

SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS OF EARLY ONSET

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Psychotic disorders are associated with impairment in emotional, cognitive and social functioning, potentially leading to long term disability. There is also an increased risk of suicide and harm to others, particularly when acutely unwell. Early and expert treatment is crucial, with optimal results obtained with prompt referral to psychiatric services and intensive treatment by a mental health team, including a psychiatrist, in the acute phase of the illness. Furthermore, these disorders are highly stigmatized in most cultures, making treatment and integration into the community difficult.

Psychotic symptoms in children

Schizophrenia is an extremely rare condition in prepubertal children; psychotic symptoms in this age group need careful evaluation and may be due to many other disorders. This section discusses the presentations of these symptoms in children.

Childhood onset schizophrenia, where children's symptoms meet criteria for schizophrenia and where symptoms start before the age of 13, is a very rare disorder with a prevalence of less than 1/10,000 (Asarnow et al, 2004). The latest information about childhood onset schizophrenia comes from large research cohorts such as the Childhood-onset Schizophrenia Study at the NIMH (Rapoport & Inoff-Germain, 2000). These studies drew from a wide geographical area and had strict exclusion criteria. Information from these cohorts suggests that childhood onset schizophrenia is a severe form of the late adolescent/early adult onset disorder. Findings from these cohorts include more premorbid impairment than seen in those with later onset, with an increased prevalence of cytogenetic (Addington & Rapoport, 2009) and developmental abnormalities including pervasive developmental disorders and mental retardation (Rapoport et al, 2009). Premorbid social difficulties, motor abnormalities and a family history of schizophrenia were more common than in controls. The onset of the illness was often insidious with cognitive deterioration (Bedwell et al, 1999) and neuroanatomical changes (Arango et al, 2008) occurring

Terms used in this chapter

- *Psychotic* (symptoms) is a word used to describe situations when perceptions, thoughts or emotions are disordered so severely that contact is lost with external reality. The two most common mental illnesses where psychotic symptoms are a predominant feature are schizophrenia and bipolar disorder. Psychotic symptoms include:
 - *Hallucinations* (false sensory perceptions in the absence of external stimuli). Auditory hallucinations ("hearing voices") are the most common but visual hallucinations are also seen in children and teenagers with psychosis.
 - *Delusions* (strongly held beliefs, not shared by other members of the community, arising from an incorrect interpretation of external reality, incompatible with a person's social or religious background).
- *Positive symptoms* describe an excess or distortion of normal functions (such as hallucinations or delusions).
- *Negative symptoms* is used to describe a reduction or loss of normal functioning (for example loss of normal emotional reactivity or impaired cognitive functioning)
- *Prodrome* is the period of time before the onset of psychotic symptoms where functioning is impaired.
- *Acute psychosis* is the period of time when hallucinations and/or delusions are predominant and behavior is often disturbed.

early in the illness. However, few children with psychotic symptoms fulfill diagnostic criteria for childhood onset schizophrenia and by the time diagnostic criteria are met they are chronically ill, with significant disability.

Other psychotic disorders presenting in childhood include bipolar disorder (discussed in Chapter E.2). However, most children who present with psychotic symptoms do not have schizophrenia or bipolar disorder. They are more likely to show transient auditory hallucinations as well as mood or anxiety symptoms with associated distress. At first presentation these children often meet diagnostic criteria for depression, post-traumatic stress disorder (PTSD), anxiety or behavior disorders but not for any of the psychotic disorders. Many have a long history of developmental, behavioral and emotional problems and may display a confusing mix of symptoms. There are very few studies following up such children to see if they go on to develop schizophrenia but the available evidence is summarized below.

Auditory hallucinations are not uncommon in non-psychotic children attending child psychiatry services (Dhossche et al, 2002). While most appear to recover, a subgroup of those with hallucinations develops a psychotic illness. In a clinic sample of 90 children it was found that half of the 15% who reported hallucinations initially were hallucination free at 12 months, while a third had ongoing symptoms and came close to meeting criteria for either schizophrenia or bipolar disorder (Askenazy et al, 2007). Sixty percent of a sample of 80 children with auditory hallucinations reported no hallucinations three years later but 16% had developed delusions (Escher et al, 2002). Hallucinations were more likely to persist in those with diagnoses of anxiety, depression or dissociative disorder. Other risk factors were behavior problems, negative symptoms and more frequent auditory hallucinations or hallucinations with negative content (Escher et al, 2004). Children and adolescents with PTSD are also more likely to report auditory hallucinations (Scott et al, 2007a). Children in community samples report auditory hallucinations relatively often, two studies reporting a rate of 8% (McGee et al, 2000; Scott et al, 2006). Hallucinations were more likely in children with anxiety, depression, family dysfunction and inattention or hyperactivity. When the cohort reported by McGee and colleagues was followed up 15 years later, at the age of 26, a quarter of those with psychotic symptoms at age 11 met criteria for schizophreniform disorder (Poulton et al, 2000).

In summary, the differential diagnosis of psychotic symptoms in childhood can be difficult and a longitudinal perspective is essential. It may be more useful to describe “diagnostic hypotheses” rather than a specific diagnosis, especially at first presentation (Lee et al, 2003). While the majority of children with isolated psychotic symptoms will not go on to develop schizophrenia, schizophrenia or bipolar disorder will develop in a significant minority either within one to two years of hallucinations first appearing or they will remain comparatively well in adolescence but develop schizophrenia as an adult.

Psychotic symptoms in adolescence

Psychotic disorders of all types increase in prevalence during adolescence, to a prevalence of one in 500 among 18 year olds. Retrospectively, about one third of adults with psychotic disorders report that their illness started before the age of 20 and the lifetime prevalence of all psychotic disorders in the adult population



Click on the picture to access a video clip in which a young woman describes her psychotic symptoms that had started during her childhood (7:31).



Click on the picture to hear a university student talk about psychosis and what it is like to go through an early detection service (9:59).

Table H.5.1 Diagnostic criteria for schizophrenia

1. Two or more of the following present for at least a month:
 - Hallucinations
 - Delusions
 - Disordered thoughts and speech (speech can be incoherent or greatly reduced)
 - Severely disorganized behavior (including catatonia, or severe motor slowing)
 - Negative symptoms
2. Deterioration in social, educational or work functioning
3. Duration of illness of at least six months, including the prodrome, if present (if duration is less than six months, it is labeled *schizophreniform psychosis*)
4. Not due to another mental illness such as a mood disorder, or a medical condition.

is 2%-3% (Kendler et al, 1996). While some adolescents with psychosis come from similar high risk groups to those with childhood onset schizophrenia, the majority had previously normal functioning. In this group the typical illness course starts with a prodrome, with nonspecific symptoms including low mood, anxiety, cognitive and functional deterioration.

The risk factors for schizophrenia in adolescents and young adults are well described. These include a schizotypal personality, sub-threshold psychotic symptoms (such as brief, indistinct auditory hallucinations), functional decline and a family history of schizophrenia (Owens & Johnstone, 2006; Yung et al, 2004). Combinations of these symptoms have been described as the “ultra high risk” mental state. The likelihood of transition to psychosis with these risk factors was thought to be high, but recent studies suggest that, in help-seeking young people, the risk decreases from 40% to 16% (Yung et al, 2008). Poor functioning at presentation, low-grade psychotic symptoms, depression and a long duration of prodromal symptoms make transition to psychosis more likely.

Currently, the debate in the adolescent-onset group is at what stage to treat the psychotic symptoms. Trials of antipsychotic medication have been shown to reduce the transition from the “ultra-high risk” state to a psychotic disorder, but as the risk of transition to psychosis drops in the clinic cohorts, the risk of using antipsychotic medication in adolescents who are unlikely to later develop psychosis becomes less acceptable (Yung et al, 2007).

ETIOLOGY

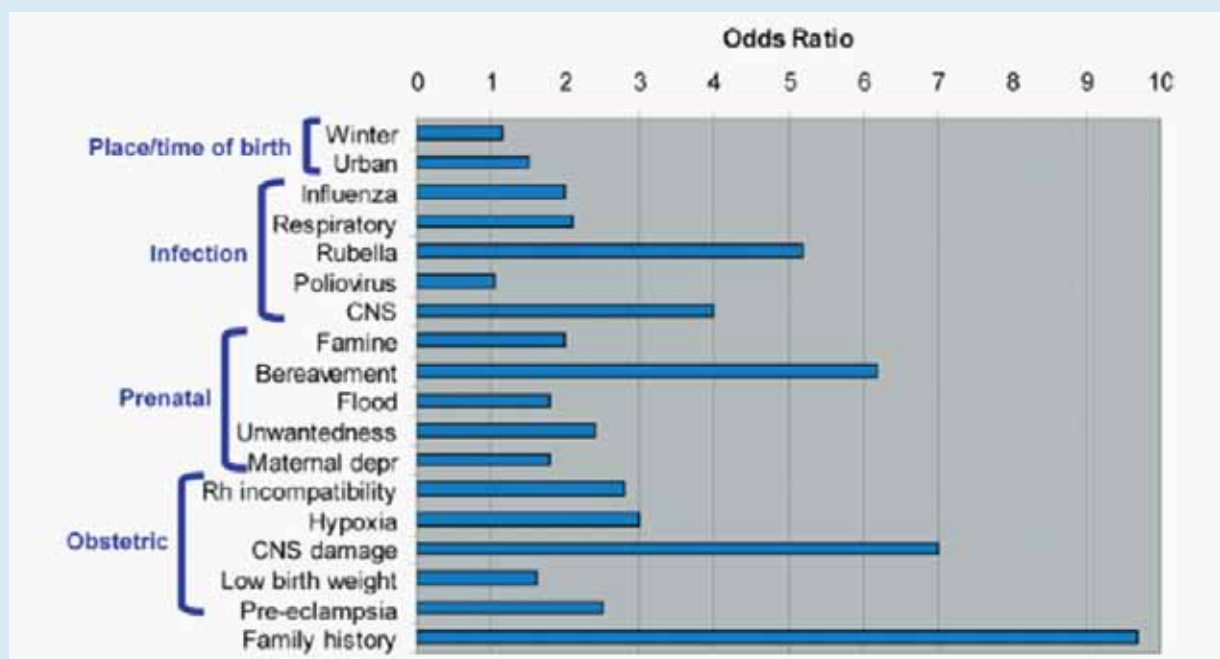
The pathophysiology of schizophrenia or any of the other psychotic disorders is still unclear. All psychotic disorders have a genetic vulnerability but there is no clear single gene implicated in causation. Recent research reports multiple genes associated with the development of schizophrenia, but most have a small effect. Most of these genes are nonspecific and some genes linked to schizophrenia are also linked to autism and bipolar disorder. There are also multiple other organic and psychosocial risk factors. A summary of risk factors and their associated odds ratios can be seen in Figure H.5.1. Additional risk factors include being male or an immigrant. Children, and to a lesser extent teenagers, with psychosis are likely to have more risk factors than those with a later age of onset.

When talking to young people and their families, the most easily understood



Click on the picture to hear a young man describing his struggle with schizophrenia and its treatment (8:13).

Figure H.5.1 Comparison of a selected set of relatively well-established risk factors for schizophrenia, focusing mainly on pre- and ante-natal factors.



CNS: central nervous system; depr: depression; Rh: Rhesus. Source: Sullivan PF. *The genetics of schizophrenia*.

model for the etiology of schizophrenia is the stress/vulnerability model. Risk factors (or vulnerabilities) for the development of schizophrenia include:

- Family history of psychosis, particularly in first degree relatives
- Personality in the schizotypal, schizoid or paranoid spectrum, and
- Being an older teenager or a young adult.

Factors that may precipitate a psychotic episode include organic factors such as illicit or medical drug use, a severe physical illness, trauma or other psychological stress such as starting a more difficult course of study.

SYMPTOMS OF PSYCHOSIS

Positive symptoms

- Hallucinations, most commonly auditory hallucinations or hearing voices. Visual hallucinations are more common in children than in adults (up to 50% in some cohorts)
- Delusions, generally persecutory or grandiose in nature

Negative symptoms

- Reduced motivation
- Flat or blunted affect
- Social withdrawal
- Impaired cognitive performance in domains such as attention, concentration, memory and planning.

These negative and cognitive symptoms best predict long term outcome and may precede the onset of hallucinations or delusions by many months. In addition changes in mood, anxiety and levels of agitation are common.

The two most common psychotic disorders are schizophrenia and bipolar disorder. Table H.5.1 summarizes the criteria for the diagnosis of schizophrenia. The prominent symptoms are hallucinations and/or delusions. People who are given a diagnosis of schizophreniform disorder have the same symptoms as those with schizophrenia but for less than six months. In both conditions there is also associated disturbed behavior and deterioration in functioning, including school performance and social functioning. In bipolar disorder, a distinct period of mood symptoms is the predominant feature, with mania (at least one episode of severely elevated mood affecting all areas of functioning including sleep and cognition for a period of at least seven days) being the most prominent. Delusions and hallucinations in psychotic bipolar disorder tend to be grandiose if the patient is manic and depressive (e.g., of guilt, ruin, worthlessness) in psychotic depression. The initial episodes of a bipolar disorder are often depressive, so diagnosis is not clear until after the young person has a manic episode (see Chapter E.2). The diagnosis of both schizophrenia and psychotic mood disorders have poor reliability at first presentation, with low agreement between clinicians and diagnostic instability over time.



Click on the picture to hear a description of psychotic phenomena she had as a teenager in a person with bipolar disorder (3:06)

COURSE AND OUTCOME

A good outcome in early onset psychosis includes not only the resolution of acute psychotic symptoms such as hallucinations and delusions, but also a reduction in negative symptoms and a return to education and friendship networks. A rapid recovery is more likely with early treatment, a more acute onset and an illness with fewer negative symptoms. Early onset is associated with a poorer prognosis, particularly childhood onset (Hollis, 2000), although those with illness onset prior to the age of 18 tend to have a worse outcome than those with adult onset (Schimmelmann et al, 2007). Male gender, ongoing substance use, pervasive developmental disorder, poor premorbid function and insidious onset are also associated with poorer outcomes.

Early treatment, not only reduces the severity of the first episode, but also helps prevent relapse. While recovery may be good after the first episode – about 20% of young people with schizophrenia will have only one episode – a relapse is not only extremely disruptive to educational, vocational and personal development but may also be less responsive to treatment. Active follow up after recovery from the first episode, including a clear plan to monitor for early warning signs (subtle signs of deterioration in mental state), as well as continuing antipsychotic medication for twelve months after recovery will reduce the risk.

PSYCHOSIS IN SPECIFIC GROUPS

Developmentally disabled

Young people with developmental disability, in particular pervasive developmental disorders, have an increased risk of psychosis but are also more likely to be wrongly diagnosed as psychotic. Pervasive developmental disorders, also called autistic spectrum disorders, are discussed in Chapter C.2. These disorders manifest themselves with deficits in social interaction, impaired verbal and nonverbal communication, restricted and idiosyncratic interests, and stereotyped behaviors. Because the core deficits in pervasive developmental disorders lead to difficulties in social interaction, repetitive or other unusual behaviors, and odd

preoccupations, it can be difficult to differentiate between these symptoms and other psychiatric disorders. Behaviors or cognitions associated with pervasive developmental disorders may appear similar to those of disorders such as anxiety, obsessive-compulsive disorder or even schizophrenia. The broad phenotypes seen more commonly in relatives of children with autism, such as delayed language, poor social functioning and executive control deficits are also risk factors for schizophrenia (Losh et al, 2008), suggesting some common causative factors.

There is so much overlap of symptoms between pervasive developmental disorders and psychosis that before the 1970s, the term childhood psychosis was widely used to refer to both childhood-onset schizophrenia and autism. Much of the later work in this area, such as the seminal studies by Kolvin (Kolvin, 1971), concentrated on identifying the differences between autism and schizophrenia, including age at onset and differing outcomes. During the past two decades, the core syndromes of pervasive developmental disorders and childhood-onset schizophrenia have been clearly delineated and research has focused on the identification of comorbid psychosis and other mental illnesses in the pervasive developmental disorder population.

In clinical practice, the main difficulty is making a differential diagnosis in a young person with pervasive developmental disorders and either increasingly odd behaviors or a decline in functioning (Starling & Dossetor, 2009). It is important to consider beliefs and behaviors in a developmental context, particularly in young people with intellectual impairment. In this population, anxiety or depression can also manifest with unusual behaviors. Psychosis should not be diagnosed in individuals with pervasive developmental disorders without the presence of hallucinations or delusions, as disturbed behavior alone is not sufficient.

Young people with a history of trauma

Rates of psychotic disorders are significantly increased in adults with a history of childhood sexual abuse (Cutajar et al, 2010). A history of psychological trauma or maltreatment also increases the risk of transition from prodromal symptoms to a psychotic disorder in young adults (Bechdolf et al, 2010b). There is less evidence of a link between trauma and psychosis in children and teenagers, but traumatized young people are more likely to report hallucinations, sometimes as a symptom of post-traumatic stress disorder (Shevlin et al, 2007). There is some debate about whether auditory hallucinations reported by young people with a childhood history of trauma are different from those without a history of abuse. Some studies found that hallucinations directly related to the trauma experience were more likely, while others found no difference in symptoms (Scott et al, 2007b).

A history of childhood trauma also increases the risk of aggression, self-harm, suicide attempts and substance abuse in patients with psychosis (Hainsworth et al, 2011). Clinically this means that young people with psychosis and a traumatic background are likely to be more difficult to treat and potentially more dangerous to themselves and others. They are also more likely to live away from their families or have less family support. It is important to be aware of the reasons for the disturbed behavior and also provide treatment for the trauma symptoms as well as for the psychotic disorder.

Substance use

The relationship between drug use and early psychosis is complex. There is good evidence that early cannabis use increases the risk of psychosis in later life, with some young people being more vulnerable than others. Research from a New Zealand cohort suggests that there is a tenfold increase in the risk of psychosis with cannabis use in people with a functional polymorphism of the catechol-O-methyltransferase (COMT) gene – associated with the production of dopamine in the brain – suggesting a gene-environment interaction (Caspi et al, 2005). Drug use, particularly cannabis, psychostimulants and hallucinogens can precipitate a psychotic episode, reduce response to treatment and increase the risk of relapse after recovery. Cannabis use can worsen cognitive deterioration. Acute drug intoxication can also mimic psychosis, although symptoms generally last only hours or days. Symptoms lasting days to weeks suggest either severe ongoing substance abuse or a psychotic illness (Volkow, 2009).

Illicit drugs may also be used to self-medicate distress in the prodromal stage of schizophrenia so, the psychotic illness predate the substance abuse, but ongoing use makes hallucinations and delusions less likely to respond to medication. Strategies for helping teenagers with psychosis and substance use are detailed on the [EPPIC website](#).

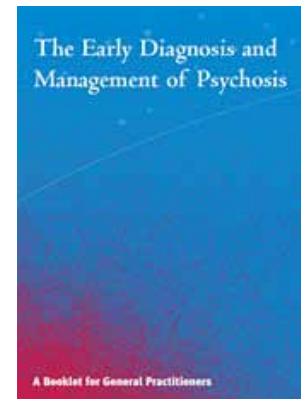
ASSESSMENT

The goal of the initial assessment of a young person presenting with a psychotic disorder is not just to make a diagnosis but also to develop rapport and set the stage for the ongoing treatment of a frequently chronic illness. While going slowly and cautiously at this stage can be seen as wasting time, forcibly treating without adequate discussion, education and understanding of the patient and family, can lead to later avoidance of services and relapse or recurrence of the illness.

Individual assessment

Obtaining a history of psychotic symptoms can be difficult. Young people often avoid discussing such symptoms because they are frightened of being seen as “crazy”. They need to be given the choice as to whether they would prefer to be seen alone or with the support of a trusted adult, often a parent – although seeing young people by themselves for a short period is always necessary, e.g. to assess suicidality. Starting the interview with a discussion of more neutral topics such as family, school, hobbies and friendships helps to build rapport and assemble a picture of their general functioning. The interviewer can then move on to ask about specific worries or concerns and explore those in more detail.

Asking about symptoms of anxiety and depressed or elevated mood is crucial, as is discussing thoughts of self-harm or suicide. Finally there needs to be specific enquiries about psychotic symptoms, where it is important to be neutral but direct, for example saying “*I am going to ask you some questions that seem really strange but are important to help me understand what is happening with your thoughts*”. It may take several interviews to fully elicit symptoms; it can be difficult for confused young people to put the chaos of their thoughts into words. Examples of questions to use for a comprehensive assessment of psychotic symptoms are given in Table H.5.2.



Click on the picture to access an overview of the early identification, assessment and treatment of psychosis by ORYGEN Youth Health

Table H.5.2 A mental state assessment for psychotic symptoms

	Interview questions	Rationale for questions
Appearance and behavior	Observation at interview	Unusual behavior or dress should be described and if possible understood during the interview
Insight	<ul style="list-style-type: none"> – Could you tell me why you have come to see me? – Do you think there is anything that you need help with? 	If they understand that they are unwell and if they see the need for treatment, cooperation is more likely
Mood: depressed	<ul style="list-style-type: none"> – Have you been feeling depressed or down recently? – Have you lost interest in things you usually enjoy? – Have you had problems sleeping? – Have you had thoughts of hurting yourself? – If yes to any of the above, ask also about eating, agitation, concentration, thoughts of guilt or hopelessness and suicidal ideas or plans 	Checking for a current and past history of depression and risk of self harm or suicide
Mood: elevated	<ul style="list-style-type: none"> – Have you ever had a period of time where you were feeling so good, excited or hyper that you felt out of control, or did worrying things? – If yes ask for more details 	A period of elevated mood may be a manifestation of bipolar disorder
Thought form	Observation of speech flow and thinking at interview	Thought disorder is often seen in psychosis and the type will help with diagnosis. Thought disorder is where thoughts are poorly connected. Speech can be also rushed in bipolar disorder or slowed in depression.
Perceptual abnormalities: hallucinations	<ul style="list-style-type: none"> – Did you ever hear things that other people couldn't such as noises or people's voices? – If yes, what did you hear and how often? – If voices, did they comment on what you were thinking or doing? – How many voices did you hear? Were they talking to each other? – Did you have visions or see things that other people couldn't? (ask for details) – Also ask about tactile, olfactory and gustatory abnormalities 	These questions seek to elicit core psychotic symptoms. As hallucinations become more complex (more often, say more things, more than one voice) a psychotic disorder is more likely.
Thought content : delusions	<p>Start with "I would like to ask you about unusual experiences people sometimes have"</p> <ul style="list-style-type: none"> – Has it ever seemed that people were talking about you or taking special notice of you? – Have you ever received special messages from the TV, radio, or other things around you? – What about anyone trying to give you a hard time or hurt you? – Have you ever felt that you were especially important or could do things that others could not? – If yes to any, get further details 	As delusions become more complex (e.g., not just people looking at me but having an elaborate plan to hurt me) a psychotic disorder is more likely. Paranoid delusions are most likely in schizophrenia spectrum disorders, and grandiose delusions in bipolar disorder.
Cognitive functioning	Ask about current and past functioning at school including concentration, motivation, ability to learn and academic grades	Premorbid cognitive functioning affects prognosis, while deterioration is not only seen in psychotic disorders but also in depression.

A discussion of the rules of confidentiality is also important. While a teenager's thoughts or feelings should be kept confidential, if they talk about harming themselves or others there is often a duty of disclosure for safety reasons. Similarly a history of past sexual or physical abuse may also require disclosure to the relevant authorities, depending on the laws of the country they live in.

It is important to remember that it is rare for a psychotic disorder to exist in isolation. Common co-morbidities include substance misuse (ask about tobacco, cannabis and stimulants), anxiety, depression, behavior disorders, a history of trauma or developmental disorders.

Other assessments

Parents can provide a developmental history including pregnancy (viral infections, maternal drug or alcohol use, other complications) birth trauma (such as emergency caesarian section, hemorrhage or hypoxia) or developmental abnormalities, and can also describe symptoms that the young person is reluctant to talk about or even unaware of. Siblings often have important information to add, particularly about interactions and social functioning. Past or family psychiatric history can be an important pointer for diagnosis.

Corroborative information from schools, about academic and social functioning, health services and other care agencies will also be needed for an accurate assessment not just of mental state but also of current and previous levels of functioning.

DIFFERENTIAL DIAGNOSIS

The first consideration is to decide if the reported symptoms are truly the manifestation of a psychotic illness or due to another disorder. For example a depressed teenager may describe hearing a voice saying that they are useless, but are actually talking about their own thoughts, or an anxious adolescent may see shadows by their bed and be convinced that burglars have broken into the house.

Symptoms may also appear related to a psychosis but do not meet full diagnostic criteria. Many individuals with schizophrenia have a prodrome, with disturbances in mood, thoughts and behavior and some deterioration in functioning. However, these symptoms are non-specific and can have other causes, such as an adjustment disorder or depression. Research has also identified *psychotic-like experiences* – bizarre beliefs, persecutory ideas and magical thinking. All these symptoms except magical thinking increase the risk of later developing psychosis (Yung et al, 2006).

Even if it is clear that the young person meets criteria for a psychotic disorder, it can be difficult to make a specific (e.g., whether schizophrenia or bipolar) diagnosis early. Many diagnoses made at first presentation are found to be incorrect later (McGorry et al, 1995). Thus, some experts prefer to use the term *early onset psychosis* because it reflects this diagnostic uncertainty and provides more treatment flexibility. If there is a definite psychotic illness, early treatment is crucial, irrespective of its nature (e.g., schizophrenia, mood disorder). The longer the duration of untreated psychosis the more difficult the symptoms are to treat and the greater the risk of long term disability (Leeson et al, 2011). It is also

Table H.5.3 Investigations recommended at baseline assessment for early onset psychosis

Investigation	Rationale
Full blood count	<ul style="list-style-type: none"> • Detection of pre-existing hematological disorders such as anemia • Monitoring side effects of mood stabilizers
Urea, electrolytes, liver function tests	<ul style="list-style-type: none"> • Exclusion of pre-existing abnormalities (rare, but polydipsia can be seen in psychosis). • Monitoring for medication side effects (some antipsychotics and antidepressants can cause hyponatremia, mood stabilizers can impair liver function)
Fasting glucose, cholesterol and triglycerides	<ul style="list-style-type: none"> • Detection of insulin resistance or lipid abnormalities. Initial and six monthly monitoring as most antipsychotics can cause weight gain and insulin resistance
Thyroid function	<ul style="list-style-type: none"> • Thyroid abnormalities can cause mood elevation or depression and are a side effect of lithium treatment
Calcium levels	<ul style="list-style-type: none"> • Abnormalities a rare cause of psychosis
Prolactin	<ul style="list-style-type: none"> • Exclusion of pre-treatment hyperprolactinemia (e.g., due to pituitary tumor). • To monitor possible antipsychotic induced hyperprolactinemia,
Brain imaging (Computerized Axial Tomography, CAT; Magnetic Resonance Imaging, MRI)	<ul style="list-style-type: none"> • Exclusion of preexisting neuroanatomical lesions (injuries, malignancy) • MRI preferable because of higher resolution image and less radiation exposure but noise and claustrophobia may not be tolerated by patient
EEG	<ul style="list-style-type: none"> • Exclusion of a seizure disorder
Urine drug screen	<ul style="list-style-type: none"> • To rule out recent drug use or identify illicit drugs taken recently

important not to miss depression or elevated mood and so to misdiagnose a mood disorder as schizophrenia.

Other differential diagnoses include pervasive developmental disorders, PTSD with flashbacks, delirium and drug intoxication or drug induced psychosis, as discussed earlier. Finally, it is important to exclude possible organic disorders that can be confused with psychosis such as delirium, neurological disorders and other medical conditions such as thyrotoxicosis or Vitamin B12 deficiency, by a physical examination and physical investigations as detailed below.

Investigations

Investigations are detailed in Table H.5.3. They are not only performed to exclude treatable organic causes for psychosis but also as a baseline to monitor, prevent and manage side effects of treatment. A full physical examination is also essential, with particular emphasis on developmental or neurological abnormalities. Weight, height, waist measurement, blood pressure and pulse need to be recorded initially and monitored regularly. There are acute autoimmune or inflammatory illnesses that can mimic psychosis, especially when onset is acute (symptoms in these cases could be of delirium). Appropriate pediatric or other medical consultations may be required.

MANAGEMENT

Least coercive treatment

Assessment should always consider risk, both to the young person and to others. Ideally assessment and treatment should occur while patients remain at home with their family, but an admission to hospital may be needed if:

- There are concerns about high risk of suicide
- There is risk aggression to others (e.g., because of delusional beliefs)
- The patient is at serious risk of exploitation by others while unwell
- The young person is homeless
- Carers are exhausted. For example when teenagers have required round the clock supervision for days and their family can no longer manage this
- There are physical symptoms such as fluctuating levels of consciousness that require urgent medical investigation.

Taking into account the risk, the option least restrictive of patient's liberty should generally be used. If the risk is high, admission may need to be involuntary if the consent of either the young person or their family cannot be obtained, or there is concern that the young person is not well enough to make rational decisions about treatment. The laws about involuntary hospitalization vary according to country, but many only allow treatment against an individual's wishes if there is serious danger to themselves or others. [Click here](#) to see an example of legislation for involuntary hospitalization.

While it is possible to admit a child under the age of sixteen with their parents' consent (in many countries individuals have the capacity to give consent to treatment at 16 years of age, see Chapter A.1), it is also important to respect the child's rights, including the right to have their views about treatment considered and to be protected from violence (protection from being hurt physically and mentally by caregivers). This means that, even if young people are admitted against their will, every effort should be made to discuss their treatment with them, take their preferences into account wherever possible and to keep the use of coercive practices such as restraint to an absolute minimum.

Summary of management

Biological

Antipsychotic medication is essential for the treatment of psychosis. Most treatments are extrapolated from the results of adult studies. Studies in children include one small randomized controlled trial (RCT) showing haloperidol to be superior to placebo (Spencer & Campbell, 1994), and a small RCT (21 cases) showing that clozapine was superior to haloperidol (Kumra et al, 1996). Studies in adolescents show similar efficacy to adults for olanzapine, risperidone and haloperidol, but with differing side effect profiles and a non-significant trend for olanzapine and risperidone to be more effective (Gothelf et al, 2003; Sikich et al, 2008). These findings are similar to those in adult treatment trials.

Table H.5.4 Common side effects of selected antipsychotic medications used in early onset psychosis

Medication	Dose (mg)	Extra pyramidal side effects	Sedation	Weight gain	Prolactin	Postural hypotension	Potential disadvantages	Comments
Risperidone	1-6mg	++	++	++	+++	++	<ul style="list-style-type: none"> Galactorrhea, Sedation 	Most data comes from use in adolescents (including in autism)
Quetiapine	200-800mg	+	++	++	+	+	<ul style="list-style-type: none"> Initial sedation, often settles 	Useful for psychosis with mood disorders or anxiety
Aripiprazole	10-30mg	++	+	+		+	<ul style="list-style-type: none"> Initial agitation 	Sedation, weight gain and elevated prolactin are rare
Olanzapine	5-20mg	+	+++	+++	+	+	<ul style="list-style-type: none"> Very significant weight gain Sedation. Not recommended long term 	Sedating and calming when acutely unwell
Chlorpromazine	50-300mg	+	+++	++	++	++	<ul style="list-style-type: none"> Weight gain, sedation 	Sedating and calming when acutely unwell
Haloperidol	1-10mg	+++	++	+	+	+	<ul style="list-style-type: none"> Severe extra pyramidal side effects including stiffness and agitation 	Less sedating, strong antipsychotic effects

Psychological

Interventions include psychoeducation and cognitive behavioral therapy. Again, the evidence is from adult and late adolescent cohorts, with multiple trials showing benefit from these therapies (Bechdolf et al, 2010a).

Social

These therapies include family interventions and social skills training and again show benefit in multiple adult trials (Addington et al, 2005; 2010).

Pharmacotherapy***Acute sedation***

If there is acutely disturbed behavior or imminent danger, emergency sedation may be needed. Rapidly acting oral medication such as lorazepam (1mg-2mg), risperidone (0.5mg-1mg) or olanzapine (2.5mg to 5mg) are preferred. Oral wafers are absorbed more quickly and also dissolve in the mouth so are difficult to spit out. If oral medication is refused, intramuscular lorazepam (1mg-2mg) or haloperidol (2.5mg-5mg) are recommended. Intramuscular sedation usually requires physical restraint and is very distressing for the child and family. It is important to use the least coercive method of sedation not only to respect young person's rights, but also because the first experience of mental health treatment can be very aversive and make the difference between ongoing compliance or avoidance of further treatment.

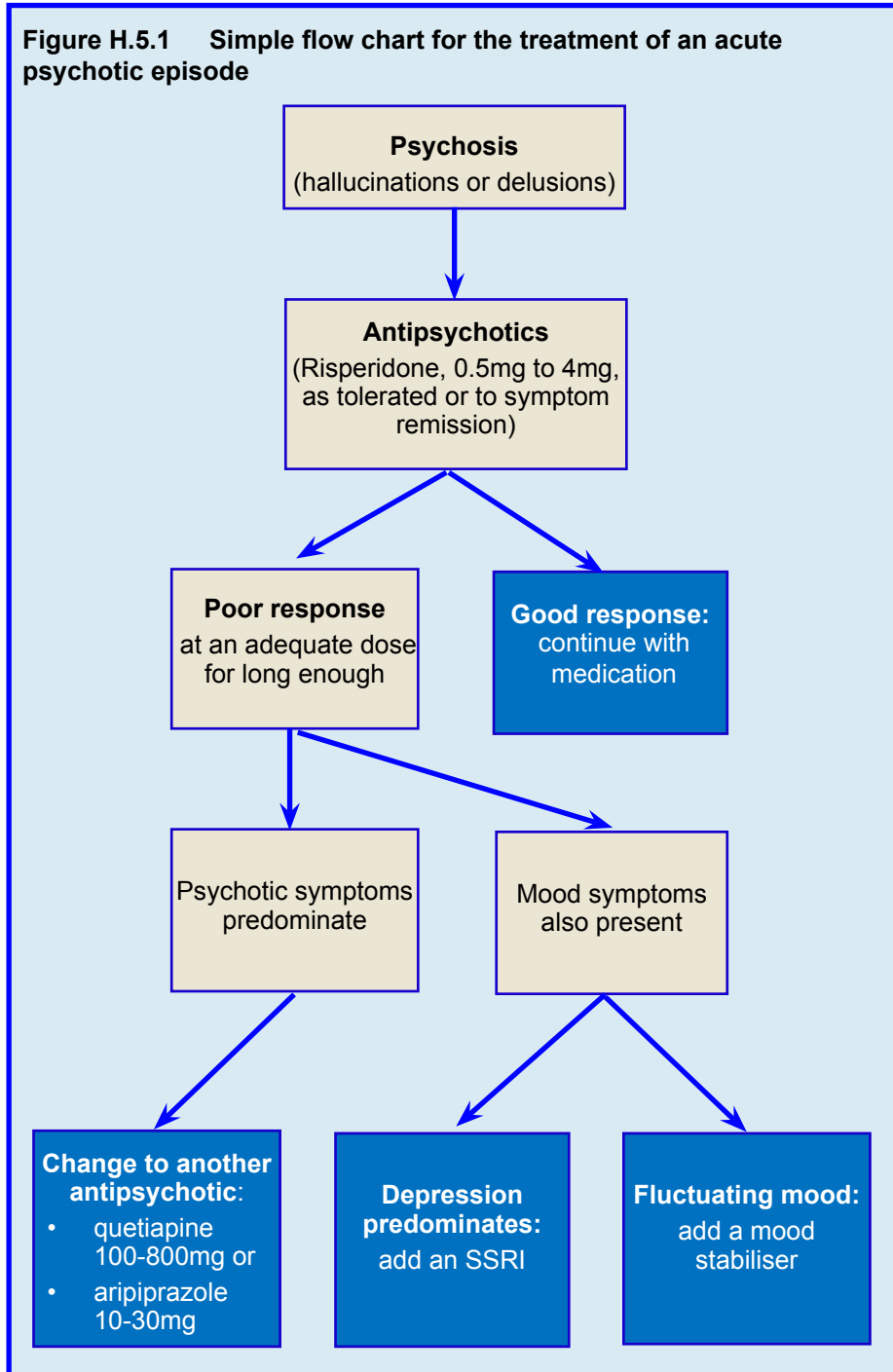
Ongoing management of medication

If no emergency treatment is needed, medication decisions in early psychosis aim to control psychotic symptoms and manage associated impairments as summarized in Figure H.5.1 (for management of psychotic depression and manic episodes see Chapters E.1 and E.2 respectively). An antipsychotic is used to treat hallucinations and delusions. In psychotic depression an antidepressant is added. When there is mania a mood stabilizer may be more appropriate. Table H.5.4 summarizes side effects of the most commonly used antipsychotic medications. It is recommended to *start low and go slow* with doses of antipsychotic medication. This is to avoid side effects and maximize adherence to treatment. (For a detailed, evidence based summary of treatment algorithms, the use of specific medications and side effects please see Taylor, 2012).

A second generation (atypical) antipsychotic is recommended as first line treatment if possible because of marginally better treatment outcomes in acute psychosis and the lower risk of movement disorder, particularly tardive dyskinesia, as demonstrated in individual RCTs and meta analyses (Davis et al, 2003; Leucht et al, 2009). However, second generation antipsychotics are expensive, so it may be necessary to use a first generation antipsychotic such as haloperidol, which is still highly effective (Schooler et al, 2005), although has more side effects than risperidone, for example.

When there is no response to antipsychotic medication after two weeks, a medication review is needed – some response in positive psychotic symptoms is usually seen by that time. If the maximum tolerable dose of a particular medication has been reached without effect a choice needs to be made about either changing medication or augmentation with another medication class (Figure H.5.1). Failure

Figure H.5.1 Simple flow chart for the treatment of an acute psychotic episode



Click on the picture to access a metabolic monitoring algorithm for young people prescribed antipsychotic medication

to respond to two or more antipsychotics for an adequate length of time and at adequate doses should prompt referral to a specialist service for consideration of clozapine.

Long term antipsychotic use increases the risk of obesity, type two diabetes and cardiovascular disease. It is crucial to monitor height, weight and waist measurement at the start of prescribing, and then at one, three, and then six monthly intervals, with intervention as needed (see metabolic monitoring algorithm in side box).

Clozapine for treatment resistant schizophrenia

Clozapine is an atypical antipsychotic that is extremely effective in schizophrenia; it should be used if there is a poor response to two other antipsychotic agents, each given at adequate doses for at least a four week trial. It is not recommended except for treatment resistant cases because of the risk of life threatening side effects and therefore the need for close monitoring. The minimum frequency of monitoring is weekly white blood cell counts for the first 18 weeks, with caution being used when neutrophils fall below 2 per 10⁹/Litre. Clozapine should be ceased at a neutrophil count of 1.5 per 10⁹/Litre. Many health services require registration of patients on clozapine so that these monitoring requirements are met before clozapine is dispensed. An example of the monitoring requirements can be found [here](#).



Click on the picture to access Get Help Early (Ontario Working Group on Early Intervention in Psychosis, Canada). It includes stories and artwork.

Table H.5.5 Severe and common side effects of clozapine and their management

	Side effect	Signs and symptoms	Monitoring and treatment
Life threatening	Agranulocytosis or neutropenia	<ul style="list-style-type: none"> Falling white cell count Infections 	<ul style="list-style-type: none"> Weekly white cell counts as per clozapine protocols, regular temperature and health checks. Stop clozapine if low neutrophils
	Cardiomyopathy	<ul style="list-style-type: none"> Tachycardia Fever Fatigue Chest pain 	<ul style="list-style-type: none"> ECG prior to starting clozapine, monitoring temperature and heart rate, troponin levels if available. Stop clozapine if it occurs
Other common side effects	Sedation		<ul style="list-style-type: none"> Give most of dose at night
	Hypersalivation	<ul style="list-style-type: none"> Dribbling, especially at night 	<ul style="list-style-type: none"> Small doses of hyoscine
	Constipation	<ul style="list-style-type: none"> Remember to ask patients about this 	<ul style="list-style-type: none"> High fibre diet
	Other cardiovascular effects	<ul style="list-style-type: none"> Hypotension Tachycardia. 	<ul style="list-style-type: none"> Monitor if minor, if significant refer to cardiologist
	Weight gain	<ul style="list-style-type: none"> Can be severe (10kg and more) 	<ul style="list-style-type: none"> Monitor weight and waist measurement Diet management
	Seizures		<ul style="list-style-type: none"> Stop for a day Reduce dose Use anticonvulsant
	Bed wetting	<ul style="list-style-type: none"> Seen in 1 in 5, possible worse on teenagers 	<ul style="list-style-type: none"> Reduce fluids at bed time Change dose regime

Other common side effects are detailed in Table H.5.5, but this list is by no means complete. It is recommended that clozapine be prescribed only by specialists who are aware of the side effects and able to manage the risks appropriately.

Other interventions

There is good evidence of effectiveness for several other therapies in the treatment of early psychosis. All have been shown to reduce the risk of relapse and, most importantly, help young people and their families feel more in control of their symptoms and their treatment.

Psychoeducation

Psychoeducation is a structured way of providing information about psychotic disorders and their treatment for both young people and their families. There are manualised programs available and evidence that psychoeducation reduces the rate of relapse in early psychosis (Xia et al, 2011).

The ingredients of effective psychoeducation include:

- Providing information about the illness and treatment options
- Offering a forum for the young persons to discuss their illness and concerns
- Involving family members in the education process, whether with their children or in parent groups.

If successful, the rate of relapse is reduced by increased adherence to medication, reduction in maladaptive behaviors such as substance misuse, and early recognition of symptom return or deterioration. Coping skills and problem solving training can also be part of the education program (Xia et al, 2011).

While face to face psychoeducation programs are useful they may not be available in remote or rural areas or may not be run at convenient times. Web based resources are also an excellent way of obtaining information and becoming part of a supportive network.

Cognitive behavioral therapy (CBT)

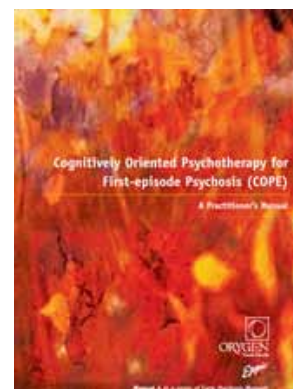
Some young people find CBT helpful in understanding and managing their symptoms. The goals of CBT vary depending on the symptoms of concern, but can include coping strategies for psychotic experiences and managing low mood. Directly addressing the psychotic symptoms is most effective in the recovery rather than the acute phase of the illness. However, CBT is also useful for managing residual symptoms such as hallucinations that persist despite antipsychotic treatment. Strategies include:

- Exploring and challenging delusional beliefs
- Finding coping strategies to minimize the impact of hallucinations
- Managing feelings of hopelessness and low mood using similar techniques to those used in CBT for depression.

Working with families

As well as providing support, initial work with families involves a psychoeducational approach, providing information about the illnesses and how it affects thoughts and behaviors. Problem solving skills and communication strategies help families deal with difficult situations and reduce distress in the household. This

Click on the picture to access the Cognitively Oriented Psychotherapy for First-Episode Psychosis (COPE) manual.



reduces the risk of relapse, as well as preventing family estrangement (Addington et al, 2005).

Maintenance medication and management of side effects

Use of antipsychotic medication is recommended for at least 12 months after symptom remission to reduce relapse. Careful monitoring and management of side effects is essential. Weight gain and associated metabolic abnormalities are the most frequent, but sedation and cognitive slowing can also cause distress. There is some evidence from meta-analyses – of adult treatment trials – that the second generation antipsychotics are more effective at preventing relapse than the first generation ones (Alvarez-Jimenez et al, 2011). Six monthly monitoring is required for:

- Involuntary movements (the recommended scale is the [AIMS – Abnormal Involuntary Movement Scale](#))
- Weight, waist measurement, pulse rate and blood pressure
- Fasting glucose and lipids.

Movement disorders, including Parkinsonism and akathisia, are less common with second generation antipsychotics. If these occur, try small doses of an anticholinergic drug, for example benztropine 0.5mg a day. Reducing the dose of antipsychotic is often more effective. Tardive dyskinesia, a rare, chronic movement disorder, is often first seen as small movements in the face, tongue or fingers. Early identification is important as tardive dyskinesia may persist after medication is ceased. The most commonly used mood stabilizers (in particular lithium carbonate, sodium valproate and carbamazepine) are teratogenic and this needs to be discussed with sexually active adolescents. The use of lithium requires clear instructions about the need to avoid dehydration and have regular lithium levels and thyroid function tests to monitor for possible toxicity (see Chapter E.2).

Prevention of relapse

The first step to relapse prevention is to develop an individual plan to detect warning signs such as difficulty sleeping, increased anxiety or the first signs that hallucinations or delusions are reappearing. If medication is being slowly reduced, recurrence of any symptom suggests that a return to the higher effective dose is required, or to resume previously effective medication if it had been stopped. Ongoing monitoring by mental health professionals during this time is essential. There are few studies examining relapse rates in children and adolescents but one study on first episode psychosis found a 17% relapse rate when medication was stopped after 12 months (Gaebel et al, 2011). As with the first episode, the earlier a relapse is treated the better the recovery. Relapses can also cause further cognitive and social deterioration.

Services for early psychosis

While schools, general practitioners, pediatricians and other health care providers often identify young people at risk of psychosis, once early psychosis is identified it is essential that mental health services be involved if at all possible. In Australia these services include child and adolescent mental health services—community based teams who treat young people up to the age of 18 and youth mental health services, for ages 12-25. All these services use a *case management model*, with a case manager (mental health professional) and consultation with a



Click on the picture to view a 25 minute documentary on schizophrenia. This website, which has information for patients and families, is sponsored by Janssen Pharmaceuticals

psychiatrist as needed. Some services also provide *assertive case management* (a more intensive case management used for difficult to treat patients, with active follow up including home visits), drug and alcohol services, general health and sexual health services or help with financial management, housing and employment.

Specialized services in remote or rural areas are few or non-existent. Local family doctors provide most of the care with support from a mental health worker, often a nurse. Internet resources listed can be useful both to guide treatment and to provide education for young people and their families.

RECOVERY, RETURN TO EDUCATION AND OUTCOME

It is important to be both optimistic and honest when talking to young people and their families. They need to know that, while acute psychotic symptoms almost always remit within days to weeks, negative symptoms such as poor motivation, concentration and cognitive slowing may continue for many months, particularly in the case of schizophrenia. While the majority of symptoms improve in the first six months of treatment, improvement can continue for up to two years. Schizophrenia spectrum disorders tend to have the slowest response, the highest rate of residual deficits and a lifelong risk of relapse of up to 90%. A better prognosis is more likely with a rapid onset of psychotic symptoms, prominent mood symptoms, good social and educational functioning prior to the illness and a rapid response to treatment.

Returning to school may be difficult because of negative symptoms, cognitive difficulties or the amount of time missed, including explaining absences to others. Options depend on what local health and education services are locally available. Meeting with the young persons' school and negotiating part-time attendance is desirable. Where school counselors or similar are available, their involvement is crucial. Some countries offer education programs with smaller classes and staff trained to manage young people with psychological disorders. For those who have reached school-leaving age, institutions that deliver vocational training may provide support for these patients. Partial hospitalization (e.g., day programs) or work preparation programs may be needed for those whose recovery is slower. Additional evidence-based interventions such as social skills training or cognitive remediation strategies may also be useful (Poletti et al, 2010; Addington et al, 2010).

Incomplete recovery

Some young people with schizophrenia do not fully respond to treatment and have ongoing positive or negative symptoms. Reasons for incomplete recovery include:

- *Factors in the young person*, including adherence to treatment. Compliance may be poor because of lack of insight into their illness, concern about side effects such as weight gain or extra pyramidal symptoms. Comorbid disorders such as drug and alcohol abuse, a history of trauma or a pervasive developmental disorder make psychosis harder to treat
- *Illness factors*. Some young people have a more severe form of the illness with a long prodrome and prominent negative symptoms, which



Click on the picture to view a clip about early intervention and treatment from the US Maine Medical Centre's PEIR Program. Other useful websites are the one from the [International Early Psychosis Association \(IEPA\)](#), a network for people involved in the study and treatment of early psychosis, and the [Early Psychosis Prevention and Intervention Centre \(EPPIC\)](#) website. This Australian website has a wide range of information about the identification and treatment of early psychosis. Mental Health professionals can register with the site and log on for forums and education sessions.

As well as many of the websites already mentioned the [Schizophrenia Fellowship](#) and [Arafmi](#) are two Australian non-government organizations that provide support and information for family members and others who care for people with mental illness.

takes longer to respond to treatment, or may never respond completely

- *Treatment factors.* Poor response is more likely if the first experience of treatment was coercive or patients do not have active follow up. Ongoing stress at school or in their family (e.g., high expressed emotion) make relapse more likely. Psychological treatments such as CBT or family therapy help to prevent relapse by teaching strategies to manage early symptoms and reduce and manage stress.

Support for family and other carers

Caring for young persons with a chronic mental illness can be exhausting for their families. As well as family psychoeducation, informative websites and support groups can help families and carers feel less alone.

SUMMARY AND CONCLUSIONS

Psychotic symptoms in children and adolescents can be confusing and difficult to assess in the early stages. However, early symptoms, such as functional decline or hallucinations, should be taken seriously. While many symptoms remit with time, early symptoms are associated with an increased risk of schizophrenia spectrum disorders in adult life. There is also good evidence that early treatment reduces the morbidity and mortality associated with this group of severe mental illnesses.



Encouraged by Henri Laborit, a French surgeon and researcher, the French pharmaceutical company Rhône-Poulenc synthesized chlorpromazine in 1950. The first systematic study of chlorpromazine's effect on Schizophrenia, which included 38 patients, was published by the French psychiatrists Jean Delay and Pierre Deniker in 1952. Jean Delay created the word "psychopharmacology", proposed the definition of neuroleptic drugs (literally, "substances that take the nerves") and together with Deniker established the first classification of psychotropic drugs. Chlorpromazine is still in clinical use today.

Photo: Delay (left) and Deniker

Resources in languages other than English

There is a wealth of resources available on the Internet, some examples are given below.

- Many international resources are indexed at schizophrenia.com
- The [Quebec Early Psychosis Program \(AQPPEP\)](#) has a site in French
- The [Swiss Early Intervention](#) site has interactive information in German, French and English
- [P3 Programa de Prevención de Psicosis](#) is a Spanish site with resources in Spain
- Chinese sites (Cantonese) include the [Hong Kong Early Psychosis Intervention Society](#); [EASY](#), an animated website for people aged 15-25 with information about psychosis, self-assessment, news, and where to get help; and [Radio-I-Care](#), an online radio broadcast with a range of topics on mental illness, intervention, and how to live with psychosis.
- The pharmaceutical company Astra Zeneca funds an educational site about psychosis and bipolar disorders in several languages ([German](#), [Russian](#), [Turkish](#) and English).

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