Schizophrenia is a chronic mental health condition characterised by a distortion of perceptions and thinking. It is thought to be caused by a combination of biological, social and psychological factors.

Schizophrenia
clinical features and diagnosis

By Michele Sie, MSc, MRPharmS

Schizophrenia is a severe and enduring mental health disorder that is often diagnosed in late adolescence or early adulthood. It can present with a wide assortment of symptoms that distort the form and content of thinking and perceptions, which can lead to the development of strange behaviours.1 Schizophrenia can be chronic or relapsing and remitting.

In the 1890s Kraepelin, a German psychiatrist, used the term “dementia praecox” (early dementia) to describe a cluster of symptoms including psychosis and deterioration in cognition. The term “schizophrenia” was introduced in 1911 when Bleuler, a Swiss psychiatrist, used it to describe a syndrome of distorted perceptions and behaviours. However, it was not until 1959 that the first diagnostic criteria were proposed.2 Today, schizophrenia is classified into several different subtypes based on presenting symptoms.3

People with schizophrenia have a lower quality of life than the general population. This may be related to the side effects of medicines, financial difficulties, lack of social support networks and stigma associated with the disorder.4,5

Epidemiology

The World Health Organization estimates that schizophrenia is the 10th most common non-fatal disease worldwide.6 Although the yearly incidence is low (0.015%), due to the chronic nature of the disorder the lifetime prevalence is around 1%.1,7 Schizophrenia is more common among men and among immigrants and urban populations.1 The average age of onset is 18 years for men and 25 years for women. Women also have an increased risk of developing schizophrenia in their mid forties.

It has been estimated that in the UK the direct costs of schizophrenia treatment and care amount to £2bn per year.4 The condition is also associated with indirect costs including: loss of productivity of patients and their carers, criminal justice system costs and benefit payments. People with a diagnosis of schizophrenia are at a higher risk of suicide than those in the general population. Approximately 10% commit suicide — the most common cause of premature death in this patient group.9

Psychiatric comorbidity

Psychiatric comorbidities are frequent among patients with schizophrenia. Substance misuse is also common; conservative estimates suggest at least half of patients are affected. Comorbid depression occurs in 50% of patients. Anxiety disorders (particularly panic disorder, post-traumatic stress disorder and
obssessive-compulsive disorder) can also be present to varying degrees.10

Causes
The cause of schizophrenia is uncertain — the so-called nature-versus-nurture concept is heavily debated. The most established theory is the “stress-vulnerability” model. This model proposes that schizophrenia is caused by a combination of three types of factors, specifically:1,11

- Biological — for example family history (a genetic cause is suggested, but no single gene has been found to be responsible and it is more likely that there are small changes in several genes) or brain injury (caused by birth trauma or fetal exposure to infection)
- Social — such as low socioeconomic status, poor housing, social isolation, loss of cultural identity and discrimination
- Psychological — including early living environment and stressful life events

Pathophysiology
In the 1970s the “dopamine hypothesis of schizophrenia” was first proposed, which suggested that psychotic symptoms arose from a hyperactivity of dopamine in certain neural pathways. This hypothesis came from the observation that all medicines with antipsychotic properties acted as antagonists at dopamine receptors and that substances that were dopaminergic induced psychotic symptoms.

There are four neural pathways that are important to consider in the pathophysiology and treatment of schizophrenia — the mesolimbic, mesocortical, tuberofundibular and nigrostriatal pathways. Overactivity of dopamine in the mesolimbic pathway is thought to produce the positive symptoms of schizophrenia (see below). The mesocortical pathway is believed to be responsible for the negative symptoms (see below). The causes of these dopamine imbalances are still unclear. The nigrostriatal pathway controls movement, and blockade of dopamine receptors in this pathway causes the extrapyramidal side effects observed with some antipsychotic medicines. Blockade of dopamine in the tuberofundibular pathway leads to the adverse effect of hyperprolactinaemia (for more on the treatment of schizophrenia see the accompanying article, p47).12

Although the dopamine hypothesis remains the preferred neurochemical theory explaining schizophrenia, involvement of other neurochemical pathways has been proposed, including the serotonergic system and the glutamatergic system.

Symptoms
Schizophrenia symptoms are classified into two groups: positive and negative. Positive symptoms are those which cause an excess or distortion of normal function, including:

- Delusions — delusions can be somatic (involving false beliefs about physical illnesses), grandiose (containing beliefs of self-importance and having special powers or abilities) or paranoid (where there are beliefs of persecution)
- Hallucinations — hallucinations can be auditory, tactile, visual, olfactory or gustatory, characterised by experiences when there are no external stimuli
- Disorganised speech and behaviour
- Thought disorders — thought disorder is characterised by disorganised speech, which is believed to be due to abnormal thoughts; thoughts can be blocked (where little or no thoughts occur), or can appear to have been inserted into, or withdrawn from, the mind by others
- Ideas of reference — ideas of reference occur when a person believes that certain external phenomena such as TV, radio or newspaper articles are reporting about them or talking directly to them (ideas of reference can also be considered delusions if there are beliefs that external happenings relate directly to the individual)

Negative symptoms are those that lead to a decrease or loss of normal function, including lack of emotion, apathy, poor or non-existent social functioning, lack of motivation, reduced speech, lack of initiative, slow movements and poor self-care.

It is common for people with schizophrenia to lack insight to such an extent that they do not believe they are ill.1

Diagnosis
Schizophrenia is diagnosed using the International Classification of Diseases Version 10 (ICD-10) criteria.
For a diagnosis to be made there must be clear evidence of either:

- One of the following — hallucinations, delusions or thought disorder
- Two of the following — catatonia, negative symptoms or a consistent change in personal behaviour

These symptoms must be present for the majority of a one-month period.

Generally, a diagnosis of schizophrenia will not be made based on a single episode of psychosis. This is because psychosis can occur as part of a number of different mental health conditions or be due to another cause (see below).

The onset of the first episode of psychosis of schizophrenia is usually preceded by a prodromal phase. This phase includes symptoms that can cause a deterioration in functioning, such as reduced concentration and attention, reduced drive and motivation, sleep disturbance and anxiety.

Young people often fail to complete further education and become isolative and socially withdrawn. Delay in diagnosing and treating first episode psychosis increases the risk of more severe long-term positive and negative symptoms.

The ICD-10 criteria are also used to classify a patient with schizophrenia based on his or her prominent symptoms at presentation (see Box 1). For example, paranoid schizophrenia has prominent symptoms of paranoid delusions accompanied by auditory hallucinations.

**Box 1: Summary of ICD-10 classification of schizophrenia**

<table>
<thead>
<tr>
<th>PRESENTATION</th>
<th>KEY FEATURES</th>
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<tbody>
<tr>
<td>Paranoid schizophrenia</td>
<td>Prominent affective changes, thought disorder, fleeting and fragmented delusions and hallucinations, irresponsible and unpredictable behaviour, mannerisms, incoherent speech and social isolation</td>
</tr>
<tr>
<td>Hebephrenic schizophrenia</td>
<td>Fluctuating psychomotor disturbances (including hyperkinesis [overactive restlessness] and stupor), long periods of posturing (voluntary inappropriate or bizarre postures), vivid scenic hallucinations may be present</td>
</tr>
<tr>
<td>Catatonic schizophrenia</td>
<td>Used when symptoms are not within the above three categories or when symptoms fall into more than one of these sub-types</td>
</tr>
<tr>
<td>Undifferentiated schizophrenia</td>
<td>A depressive episode following an episode of acute illness. Some positive or negative symptoms of schizophrenia must still be present but they are no longer dominating the clinical picture</td>
</tr>
<tr>
<td>Post-schizophrenic depression</td>
<td>Long standing negative symptoms</td>
</tr>
<tr>
<td>Simple schizophrenia</td>
<td>Progressively strange behaviours, poor social functioning, deteriorating daily functioning, negative symptoms, overt psychotic symptoms are generally not present</td>
</tr>
<tr>
<td>Other schizophrenia</td>
<td>For example: cenesthopathic schizophrenia (somatic hallucinations causing abnormal bodily sensations)</td>
</tr>
<tr>
<td>Schizophrenia, unspecified</td>
<td>Any disorder where symptoms have not been fully assessed and classified as above</td>
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Differential diagnoses

Some medical conditions can present as psychosis. Thought disorder, delusions, visual and auditory hallucinations and paranoia have been documented with long-standing untreated hypothyroidism and hyperthyroidism. Olfactory hallucinations are commonly experienced in temporal lobe epilepsy. Systemic lupus erythematosus, central nervous system tumours, migraines, diabetes, human immunodeficiency virus, head injury and delirium have also all been associated with psychotic symptoms.11

There are a number of medicines that can induce psychosis. Levodopa (the amino-acid precursor of dopamine) and dopamine agonists such as bromocriptine and pergolide can all cause psychotic symptoms. Furthermore, psychotic symptoms can be caused or worsened by some medicines, including antimuscarnics, some anti-infectives (eg, isoniazid), beta-blockers, corticosteroids and amphetamines.12 Psychoactive substances (such as alcohol, hallucinogens, opioids and cannabis) have also been associated with psychotic symptoms.13

Cannabis

One of the pharmacological effects of cannabis is to increase dopamine release in the brain. As already discussed, an overactivity of dopamine is considered to be the neurochemical basis for schizophrenia. Drug-induced psychosis is a commonly observed syndrome and there are concerns about the long-term effects of cannabis use on the risk of developing schizophrenia. Recent research has indicated that heavy cannabis users have a sixfold increased risk of developing schizophrenia compared with non-users.17

Baseline tests

A range of baseline tests should be carried out for those with a suspected diagnosis of schizophrenia to exclude any physical conditions that could account for the psychotic symptoms. These should include:

- Thyroid function tests to assess for hyper- or hypothyroidism
- Liver function tests to assess alcohol use
- Blood sugar level to assess for diabetes
- Urine drug screening to rule out (or identify) substance misuse

References