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Schizophrenia

Schizophrenia is a mental illness associated with symptoms which include hallucinations (can include seeing and hearing things), delusions (false ideas), disordered thoughts, and problems with mood, behaviour and motivation. It can cause a person to lose touch with reality and thus become unable to tell what is real and what is not. The cause is not clear. In many people symptoms recur or persist long-term, but some people have just one episode of symptoms that lasts a few weeks. Like other mental illnesses, there is a general misunderstanding of schizophrenia amongst the general public. For example, there is a general misconception that schizophrenia sufferers have a split or “Jekyll and Hyde” type personality which is not true. There is also a misconception that schizophrenia sufferers have a tendency to be violent; the truth is that the vast majority of schizophrenia sufferers are not violent. Schizophrenia is like many other mental health problems in that it is caused by an imbalance of chemicals in the brain. Like any other long term illness, it is a major inconvenience and disruption on somebody’s life, however it is not something to be embarrassed about and with proper treatment you can lead a normal life. The good news nowadays (especially over the last 20 years) there is very effective treatment options which allow a person suffering from schizophrenia lead a normal life.

When does it generally occur?

Schizophrenia occurs in about 1 in 100 people; this rate is the same for all ethnic groups. It occurs equally in men and women. It most often first develops between the ages of 15 to 25 in men and 25 to 35 in women. First diagnosis of schizophrenia is rare after the age of 45. It normally continues throughout life however symptoms can be kept to a minimum with proper treatment. If a person develops schizophrenia in their teens, early diagnosis can be difficult. This is because the first signs can include a change of friends, a drop in grades, sleep problems, and irritability, all of which are behaviours that are common among teenagers. A combination of factors and behavioural changes can help doctors predict schizophrenia in up to 80% of youths who are at high risk of developing the illness. These factors include isolating oneself and withdrawing from others, an increase in unusual thoughts and suspicions and a family history of psychosis. Psychosis is a serious mental condition that is caused by a disturbance in brain functioning. A person with psychosis experiences a loss of contact with reality, characterised by changes in their thoughts, beliefs, perceptions and/or behaviour.

Initial signs

The onset of schizophrenia can be abrupt. However most people undergo a “prodromal phase” characterised by a slow and gradual development of symptoms, including social withdrawal, loss of interest in school or work, deterioration in hygiene, becoming uncharacteristically unkempt, unusual behaviour, or outbursts of anger. Family members may assume that the person is just “going through a phase”, especially in the case of adolescents who are notorious for going through difficult phases. Often it is only after the appearance of classic symptoms associated with schizophrenia (e.g., psychosis such as delusions and hallucinations) that the diagnosis of schizophrenia is made.

Symptoms

The symptoms are classed as either positive or negative. Positive symptoms are abnormal mental functions while negative symptoms are best described as loss of normal mental

functions. Positive and negative symptoms vary in intensity over time; people with schizophrenia display predominantly one type at any particular time.

Negative symptoms

Negative symptoms include loss of motivation (including loss of interest in social activities, mixing with people, loss of concentration and inability to complete activities you previously had no problem completing), loss of a sense of pleasure, slow movements, lack of facial expression and low or flat mood. The person may uncharacteristically neglect their appearance and look unkempt. The negative symptoms of schizophrenia are very similar to the symptoms of depression and can be misdiagnosed as depression; the biochemical reactions in the brain that cause negative symptoms are similar to those that cause depression.

Positive symptoms

Positive symptoms are psychotic behaviours not seen in healthy people; they cause people to temporarily lose touch with reality. The symptoms come and go so at times they can be severe and at other times they can be hardly noticeable.

Delusions
These are false beliefs that are not part of the person's culture and most people of the same culture would agree are not true. For example the person may believe that aliens are coming to get them, that television is directing special messages to them or that people are plotting to kill them; the delusions can be anything, there is no set trend for the types of delusions a person may experience.

Hallucinations
This can include hearing, seeing, feeling, smelling, or tasting things that are not real. Hearing voices tends to be the most common type of hallucination. Some people with schizophrenia appear to talk to themselves as they respond to the voices. People with schizophrenia believe that the hallucinations are real.

Disordered thoughts
Thoughts become jumbled or blocked. Thought and speech may not follow a normal logical pattern. The person may make up meaningless words or "neologisms". Types of thought disorder with schizophrenia include *thought echo* (person hears their thoughts as if they were being spoken aloud), *knight's-move thinking* (person moves from one train of thought to another that has no apparent connection to the first) and *disorders of thought possession*. Disorders of thought possession include *thought insertion* (when someone believes that their thoughts are being put there by someone else), *thought withdrawal* (when someone believes that their thoughts are being removed from their mind by an someone or something else), *thought broadcasting* (when someone believes that their thoughts are being read or heard by others) and *thought blocking* (when there is a sudden interruption of their train of thought meaning the person stops talking mid-sentence, the person often cannot recall what he or she has been saying).

Movement disorders
Movement disorders may appear as agitated body movements. A person with a movement disorder may repeat certain motions over and over. In the other extreme, a person may become catatonic. Catatonia is a state in which a person does not move and does not respond to others. Catatonia is rare today due to the availability of modern antipsychotic medication to prevent it.

Causes

While the exact cause of schizophrenia is not known there is evidence that the balance of some brain chemicals (neurotransmitters) is altered which means that the messages from the brain do not pass correctly. The neurotransmitter dopamine appears to play an important role. Most antipsychotics decrease the neurotransmission of dopamine. There is a genetic influence meaning that it does tend to run in families; 70% of the risk of schizophrenia is thought to be hereditary. For example, a close family member (child, brother, sister, parent) of someone with schizophrenia has a 10% chance of also developing the condition. This is 10 times the normal chance. A child born to a mother and father who both have schizophrenia has a 1 in 2 chance of developing it too.

However certain triggers appear to be needed to trigger the condition in people who are genetically prone to it. There are various theories as to what these might be and they are thought to account for 30% of the risk of developing schizophrenia (other 70% of risk is hereditary). These include:

- Stress such as relationship problems, financial problems, separation from family when a child, social isolation, bereavement
- A viral infection during the mother's pregnancy, or in early childhood.
- Childhood brain injury (eg) a lack of oxygen at birth may damage part of the brain
- Illegal or street drugs may trigger the condition in some people. Those who use cannabis heavily are six times more likely to develop schizophrenia than nonusers. Many other drugs of abuse such as amphetamines, cocaine, ketamine, and lysergic acid diethylamide (LSD) can trigger a schizophrenia-like illness.

Other conditions that can be confused with schizophrenia

Substance abuse can cause symptoms that are similar to schizophrenia. Substance abuse including the abuse of multiple substances (e.g., hallucinogens, narcotics, alcohol) and the withdrawal from these substances can cause delusions and hallucinations. Therefore diagnosis of schizophrenia should not be made while a person is still taking drugs.

Bipolar disorder and depression can also cause psychotic type symptoms which can lead to misdiagnosis of schizophrenia. On the flip side, schizophrenia can be misdiagnosed as bipolar disorder or depression (especially when negative symptoms predominate).

Delirium can have features that are similar to the positive symptoms of schizophrenia (e.g., hallucinations, delusions). Delirium is a confused state that is brought on by medical illness. The main feature that distinguishes schizophrenia from delirium is the timing. Symptoms of schizophrenia generally develop over weeks or months, whereas delirium usually develop quite rapidly and is mostly associated with medical illnesses. Delirium tends to be a lot shorter lasting than schizophrenia. The diagnosis of new-onset schizophrenia should be made cautiously while a patient has an existing serious medical illness.

Some illnesses can cause symptoms similar to schizophrenia. These include hypoglycaemia (low blood sugar), hepatic encephalopathy (worsening brain function due to liver failure), electrolyte abnormalities such as hyponatraemia (low sodium levels), hypercalcaemia (raised calcium levels), hypocalcaemia (low calcium levels), hypomagnesaemia (low magnesium levels) and sepsis (severe infection). The symptoms resolve once the condition is controlled. Delirium explains the psychotic symptoms in some of these conditions. Some prescription medication can cause schizophrenia like symptoms. These medicines very rarely cause these symptoms and it generally only occurs when then the blood levels go too high. Examples of drugs that can cause schizophrenia like symptoms include

anticholinergics (used to treat various conditions including urinary incontinence, COPD and allergies), benzodiazepines (for anxiety and insomnia), digoxin (for cardiac arrhythmias), phenytoin (for epilepsy), steroids (for inflammatory) and opioid analgesics (for severe pain). These drugs are safe in the majority of patients when prescribed appropriately and psychotic type symptoms only occur in exceptional situations; for example, when they interact with other drugs or if the patient has a medical illness which causes the effect of the medication to be exaggerated.

Treatment

Often people suffering from schizophrenia do not realise they have a mental illness. They may not think they need help because the condition makes you believe the delusions or hallucinations are real. Therefore it is often up to family and friends to seek treatment.

The causes of schizophrenia are still unknown; therefore treatment focuses on eliminating the symptoms of the disease. While medication is not the only treatment option for schizophrenia, medication forms an important component of the treatment regime. Antipsychotics are mainly used to treat schizophrenia. They work by altering the balance of some neurotransmitters in the brain thus controlling symptoms. Positive symptoms respond well to antipsychotic drugs however they do not work as well on negative symptoms. Therefore, antipsychotic medication is usually taken on a long-term basis to prevent relapses. Antipsychotic drugs are broadly divided into two categories; typical or atypical antipsychotics.

Older typical antipsychotics
These are sometimes called ***first generation*** antipsychotics and were the first type of antipsychotics developed in the 1950s for psychosis, especially schizophrenia. Examples include chlorpromazine (Largactil®), trifluoperazine (Stelazine®), haloperidol (Serenace®), flupentixol (Depixol® Injection, Fluanxol® tablets), zuclopenthixol (Clopixol® Injection), and sulpiride (Dolmatil®). 30% of patients have a relapse during treatment with first-generation antipsychotic drugs compared with 80% without treatment.

Newer or atypical antipsychotics
These were first introduced in the 1990's and are also known as ***second generation*** antipsychotics. Examples are amisulpride (Solian®), aripiprazole (Abilify®), clozapine (Clozaril®), olanzapine (Zyprexa®), quetiapine (Seroquel®) and risperidone (Risperdal®). There are now generic equivalents of most of these drugs now available. Atypical antipsychotics are often used as the treatment of first choice for people newly diagnosed with schizophrenia. This is because they demonstrate good balance between chance of success and the risk of side-effects. However, for people already stabilised on typical antipsychotic there is no need to change to a newer one.

Depot injections of an antipsychotic drug
In some cases, an injection of a long-acting antipsychotic drug is used once symptoms have eased. The drug from a depot injection is slowly released into the body and is given every 2 to 4 weeks. This aims to prevent relapses. The main advantage is that it prevents non-compliance which is when people forget to take their medication or decide not to take their medication. Not taking prescribed medication can be a problem with schizophrenia as the person often does not realise they have a problem or do not feel that they are ill. An American study showed that 74% of patients with schizophrenia discontinued medication within 18 months without consulting with their doctor leading to relapses. Non-compliance is similar for atypical and typical antipsychotics; depot injections can be a solution in these situations. Depot injections are administered by a trained nurse usually through the local community mental health service.

Choice of Drug

There are some differences between the various antipsychotic drugs. No one drug can be considered significantly better than the others, however one may be better for one individual than another. For example, some are more sedating than others so may be suitable for patients who are agitated or cannot sleep. If one does not work so well, a different one is tried until a good response occurs. A good response to antipsychotic medication occurs in about 70% of cases. Symptoms such as agitation and hallucinations generally ease within a few days of starting medication. Symptoms like delusions usually subside within a few weeks and it can take several weeks for full improvement. Antipsychotic medication is normally continued long-term once symptoms improve. Long term treatment aims to prevent relapses, or at least limit the number and severity of relapses. There is some evidence that the newer atypical antipsychotics give lower relapse rates than older typical antipsychotics. Newer atypical antipsychotics have been shown in studies to be more effective at improving cognitive function (including attention, memory and speech) than older typical antipsychotics. Newer atypical antipsychotics also appear to be more effective than older typical antipsychotics for negative symptoms of schizophrenia. Clozapine is often prescribed for patients who have not responded adequately to treatment despite the use of adequate doses of at least two different antipsychotic drugs. At least one of the drugs should be an atypical antipsychotic before trying clozapine. Clozapine (Clozaril®) is very effective for psychotic symptoms including hallucinations and breaks from reality. Clozapine can sometimes cause a serious condition called agranulocytosis, a loss of the white blood cells which reduces the ability to fight infection. People who take clozapine must get their white blood cell counts checked weekly for the first 18 weeks and every two weeks after that for the first year and every four weeks thereafter, including the first four weeks after the drug is discontinued. Other atypical antipsychotics do not cause agranulocytosis. While all antipsychotics lower the threshold for seizures (making an epileptic fit more possible), this effect is more pronounced with clozapine. The risk of agranulocytosis and the cost of blood tests is the main reason that clozapine is generally reserved for when other medication fails which is estimated to be 30% of cases.

For patients who have only one episode of schizophrenia and who remain symptom free for two years with treatment, the medication may then be discontinued slowly under the supervision of a doctor; the patient must be closely monitored for relapse when medication is being discontinued.

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Side-effects of antipsychotic drugs

Side-effects can occur and there is a trade-off between easing symptoms and side-effects from treatment. Different antipsychotic drugs cause different types of side-effects. Sometimes one drug causes side-effects in some people and not in others. Quite often, two or more different drugs have to be tried before one is found that is best suited.

Anticholinergic side effects are more common with the older typical anti-psychotics and include dry mouth, blurred vision, flushing and constipation. These tend to be worse at the start of treatment and may ease off as the person gets used to the drug. Chlorpromazine has a tendency to cause skin rash when the person is exposed to sunlight. Sunscreen must be used if going out in strong sun while taking chlorpromazine.

Drowsiness is also common but may be reduced by reducing the dose. Movement disorders can occur with typical antipsychotics. These include:

- Parkinson type symptoms, for example, tremor and muscle stiffness.
- Akathisia, which is like a restlessness of the legs (a major cause of non-compliance)
- Dystonia, which is abnormal movements of the face and body.

- Tardive dyskinesia, which is a movement disorder that can occur with longer term treatment with antipsychotics. It causes rhythm like, involuntary movements. Tardive dyskinesia most commonly affects the mouth and can include lip-smacking, grimacing and tongue-rotating movements, although it can affect the arms and legs too. About 30% people treated with typical antipsychotics long term eventually develop tardive dyskinesia. This side effect is rarer nowadays as people are closely monitored for symptoms of tardive dyskinesia and the drug is changed once the symptoms start to develop.

If movement disorders are a problem, then other drugs may be used to try to counteract them. These include anti-cholinergic drugs such as biperiden (Akineton®). Tardive dyskinesia will not respond to treatment with anti-cholinergic drugs but usually resolves slowly after discontinuation of the typical antipsychotic. However it is irreversible in some cases. Propranolol (20 to 80 mg daily) can be prescribed by the doctor to control akathisia (restlessness).

Atypical antipsychotic drugs are less likely to cause movement disorder side-effects than typical antipsychotic drugs. This reduced incidence of movement disorders is the main reason why an atypical antipsychotic drug frequently the first choice for treatment. Atypical antipsychotics do have their own risks, particularly the risk of weight gain. Weight gain can occur and this may increase the risk of developing diabetes and heart problems (due to raised cholesterol) in the longer term; thus blood sugars and cholesterol levels should be monitored regularly. Weight gain appears to be a particular problem with clozapine and olanzapine. For example, studies show that olanzapine can cause weight gain of 5.4kg within 5 weeks of treatment and weight gain of 20kg or more after longer term treatment. Ziprasidone (Geodon®) and amisulpride (Solian®) tend to cause less weight gain than other atypical antipsychotics. Atypical antipsychotic drugs can sometimes cause the tendency to cause obsessive compulsive symptoms.

Antidepressants

Antidepressants may be used in some cases, especially for people primarily showing negative symptoms. Research suggest that taking an antidepressant drug in addition to an antipsychotic drug may be better than an antipsychotic drug alone in treating negative symptoms of schizophrenia. An antidepressant drug may also be useful to treat depression which is common in people with schizophrenia. People who display manic episodes including excitement and agitation may benefit from mood stabilisers such as lithium carbonate or sodium valproate.

Family education

People with schizophrenia are often discharged from the hospital into the care of their families. It is important that family members know as much as possible about the disease. With the help of a therapist, the GP and staff from your local HSE community Mental Health Service, family members can learn coping strategies and problem solving skills. In this way the family can help make sure their family member continues with treatment and continues to take prescribed medication.

Psychological treatments

Cognitive behavioural therapy (CBT)
Psychological treatments include a variety of talking treatments, in particular a treatment called cognitive behavioural therapy (CBT). CBT is used as a treatment for various mental health and physical problems and is being increasingly used as a treatment for schizophrenia. CBT aims to help the person change the way that they think, feel and behave. CBT is actually a wide term which includes various types of therapy. You may be asked to keep a diary of important events in your life and the way you feel about them. Your therapist may challenge your beliefs and ask you to explain them. You may be asked to try out new ways of behaving and reacting.

CBT and other talking treatments are not alternatives to drug treatment. They are often used in conjunction with medication. The National Institute of Clinical Excellence (NICE) in the UK (an internationally renowned healthcare advice organisation) recommends up to 16 CBT sessions. This is because studies have found that, on average, CBT reduces the chance of being admitted or readmitted to hospital, can reduce symptom severity and can improve social functioning.

In summary, CBT has two phases or goals. The first is to raise your awareness of the condition and what behaviours, thoughts and emotions are leading to your mental health difficulties. The second is to use this knowledge to tackle the problem and to behave in a different way so as to relieve the underlying problems such as schizophrenia, anxiety or depression.

Schizophrenia and heart disease and smoking

Smoking and nicotine addiction is more common in people with schizophrenia. They are addicted to nicotine at three times the rate of the general population (75 to 90% versus 25 to 30%).

The full reason for higher smoking rates among people with schizophrenia is not fully understood; it is thought to be partly due to the way that smoking can temporarily improve cognitive function in people with schizophrenia including attention, memory and speech as well as be perceived (incorrectly) as relaxing. The rate of smoking in people with schizophrenia is also higher than for those suffering from other mental health illnesses including depression and bi-polar disorder. The risk of death from heart disease is two to three times higher among people with schizophrenia than the general population. The reason for this is mainly attributed to the higher rate of smoking among people with schizophrenia.

What is the outlook (prognosis)?

- In most cases there are recurring episodes of symptoms (relapses). Most people live relatively independently with varying amounts of support. The frequency and duration of each relapse can vary. Some people recover completely between relapses. Some people improve between relapses but never quite fully recover. Treatment often prevents relapses, or limits their number and severity.
- In some case (approximately 2 in 10 cases), there is only one episode of symptoms that only lasts a few weeks. This is followed by a complete recovery without any further relapses.
- Up about 20% of people with schizophrenia, medication is not very effective at

controlling symptoms and they need long-term dependent care. For some, this is in secure accommodation.
- Depression is a common complication of schizophrenia.
- It is thought that up to a third of people with schizophrenia abuse alcohol and/or illegal drugs. This can make treatment more challenging.
- About 1 in 10 people with schizophrenia attempt or commit suicide.

The outlook is thought to be better if:
- Treatment is started soon after symptoms begin.
- Symptoms develop quickly over several weeks rather than slowly over several months
- The main symptoms are positive symptoms rather than negative symptoms.
- The condition develops in a relatively older person (aged over 25).
- Medication is taken as advised.
- There is good family and social support which reduces anxiety and stress.
- Abuse of illegal drugs or alcohol does not occur.

Newer drugs and better psychological treatments mean that prognosis is now better than it was in the past.

Medication	**For Schizophrenia**
First-generation antipsychotic agents	**Daily Oral Dose** *mg*
Chlorpromazine (Largactil, Clonactil)	150–1000
Trifluoperazine (Stelazine)	5–60
Haloperidol (Serenace)	2–25
Second-generation antipsychotic agents	
Clozapine (Clozaril)	100–900
Risperidone (Risperdal)	2–10
Olanzapine (Zyprexa)	5–20
Quetiapine (Seroquel)	75–750
Ziprasidone (Geodon)	40–160
Aripiprazole (Abilify)	15–30
Amisulpride (Solian)	400–1200

Intramuscular Dose	**For Schizophrenia**
Depot preparations	**Every 2 to 4 weeks** *mg*
Fluphenazine decanoate (Modecate decanoate injection)	12.5–50
Haloperidol decanoate (Haldol decanoate injection)	50–200
Flupentixol decanoate (Depixol depot injection)	20–100
Risperidone microspheres (Risperdal Consta)	25–50

Written and researched by Eamonn Brady (MPSI), Whelehans Pharmacy, 38 Pearse Street, Mullingar. 04493 34591. References available upon request