# Schizophrenia in childhood and adolescence

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Schizophrenia has been recognized in childhood since Kraepelin's description of dementia praecox. Following Kanner's account of childhood autism in 1941 as a psychosis, the two conditions became confounded, and it was only in 1971 that Kolvin's Newcastle study clearly delineated schizophrenia and autism.[1] Subsequent studies have begun to categorize other psychotic conditions with onset in childhood and early adolescence. Schizophrenia, although rare in this age group, is diagnosed by the same criteria as in adults (ICD-10 or DSM-IV), but the clinician needs to be aware of the modifications to the clinical picture caused by the young person's developmental level.

## Epidemiology

Child and adolescent onset schizophrenia (CAOS) is conventionally divided into two: very early onset (VEOS) prior to 13 years of age, and early onset (EOS) occurring between 13 and 19 years of age. The incidence rises rapidly during adolescence and beyond, to give a peak incidence at around 25 years of age.

VEOS is extremely rare, with population-based studies giving point prevalence rates between 1.6 and 1.9 cases per 100,000.[2] Some clinic-based studies offer higher prevalence rates, for reasons that are not entirely clear, but diagnostic inaccuracy was probably a significant feature in earlier studies. Males appear to predominate with a ratio of about 2:1. Around the age of 13 the incidence and prevalence of the illness rises rapidly, to reach a teenage population prevalence of 2 to 3 per 1000. The excess in males falls to parity, before rising again in early adulthood.

## Aetiology

Traditionally, psychiatry divided psychoses into 'functional' and 'organic', because in most cases of schizophrenia it was not possible to identify any neuropathology. However, neurobiological and neuropsychological abnormalities are increasingly recognized, particularly with early-onset illness and this distinction is outdated.

### Genetics

Rapoport's ongoing study of treatment-resistant VEOS has identified about 10% of children with a cytogenetic abnormality, including 22q11 deletions, the Fragile-X expansion and mosaic 45,XO, which is considerably in excess of the population base rate. The longitudinal 'high-risk' studies (which identify study children of

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schizophrenic parents who carry an increased genetic risk) in New York and Scotland have indicated that familial loading is associated with earlier age of onset and greater neurodevelopmental and behavioural disturbance prior to onset.

### Neurodevelopment and symptomatic psychosis

Developmental abnormalities, dyspraxia and dyslexia and poor academic achievement, are extremely common in EOS, and particularly VEOS. Pre-existing speech and language disorders, receptive and expressive, are found in up to 80% of patients.[3] Psychosis and schizophrenia-like illness are well-recognized complications (secondary or symptomatic) of numerous childhood neurological conditions, most notably tuberous sclerosis, partial complex seizure disorder and neurodegenerative conditions such as the leucodystrophies. In keeping with adult studies, smooth pursuit eye-tracking has been found to be impaired in children who have developed schizophrenia and other psychotic illnesses, and also impaired in their close relatives, which may indicate it is a trait marker for neurodevelopmental risk.[4]

### CNS development

The advent of non-invasive imaging techniques has permitted extensive cross-sectional and, more importantly, longitudinal studies of brain development in schizophrenic and control populations. Diagnostic instability and patient selection problems have led to some conflicting results. However, some consistent findings are emerging. In adolescents, ventricular size increases post-illness onset compared to normal controls and is associated with loss of peri-ventricular grey matter in the thalamus and basal ganglia. The National Institute of Mental Health group have also described a pattern of progressive grey matter loss during adolescence, spreading forwards and outwards from the parietal lobes to the pre-frontal cortex.[5]

### Family environment

Just as with autism, parents have often been blamed (and blame themselves) for causing schizophrenia. High expressed emotion in the home environment strongly predicts relapse in adults. These studies have not been replicated in CAOS, and in any case, relapse is not the same as cause. However, evidence is emerging of significant gene–environment interactions, whereby good family functioning protects an adopted child who is at high genetic risk. Conversely, poor functioning exposes the genetic vulnerability in schizophrenia spectrum disorders.[6]

### Gene–environment

Neuchterlein organizes the different components of research into an interactive stress-diathesis model.[7] Personal vulnerability factors including dopaminergic dysfunction, reduced processing capacity (executive function), autonomic hypersensitivity and schizotypal personality traits interact with each other and personal protective factors – coping and self-efficacy attributes and use of anti-psychotic medication. External or environmental adverse influences include:

- stressful life events
- high expressed emotion
- over-stimulating environment

These interact with external protectors:

- supportive psychosocial interventions
- domestic problem solving.

The internal and external factors determine the state of pre-morbid or remission functioning. They act and interact together to give rise to prodromal and symptomatic episodes, which in turn feedback onto the internal and external components.

## Diagnosis

DSM-IV and ICD-10 use rather different diagnostic systems; the American approach is more structured, and may produce greater diagnostic stability. Hollis has recently published a study showing an 80% positive predictive value (PPV) for the 51 adolescents diagnosed with schizophrenia, confirmed at follow-up.[8] This contrasts with previous studies giving at best a 50% positive predictive value for schizophrenia. The difference is striking given that DSM-IIIR was used in the Hollis study and several of the earlier studies as well. He used OPCRIT, a software programme, to assign the diagnoses, and it may be that this is more valid and reliable than human coders when it comes to considering all the information available to formulate a diagnosis. However, data collected over many months was used to assign diagnosis. Given the improved tolerability of the newer atypical neuroleptics, and concern at the possibility of worsening prognosis with longer duration of untreated psychosis, there is now a stronger impetus to early diagnosis and treatment.

In addition to the primary criteria, DSM-IV (in childhood) requires evidence of change of social or educational function, a six-month duration of illness (not necessarily frank psychosis), and the exclusion of affective, schizoaffective and pervasive developmental disorders as well as organic causes. ICD-10 is a more discursive diagnostic system, based more closely on Schneiderian First Rank Symptoms, which are grouped together.

The associations of schizophrenia are also different in the two systems. DSM-IV leaves schizotypal disorder with the personality disorders; ICD-10 has placed it with the schizophrenias, as there is an excess of schizophrenia in relatives of index cases. ICD-10 includes the category of simple schizophrenia, which is particularly common in CAOS and typified by an insidious descent into negative symptoms, without the period of active symptoms.

It will be apparent that the epidemiology and diagnostic stability of the condition is closely linked to the ascertainment process. Diagnostic accuracy is based on the skill of the psychiatrist in executing the Mental State Examination, and its interpretation. Endophenotype studies are pointing in several directions and have not yet provided clear diagnostic boundaries, but the group mean differences in biological variables, such as brain morphometry, autonomic reactivity, and smooth eye pursuit, coupled with psychometric and symptomatic evaluation may yield significant improvements in diagnostic sensitivity and specificity in the near future.[9]

## Course

Schizophrenia usually presents floridly with positive symptoms comprising hallucinations, delusions and thought disorder. A more insidious onset, with gradual decline into the negative symptom cluster of apathy, social withdrawal and behavioural disorganization is seen more frequently in VEOS and associated with a higher incidence of neurobiological abnormalities. There is often a prodromal phase of subtle alteration of activity; school grades may