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Schizophrenia: towards better understanding and better outcomes

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Early detection in general practice of patients with psychoses and their prompt referral may improve outcomes in those with schizophrenia.

Key points

- **Although strongly heritable, the genetic basis of schizophrenia is unknown and likely to be complex. Research is turning to the study of interactions among genes and between genes and environmental factors.**
- **Cognitive impairment is a core feature of schizophrenia and is present before onset of illness, stable over time and a good predictor of long term function.**
- **Early detection and treatment of schizophrenia is important in reducing the duration of untreated psychosis and promoting better outcomes.**
- **Detection of psychotic symptoms requires asking questions about the experiencing of delusions and hallucinations.**
- **Overcoming barriers to engagement in therapy is critical in achieving a good treatment outcome. Clinicians should take the initiative in this process to establish a strong therapeutic relationship.**
- **Assertive monitoring of the patient's physical health is necessary for detection of metabolic, cardiovascular and other abnormalities that are common in schizophrenia due to combinations of medication effects and unhealthy lifestyles.**

'In my fog of isolation and silence, I began to feel I was receiving commands to do things – such as walk all by myself through the old abandoned tunnels that lay underneath the hospital. The origin of the commands was unclear. In my mind, they were issued by some sort of beings. Not real people with names or faces, but shapeless, powerful beings that controlled me with thoughts (not voices) that had been placed in my head.'

Elyn R. Saks. *The Centre Cannot Hold: My Journey Through Madness.* (Hyperion; 2007. p84.)

Schizophrenia ranks among the top 10 causes of disability in developed countries. The condition's incidence is estimated (with some variation) at 15.2/100,000 persons and its prevalence at 4.6/1000 persons.[1] These statistics translate into there being more than 40,000 people in Australia with an illness that makes it impossible or, at best, very difficult for them to form and maintain relationships, study or work productively and integrate into mainstream society. With a mortality rate two and a half times that of the general population, people with the condition have a life expectancy that is curtailed by 12 to 15 years.[2] This premature mortality is increasing.[2] Suicide occurs in 5% of people affected.

AETIOLOGY

Schizophrenia is a clinical syndrome and cannot be regarded as a disease entity; there is significant heterogeneity within it and considerable overlap between it and other psychiatric conditions. These difficulties tend to confound attempts to define the aetiology and pathophysiology of schizophrenia. Nevertheless, its genetic basis has been confirmed by family, adoption and twin studies, the latter suggesting a high heritability of approximately 80% (i.e. about 80% of the causal variance is accounted for by genetic factors).[3]

The successful mapping of the human genome and the extraordinary recent technical developments in molecular genetics have not yet pinpointed the genetic basis of schizophrenia.

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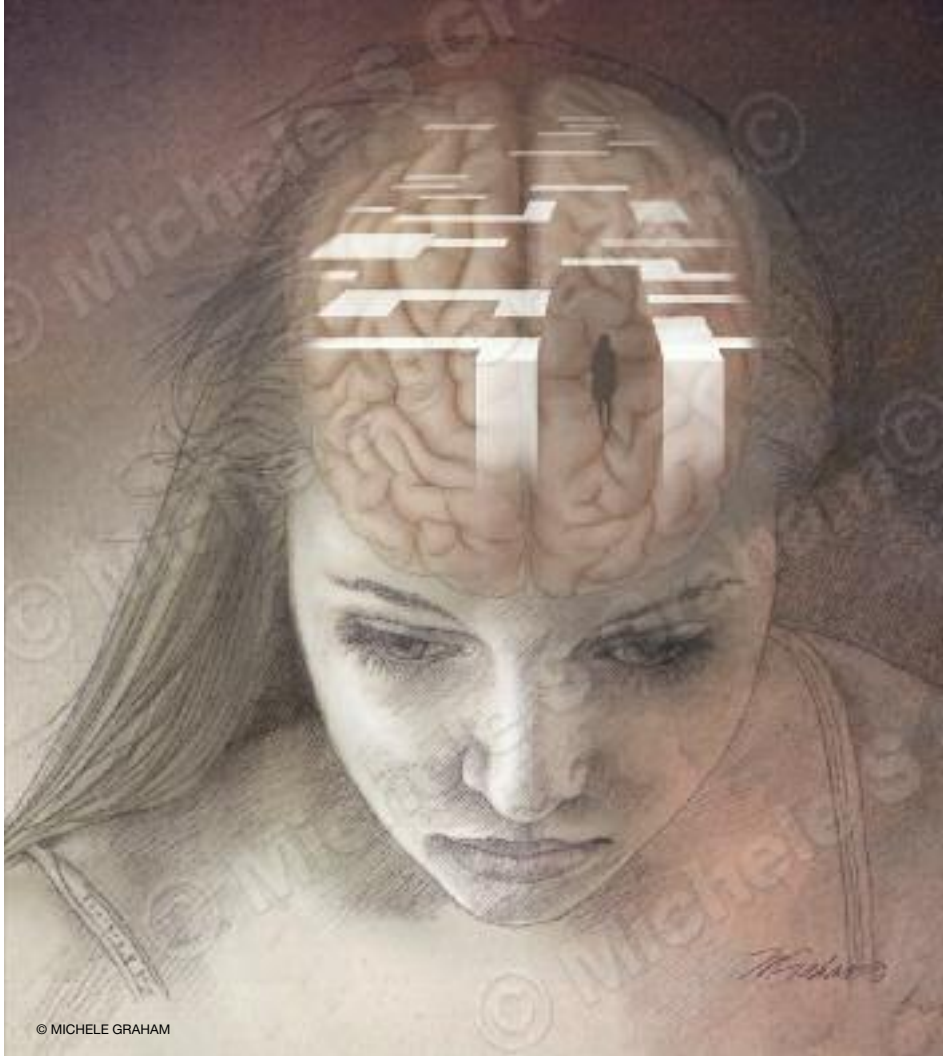
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Genome-wide association studies have so far had disappointing findings, marked by an inability to clearly identify causal genes and failures to replicate findings of promising candidate susceptibility genes. An emerging consensus is that schizophrenia is a genetically complex disorder, similar to diabetes and cancer, involving multiple genes of small effect interacting with each other and with environmental factors.

The response of the scientific community to this dilemma is fourfold, as discussed below.

- Ever-increasing sample sizes, in the tens of thousands, are being sought via multicentre research collaborations to achieve the statistical power necessary to identify genetic factors of small effect.
- Attempts to achieve greater phenotypic homogeneity are being pursued through the identification of subtypes based on clinical criteria (e.g. symptom pattern, course, outcome) or related criteria (e.g. onset age, cognitive deficit, neurological 'soft signs', childhood adversity, early cannabis abuse).
- Endophenotypes are being identified and their genetic determinants are being studied. The term endophenotype refers to a measurable component (e.g. neuro - physiological, brain imaging or cognitive markers) on the pathway between genotype and disease. An endophenotype must be associated with the disorder, heritable, present before, during and after acute illness episodes, co-segregate with illness in families and found in unaffected family members at higher rates than in the general population.[4] Examples of candidate endophenotypes in schizophrenia include certain electroencephalogram (EEG) measures, saccadic eye movements, regional grey matter deficits and working memory impairments.
- Factors influencing alterations in gene expression are being studied – the science of epigenetics. Examples include DNA methylation or histone acetylation in chromatin and post-transcriptional gene silencing by micro-RNA molecules. Environmental factors may affect gene expression, exerting their influence through these molecular mechanisms.

Several risk factors for schizophrenia have been identified through epidemiological research. These factors are listed in Table 1 with their relative risk ratios, which for most factors are quite small. The unanswered questions are whether combinations of these factors add or multiply together in contributing to schizophrenia and, similarly, with what combinations of genetic risk factors are they additive or multiplicative in causing the illness. Among obstetric complications, those that result in fetal hypoxia appear to be associated with a greater risk for schizophrenia.

PATHOPHYSIOLOGY

A relatively consistent finding in postmortem studies of the brain of people with schizophrenia is a reduction in cortical neuropil. This appears to be accounted for by a decrease in the density of dendrites. It has been proposed that the relative reduction in dendritic branches may be due to an excessive degree of the synaptic pruning that normally occurs during adolescence. In any event, such findings

TABLE 1. RISK FACTORS FOR SCHIZOPHRENIA

Risk factors	Relative risk*
Urban birth and upbringing (age under 15 years)	2 to 3
Migration:	
– first-generation immigrants	2 to 3
– second-generation immigrants	4 to 5
Maternal infection/malnutrition (first or second trimester)	2 to 3
Obstetric/perinatal complications	2 to 3
Winter birth	1.1
Cannabis use	2 to 3
Paternal age over 35 years	1.5 to 3
Male gender	1.4

* The relative risk (or risk ratio) is the probability of developing a disease in people exposed to a particular risk factor divided by the probability of developing the disease in those not exposed to that risk factor. Thus for cannabis use there is a two- to three-fold greater probability of developing schizophrenia in those who use cannabis than in those who do not.

suggest a reduction in neuroanatomical connectivity in the cerebral cortex in schizophrenia. In addition, there is altered placement and disarray of certain neurons in schizophrenia and an absence of gliosis. These findings, together with other evidence, have led to the view that there is a subtle but fundamental disturbance in the processes of neurodevelopment in schizophrenia.

An influential hypothesis is that an important component of this reduced neuronal connectivity is hypofunctioning of N-methyl-D-aspartate (NMDA) receptor-mediated glutamate neurotransmission, particularly those NMDA receptors located on certain γ-aminobutyric acid (GABA)-ergic inhibitory interneurons in the thalamus and cortex. The net effect of this is a reduction in the inhibitory effects of these interneurons leading to disinhibition of projection (pyramidal) neurons and resultant cortical excitotoxic effects, including loss of dendrites and synapses. Reduced inhibitory GABAergic interneuron activity disrupts the synchrony of high frequency cortical EEG oscillations, interfering with working memory and other aspects of consciousness.

The relative reduction in the functioning of these GABAergic inhibitory interneurons has, by mechanisms not well understood, the following effects:

- reduced dopamine activity in mesocortical pathways (from ventral tegmentum to prefrontal cortex), mediated by the dopamine D_1 receptor
- increased dopamine activity in mesolimbic pathways (from ventral tegmentum to nucleus accumbens and other limbic regions), mediated by the dopamine D_2 receptor.

The former effect is thought to account for the negative symptoms of schizophrenia, and the latter effect is believed to account for the positive (psychotic) symptoms of schizophrenia. The latter effect is the pathway through which antipsychotic medications have their therapeutic action.

CLINICAL FEATURES AND DIAGNOSIS

The triad of clinical features of schizophrenia – positive symptoms, negative symptoms and cognitive impairment – and a paraphrased version of the draft diagnostic criteria of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-V*; due for publication in May 2013; see www.dsm5.org) are presented in the boxes on page 18.

The traditional subtypes of schizophrenia (e.g. paranoid, catatonic, disorganised) have not been included in the *DSM-V* draft as they are regarded as having minimal utility and diagnostic stability. Otherwise, only minor changes have been made in criterion A and no changes at all in criteria B to F. However, it has been proposed that a dimensional assessment (on a 0 to 4 scale) be added of the severity of symptoms in criterion A as well as the severity of mania, depression and impaired cognition.

Cognitive impairment

In spite of its importance in contributing to disability and accumulating advances in knowledge about its scope, cognitive impairment has not been included in the draft *DSM-V* diagnostic criteria.[5] This is largely because of its lack of diagnostic specificity and uncertainty as to the impact of introducing it as a diagnostic criterion.[6]

Nevertheless, cognitive impairment is widely regarded as a core feature of schizophrenia. There is a fairly characteristic pattern of impairment, notwithstanding some overlap with bipolar disorder, and it occurs with high frequency, is stable over time and is independent of acute psychotic symptoms. Cognitive impairment is also present throughout the lifespan of people with schizophrenia, including during childhood before the onset of illness, and it is present in an attenuated form in their first-degree relatives. It is also a good predictor of long-term functioning.

Psychosis risk syndrome

There is growing interest in identifying, prior to illness onset, those young people who are likely to go on to develop a psychotic disorder, including schizophrenia. This work has been pioneered in Melbourne.[7] It represents a promising line of research, including experimental studies

CLINICAL FEATURES OF SCHIZOPHRENIA

Positive symptoms
- Delusions
- Hallucinations (typically auditory but may occur in other modalities)
- Formal thought disorder (e.g. loose associations, incoherence, neologisms)
- Disorganised behaviour (e.g. mannerisms, posturing, bizarre dress)

Negative symptoms
- Affect restricted or blunted
- Avolition (apathy, amotivation)
- Asociality (social withdrawal)
- Alogia (poverty in amount or content of speech)
- Anhedonia (loss of the capacity to experience or the motivation to seek pleasure)

Cognitive impairments
- General intelligence (IQ)
- Selective and/or sustained attention
- Working memory
- Verbal memory
- Language (verbal fluency, naming, comprehension)
- Processing speed
- Executive control (flexibility in problem solving)
- Social cognition (ability to identify and respond appropriately to social cues)

DRAFT DSM-V DIAGNOSTIC CRITERIA FOR SCHIZOPHRENIA (PARAPHRASED)*

Draft *DSM-V* Criterion A corresponds with Positive symptoms and Negative symptoms in the clinical features of schizophrenia.
Draft *DSM-V* Criteria B to F have no correspondence with any of the clinical features of schizophrenia.

Criterion A. Characteristic symptoms
Two or more of items 1 to 5 below present for a significant time during a one-month period; at least one item should be 1, 2 or 3.
1. Delusions
2. Hallucinations
3. Disorganised speech
4. Grossly abnormal psychomotor behaviour (e.g. catatonia)
5. Negative symptoms (i.e. restricted affect, avolition, asociality)

Criteria B to F
Criterion B. Social/occupational dysfunction – decline from pre-onset levels of at least one of work functioning, interpersonal relations or self-care
Criterion C. Duration – continuous signs for at least six months, including at least one month of symptoms from Criterion A; this may include periods of prodromal or residual symptoms
Criterion D. Exclusion of schizoaffective and mood disorder
Criterion E. Exclusion of the direct effects of a substance (drug of abuse or medication) or a general medical condition
Criterion F. Relationship to a pervasive developmental disorder. If there is a history of autism or other pervasive developmental disorder, the diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month

* For the full draft *DSM-V* criteria, see www.dsm5.org

of treatment in this group of high-risk patients.[8]

A proposal to include diagnostic criteria for a 'psychosis risk syndrome' is under consideration for inclusion in *DSM-V*. Even if it is not included, clinicians will be hearing more about this in the future; it is often referred to as 'ultra-high risk' for psychosis. The proposed diagnostic criteria include 'attenuated' forms of delusions, hallucinations and disorganised speech, with 'intact reality testing'.

There are several potential pitfalls with the psychosis risk syndrome, including those listed below.

- Definitions of 'attenuated' psychotic symptoms and 'intact reality testing' that can be successfully translated from the research setting to everyday clinical practice have not been established.
- Even in research settings where the staff are highly trained to identify the syndrome, there are high rates of false positives. At best, only 30% of cases make the transition to frank psychosis over two years,[9] and in most centres that are studying the syndrome the transition rates are even lower. Not only is there a need to improve the definition of the syndrome, the feasibility and reliability of introducing it in routine clinical practice have not been tested.
- There is no firm evidence for effective treatments that will reduce the transition to psychosis in these patients. There is a real risk of inappropriate prescribing of antipsychotic medications for such patients, most of whom will not require them but will thereby be exposed unnecessarily to their adverse effects for indefinite periods.

Other consequential harms include the potential for stigmatisation arising from a person being labelled as at high risk of psychosis.

Early detection

There is a substantial amount of evidence to indicate that the longer the duration

PSYCHOSIS SCREENING QUESTIONNAIRE[10]

The following questions are a guide to the types of probe questions that can be used to detect psychosis at an early stage. These questions form a screening tool for psychosis but this tool has not yet been tested in general practice. A positive response to any of these questions should prompt further enquiry.

Delusional mood
Have there ever been times when you felt that something strange and unexplainable was going on, things that other people would find it very hard to believe?

Grandiose delusions
Have you ever felt that you had special powers or talents that other people lack and are not shared by any group of people?

Delusions of persecution
Have you ever felt that people were too interested in you, singling you out or deliberately trying to harm you?

Delusions of reference
Have you ever felt that things were arranged, happened or said in a way so as to have a special meaning or message just for you?

Delusions of control, thought interference, passivity
Have you ever felt that your thoughts were being directly interfered with or controlled by another person in a way that people would find hard to believe, for instance, through telepathy?

Hallucinosis
Have there ever been times when you heard voices or noises when there was no one around and no ordinary explanation seemed possible? Have you ever seen visions or things that other people could not see?

of untreated psychosis, the worse the clinical outcome. Consequently, there is currently a clinical emphasis on attempting to reduce the duration of untreated psychosis by the early detection of psychosis and the use of intervention services.

Clinicians should, therefore, be vigilant regarding the possibility of a first episode of psychosis in teenagers and young adults, this being the age group schizophrenia is most likely to appear in for the first time. Any young person suspected of experiencing psychological distress should be asked, among other things, whether they have experienced delusions or hallucinations.

The questions listed in the box on this page constitute a screening instrument for psychosis,[10] but this tool has not yet been tested in general practice and some training for general practice use would be necessary. The list is included here only as a guide to the types of probe questions that can be used to detect psychosis. A positive response to any one of these questions is enough to prompt further clinical enquiry to establish the duration of the symptom(s), the degree of conviction as to their reality, the extent of emotional distress associated with them and whether the patient feels compelled to act upon them.

First-episode psychosis

Frequently a first psychotic episode will not fit a typical diagnostic pattern: features of schizophrenia may not be obvious, manic, depressive or other symptoms (e.g. anxiety, obsessive–compulsive phenomena) may appear prominent, and often the initial presentation occurs in the context of psychoactive substance abuse, misleading the clinician to assume the psychosis has been induced entirely by drugs. Under circumstances of uncertainty such as these it is important not to foreclose prematurely on a specific diagnosis, but to keep the diagnostic options open and treat the condition on the basis of its symptom profile.

A thorough history, mental status assessment and physical examination must be undertaken. Particular attention should be paid to the cardiovascular and neurological systems, and baseline measurements of BMI and waist circumference should be taken in preparation for initiating antipsychotic medication.

Laboratory investigations should include a full blood count, liver function tests, measurement of urea, electrolytes and creatinine levels (UEC), measurement of calcium, fasting blood glucose, fasting blood lipids and prolactin levels, and urine toxicology. A CT or MRI brain scan is also recommended by many experts. Assessment of cognitive functioning should be performed and taken into consideration in planning and conducting psychosocial treatments and rehabilitation for resumption of work or education.

An assessment of the patient's risk of suicide, self-harm and danger to others is critical. Also, the need for hospitalisation should be evaluated in light of illness severity, the available resources and services, as well as the extent of family and other social supports.

GENERAL PRINCIPLES OF TREATMENT

Although antipsychotic medications are the cornerstone of treatment for schizophrenia, engagement of the patient is a crucial factor that is often overlooked and without which treatment invariably fails. Patient engagement is taken as a given in

the treatment of all psychiatric disorders, but requires particular attention in schizophrenia. By engagement it is meant the establishment of a working therapeutic relationship between patient and clinician marked by mutual respect and commitment to working on the task of getting well and then staying well in the long term. Similarly, whenever possible, engagement of the patient's family is critical for long-term treatment because families frequently provide essential social and emotional support as well as a haven for the patient.

Barriers to engagement in young people with psychotic disorders include the impairment of insight that often accompanies psychosis and the low motivation that is an integral component of the negative symptoms of schizophrenia. The cognitive deficits that feature in schizophrenia can contribute to poor comprehension and retention of the information needed to manage the illness effectively, as well as to poor problem-solving skills. Immaturity in young patients may contribute to impulsivity, poor judgement and rebelliousness, which all interfere with engagement.

Psychotic content in conversation with the clinician can hamper engagement as it can impede reality-based communications and interfere with the development of empathy. In particular, it often generates discomfort in the listener and a tendency to try to avoid such topics or bring the consultation to a close, in spite of the patient's need to give expression to his or her psychotic experiences.

Overcoming these barriers can be difficult. The clinician should take the initiative and allocate adequate time to spend with the patient, listening attentively to the patient's worries and concerns, including psychotic material, while controlling his or her sense of discomfort with this.[11] Responding empathically to emotional cues is important in fostering the patient's sense of being understood, as is showing an interest in all aspects of the person, not just his or her symptoms and areas of disability but also his or her unique qualities, strengths, talents and interests. Because the experience of psychosis invariably damages self-confidence and self-esteem, it is important to encourage and facilitate the patient's capacities for self-efficacy. General psychological management includes the following:

- providing clear, accurate explanations and information as simply as possible
- giving realistic reassurance
- always avoiding deception or misleading information
- genuinely responding to the patient's concerns, however unusual they seem
- conveying a sense of realistic optimism.

Finally, treatment should be tailored to the individual as much as possible – one size does not fit all. Both clinician and patient should be prepared for treatment over the long term.

Pharmacological treatment

With the exception of clozapine, all antipsychotic medications, both first-generation (typical) and second-generation (atypical) drugs, are of approximately equal effectiveness for the treatment of schizophrenia. Clozapine has superior efficacy but is reserved for patients with treatment resistant schizophrenia (i.e. severe and persistent positive and/or negative symptoms following adequate trials of two or more antipsychotics). Clozapine is also useful in the treatment of schizophrenia in patients with persistent or frequent suicidal ideation or behaviour, severe and persistent extrapyramidal side effects from other antipsychotics, marked aggressive behaviour and severe comorbid substance abuse. Its use is subject to strict monitoring owing to its potential for causing agranulocytosis, myocarditis and cardiomyopathy.

A list of the available antipsychotic drugs and their doses is provided in Table 2; all except sertindole are available on the PBS.[12] Choice of drug primarily centres on tolerability in the individual patient, particularly the drug's adverse effect profile. Movement disorders (extrapyramidal effects and akathisia) are more common with first-generation antipsychotics, although they also occur with second-generation drugs. Conversely, weight gain and metabolic complications are more common with second-generation agents, especially clozapine and olanzapine, but also occur with first-generation antipsychotics. Other common adverse effects include sedation, hyperprolactinaemia (causing gynaecomastia and galactorrhoea) and sexual dysfunction.

As a general rule, antipsychotic treatment should start with a low dose and be titrated upwards over one to four weeks. Treatment is best initiated using oral preparations, with short-acting parenteral forms reserved for psychosis-related behavioural emergencies. Long-acting depot preparations are useful in maintenance treatment if medication adherence is poor or, occasionally, if the patient prefers them.

Second-generation antipsychotics (except for clozapine) are not more efficacious than first-generation antipsychotics. They show no convincing superiority in the treatment of positive (i.e. psychotic) symptoms, negative symptoms or cognitive deficits, and longer term outcomes are comparable for both groups of drugs. On the whole, second-generation drugs are generally better tolerated, but failures in treatment adherence occur with all antipsychotics, leading to treatment discontinuation in about 75% of cases within 18 months.

Monitoring physical health

With some of the newer drugs in particular, there are substantial risks of weight gain and obesity, diabetes, increased levels of serum lipids and development of the metabolic syndrome (i.e. central obesity, raised serum triglycerides level, raised LDL-cholesterol level, lowered serum HDL-cholesterol level, hypertension and raised fasting blood glucose level). The

well-known adverse health consequences of these phenomena combine with lifestyle problems all too common in patients with schizophrenia (i.e. poor diet, little exercise, tobacco smoking and alcohol and/or drug abuse) to contribute to a 20% shorter life expectancy in patients with this illness.

To avert adverse health consequences, it is therefore essential to monitor the patient's physical health closely and to initiate appropriate interventions early. BMI and waist circumference should be measured at every visit for the first six months after starting or changing antipsychotic drug treatment, and three-monthly thereafter. Blood pressure and fasting serum lipids and blood glucose levels should also be measured three-monthly for one year after starting or changing antipsychotic medication, and six- to 12-monthly thereafter. Interventions regarding advice, dietary guidance, exercise regimens, weight reduction programs, medical investigations and treatments (e.g. metformin) should occur as indicated, and the antipsychotic drug should be changed if necessary.

TABLE 2. ANTIPSYCHOTIC DRUGS AND USUAL DOSES[12]

Drug	Usual dose
Second-generation antipsychotics: oral	
Amisulpride	400–1000 mg daily (divided doses: twice daily)
Aripiprazole	15–30 mg daily
Clozapine	200–600 mg daily (special indications and patient monitoring protocol)
Olanzapine	5–30 mg daily
Paliperidone	3–12 mg daily
Quetiapine	300–750 mg daily (divided doses: twice daily); modified release formulation: 400–800 mg daily (once daily)
Risperidone	2–6 mg daily
Sertindole*	12–20 mg daily
Ziprasidone	80–160 mg daily
First-generation antipsychotics: oral	
Chlorpromazine	75–500 mg daily
Haloperidol	1–7.5 mg daily
Pericyazine	5–75 mg daily (divided doses)
Trifluoperazine	5–20 mg daily
Long-acting parenteral preparations	
Flupenthixol decanoate†	20–40 mg IM, every two to four weeks
Fluphenazine decanoate†	12.5–50 mg IM, every two to four weeks
Haloperidol decanoate†	50–200 mg IM, every four weeks
Zuclopenthixol decanoate†	200–400 mg IM, every two to four weeks
Olanzapine pamoate monohydrate‡	150–405 mg IM, every two to four weeks
Risperidone extended-release microspheres‡	25–50 mg IM, every two weeks

* ECG monitoring required before and during treatment; sertindole prolongs the QT interval: use only in people not responsive to or intolerant of at least one other antipsychotic.
† First-generation antipsychotic. ‡ Second-generation antipsychotic.
ABBREVIATION: IM = intramuscular.

Suicide risk

Approximately 30% of patients with schizophrenia attempt suicide and 5% die by this means, often within the first few years from onset of the illness. Suicide is most common in young men, especially those who are failing to fulfill their own aspirations as well as meet their families' expectations of them, as a result of which they become overwhelmed by hopelessness and despair. Suicide may occur suddenly and unexpectedly, without warning.

Comorbidity

Patients with schizophrenia have very high rates of substance abuse compared with the general population. The most frequently abused substances, after tobacco, are cannabis, amphetamines and alcohol. Psychotic relapses and treatment resistance may be induced by cannabis and stimulants, whereas alcohol is more likely to increase aggression and violent behaviours.

Nonadherence with antipsychotic treatment is often associated with substance abuse. Counselling about alcohol and drug abuse that employs motivational interviewing techniques can sometimes assist in this context. Nicotine replacement therapy may be of use in reducing tobacco smoking.

Other common comorbidities include depression and anxiety disorders, the former being associated with increased risk of suicide. Each of these conditions should be treated in its own right, as for other patients with depressive or anxiety disorders. The main barrier to treating these conditions is failure to recognise them in the context of the psychotic illness.

Continuing management

Each patient has a 'relapse signature', a characteristic sequence of evolving symptoms, signs and other experiences that presages relapse of a psychotic episode.

Helping patients and families identify the elements and timing of such a 'relapse signature' can enable them to detect the early warning signs of clinical deterioration and impending relapse so that help can be sought quickly – within hours to days. This may provide a window in which intervention with timely adjustments to medication, stress reduction and increased social support can help forestall relapse.

Medication adherence failures are all too common in patients with schizophrenia. The usual approaches to maximising treatment adherence, such as simple drug regimens, avoidance of polypharmacy, clear explanations and instructions, minimum effective doses, avoidance of adverse effects and use of reminders, do not seem to be sufficient in many of these patients. A motivational interviewing approach has been shown to be helpful in some studies. In such an approach, the relative benefits and risks of taking medication versus the benefits and risks of not taking medication are systematically examined and discussed with the patient, with the aim of 'nudging' the patient towards treatment adherence. If all these strategies fail then recourse may be had to depot injections of antipsychotic drugs.

Adequate levels of social support, beginning with the family and engagement with a treating doctor (see above), are important in the maintenance treatment of schizophrenia. Patients who are not well integrated in a supportive social environment are more likely to relapse and tend to have poorer outcomes. Social support can be improved by:

- encouraging patients to participate in group-based therapeutic activities available in mental health and related services
- promoting opportunities for social interaction through clubs and societies
- supporting patients' attempts to establish intimate, including sexual, relationships.

Education and employment also provide opportunities for social network formation, apart from their other obvious benefits. Rehabilitation efforts in these areas can thus have secondary benefits of augmenting social support.

CONCLUSION

Schizophrenia is a lifelong illness with a broad spectrum of outcomes, ranging from very poor, with chronic deterioration and low quality of life, to very good, with an episodic course and excellent social recovery. The GP can play a pivotal role in increasing the likelihood of better outcomes through early detection of psychosis, timely specialist referral and long-term patient management. This includes the provision of maintenance treatment and high quality care of the patient's physical health. MT

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