. In small studies, large doses of glycine resulted in a small improvement in negative symptoms in some patients. Researchers, however, are more interested in agents called glycine transport inhibitors, which would elevate glycine levels in the brain, and would therefore have a more potent effect. (Glycine itself is available in health stores, but such products are unlikely to have much effect.)

Alternative Treatments

Alternative remedies are often used for chronic illnesses. It should be strongly noted that not all are safe and their effectiveness, if any, cannot be guaranteed.

Gingko Biloba. In small 2001 studies, the herbal remedy ginkgo biloba was associated with few side effects and

improved symptoms when added to an antipsychotic. Although the risks for ginkgo appear to be low, there is an increased risk for bleeding and interaction with anti-clotting medications at high doses. Commercial ginkgo preparations have also been reported to contain colchicine, an agent that can be harmful in pregnant women and people with kidney or liver problems.

Vitamin B6. One very small 2001 study suggested that vitamin B6 (pyridoxine) therapy may help to alleviate depression in some schizophrenic patients. A 2002 study reported no effect on psychotic symptoms. Further research is needed.

Warnings on Alternative and So-Called Natural Remedies

It should be strongly noted that alternative or natural remedies are not regulated and their quality is not publicly controlled. In addition, any substance that can affect the body's chemistry can, like any drug, produce side effects that may be harmful. Even if studies report positive benefits from herbal remedies, the compounds used in such studies are, in most cases, not what are being marketed to the public.

There have been a number of reported cases of serious and even lethal side effects from herbal products. In addition, some so-called natural remedies were found to contain standard prescription medication. Of specific concern are studies suggesting that up to 30% of herbal patent remedies imported from China were laced with potent pharmaceuticals, such as phenacetin and steroids. Most reported problems occur in herbal remedies imported from Asia, with one study reporting a significant percentage of such remedies containing toxic metals.

The following website is building a database of natural remedy brands that it tests and rates. Not all are available yet (www.ConsumerLab.com ▶▶).

The Food and Drug Administration has a program called MEDWATCH for people to report adverse reactions to untested substances, such as herbal remedies and vitamins (call 800-332-1088).

WHAT ARE PSYCHOLOGICAL THERAPIES FOR SCHIZOPHRENIA?

Between one-fifth and one-third of all patients with schizophrenia do not respond adequately to drug treatment. And, many patients who have been successfully treated with medications experience the "awakenings" phenomena, which are painful reactions that are manifested as inner emotions and the recognition of real losses. The effects of the disease, in any case, are profoundly emotional and psychological therapies can be helpful for many patients.

Cognitive-Behavioral and Other Psychosocial Therapies

The use of cognitive-behavioral therapy is showing particular promise for improvement in both positive and negative symptoms in some patients, and the benefits may persist after treatment has stopped. This approach attempts to strengthen the patient's capacity for normal thinking using mental exercises and self-observation. Patients with schizophrenia are taught to critically analyze hallucinations and examine underlying beliefs in them.

In a 2000 study, for example, patients underwent the following process:

- In order to think analytically about the origins and the nature of their auditory hallucinations they kept a diary of the nature of the voices and the times they were heard.
- They were then taught ways of coping with the voices.
- Patients also learned to think objectively about the source of their delusions and to find the links between thoughts that jumped from topic to topic.

- After the patients gained some mastery over positive symptoms, the therapist worked on negative symptoms.
- The patients received an average of 19 individual sessions over nine months. At a follow-up period of nine months, patients continued to improve. (A comparison group of patients who received so-called befriending therapy, which involved empathy and non-directed support, also improved during treatment, but did not get better after treatment stopped.) Another interesting behavioral approach used memory exercises to correct verbal deficits.

In another study reported in 2002, training in social and interpersonal skills using behavioral methods resulted in improvement in functioning, relationships, and overall adjustment.

Not all psychosocial interactions are helpful and some can even endanger the patient. For example, brief education intervention that is not extensive or therapeutic enough to lead to behavioral change may increase suicidal thoughts.

Family and Outside Support Structures

Positive social interaction is extremely important for people with schizophrenia and may help reduce symptoms, including the number of delusional moments.

Family Support. It is deeply painful for anyone to interact with a loved one whose behavior is determined by a mysterious internal mechanism that has gone awry. Given support and direction, however, families or other caregivers can be very helpful in a number of ways:

- They can encourage patients to comply with drug treatments and to recognize early signs of serious treatment side effects.
- They can be taught to recognize impending symptoms of relapse and help the patient avoid situations that might trigger them. (Symptoms for an impending relapse after remission may include feeling distant from family and friends, being increasingly bothered by persistent thoughts, and having an increased interest in religion.)

Unfortunately, the family's own mental health is often threatened and they need help almost as much as the patient. Numerous studies have shown that schizophrenic patients do worse in families who are too emotional, hostile, critical, or even overly involved. The problem is an emotional loop:

- When affection and reason have failed to bring a loved one back to reality, overly critical or emotional family members typically react with anger and frustration.
- This generates anxiety and depression in patients.
- The subsequent expression of these emotions by the patient triggers yet more criticism or acting out. So the cycle continues.
- Eventually, out of despair and fear, the family may reject the patient completely.

Studies indicate that once the patient receives appropriate treatment and support, the family's over-emotional state also recedes. And, two studies reported that when families received help for themselves (group support or cognitive therapy) the relapse rates for the related patients were significantly lower than for patients whose families did not seek help. For example, when families received cognitive therapy, the patient relapse rate was 37% versus 72% in the group without family support. Still, fewer than 10% of families of patients with schizophrenia receive the support and education needed not only for the patient but also for themselves. [See Where Else Can Someone Get Help For Schizophrenia?]

Community Treatment Programs. Community treatment programs, in which a team of professional caregivers provides treatment and support for patients in their homes, is highly beneficial and cost effective (compared to frequent hospitalization). At this time, however, only between 2% and 10% of patients now participate in such programs.

Vocational Rehabilitation. Paid work is very important in the health of the patient. One study reported that after one year, 40% of workers with schizophrenia who were paid for their labor reported much improvement in all

symptoms and 50% reported much improvement in positive symptoms. Those who were not paid for their work did considerably less well. (The arts and crafts activities that are often used to enhance self-esteem in rehabilitation programs offer few real benefits to the patient.)

Unfortunately, at this time, less than a quarter of patients with schizophrenia are in programs that assist them in finding and keeping jobs, and up to 90% of patients with severe mental problems are unemployed.

WHAT PROCEDURES ARE USED TO TREAT SCHIZOPHRENIA?

Electroconvulsive Therapy (ECT)

Electroconvulsive therapy (ECT), often called shock treatment, has received bad press since it was introduced in the 1940s. However, refined techniques have revived its use, particularly for those with severe depression. Imaging studies have not found that current ECT techniques cause any damage to the brain's structure, and some physicians feel it is safer than drug therapy. It has not been widely studied in patients with schizophrenia. However, some small studies, including one in 2002, are suggesting it may improve symptoms, including negative symptoms, when used with medication. A major 2002 analysis found some limited proof that this approach may be useful for schizophrenia and there is no evidence to suggest that it should not be used in these patients.

Magnetic Stimulation

Some investigators are testing a procedure called transcranial magnetic stimulation (rTMS), which reduces brain activity. The procedure administers magnetic stimulation to the scalp in the area above and behind the left ear (which corresponds to the areas in the brain associated with auditory hallucinations). Some early studies are reporting reduced hallucinations in between 52% and 70% of patients receiving this therapy. Further research is under way.

WHERE ELSE CAN SOMEONE GET HELP FOR SCHIZOPHRENIA?

National Institute of Mental Health (www.nimh.nih.gov ▶▶). Call (301-443-4513).

National Mental Health Consumer Self-Help Clearinghouse (www.mhselfhelp.org ▶▶). Call (800-553-4539).

National Alliance for the Mentally Ill (www.nami.org ▶▶). Call (800-950-6264).

National Mental Health Association (www.nmha.org ▶▶). Call (800-969-6642).

American Psychiatric Association (www.psych.org ▶▶). Call (888-357-7924).

American Psychological Association (helping.apa.org/find.html ▶▶). Call (800-964-2000) to obtain the names and numbers of regional chapters, which in turn will provide lists of psychiatrists and psychologists.

Stanley Foundation Research Programs (www.stanleyresearch.org ▶▶). Call (301-571-0760).

World Fellowship for Schizophrenia and Allied Disorders (www.world-schizophrenia.org ▶▶). Call (416-961-2855).

Person-to-Person phone-in service that links patients to counselors (www.mentalwellness.com ▶▶). Call (800-376-8282).

Site assists in finding the right therapist (www.1-800-therapist.com ▶▶).

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