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PSYCHOSIS IN CHILDHOOD AND ITS MANAGEMENT

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The appearance of *psychotic symptoms in childhood,* albeit rare, is an important clinical entity. This importance extends beyond their clinical prevalence and has begun to influence our understanding of the principal psychotic conditions. The term *psychosis* is generally categoric and includes subgroups within it. It is clear that the peak onset of the most common psychotic disorders, schizophrenia and bipolar disorder, is in adolescence (1,2). This points directly toward developmental events in biological, social, and psychological domains of late childhood and adolescence that set the stage for activating psychotic disorders. However, in addition, it appears increasingly likely that certain early childhood characteristics and developmental deficits may presage psychosis and are related to the outcome of psychotic disorders.

For the purposes of this chapter, *psychosis* is defined as the presence of disruptions in thinking, accompanied by delusions or hallucinations, along with an alteration in the thought processes, termed a *thought disorder.* Delusions and hallucinations are considered to be positive psychotic symptoms. *Delusions* are fixed, false, idiosyncratic beliefs that the child cannot be deterred from, with logical reasoning, whereas *hallucinations* are percepts that arise in the absence of external sensory stimulus. Psychotic symptoms always encompass a broad range of conditions, but it is particularly so when they appear in children and adolescents. Psychotic symptoms in children present distinctive diagnostic and clinical challenges because of the powerful influences of immaturity and the moving target produced by development.

Although there may at one time have been confusion about whether children are capable of having psychotic symptoms, it is now certain that children, like adults, can and do experience psychoses (i.e., disruptions in the form of mental life). Children and adolescents experience the same range and types of psychotic symptoms as do adults. They can lose the connections between their thoughts (formal thought disorder) and have perceptions without external stimuli (hallucinations). The term psychosis as described by McHugh and Slavney (3) is intended simply to indicate that mental life has been disrupted in its capacities or forms, as a result of a process that generates new forms of psychological experience.

Psychotic symptoms can be considered as general or nonspecific phenomena emerging with different disorders and etiologic possibilities. Modern psychiatry eschews the misleading dichotomy of functional versus organic causes and recognizes that some of these disorders stem from known brain or metabolic disorders, whereas for other conditions the pathophysiologic sources have yet to be discovered. The interplay between environmental and biological forces is at work across the spectrum of these conditions. The psychiatrist who must determine whether a young patient suffers from a psychotic disorder faces a challenging array of possibilities, more extensive than when the patient is an adult. The influences of development, environment, and cognition are greater for young or developmentally immature patients than for adults. Nonbiological events are clearly more influential because, in most respects, children are more vulnerable to their surroundings. Immaturity makes children more susceptible to environmental stressors and cognitive distortions. Children routinely have intrusions of fantasy into ordinary mental life; determining when this becomes pathologic can be a matter of degree. Children learn and experiment with imitation, and they can acquire habits and strategies used by those around them. They have not developed the cognitive abilities that permit them to observe and compare their experiences in an objective manner. The range of normal functioning is greater in childhood, so the child's behavior may simply be a result of immaturity, rather than a deviation from a normal pathway.

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With the advent of categoric classification of psychiatric disorders, the criteria for psychotic disorders have become more stringent, and the concepts have been defined more narrowly. When one examines a 5-year old child who claims that he is ''superman and can fly,'' the challenge is to determine whether the child has a delusion. Similarly, in a child who complains about hearing a voice telling her to ''do bad things,'' one must determine whether she is talking about her conscience or is experiencing auditory hallucinations. This must be distinguished from *make-believe* (e.g., having an imaginary friend). Children can describe this make-believe phenomenon, and clinicians need to discern the differences as they work with children with symptoms of psychosis. Such characteristics are sought by the clinician in the child's answers to particular questions. The task and challenge as child and adolescent psychiatrists are to ask the right questions, to differentiate delusions and hallucinations from other forms of thought, such as a vivid imagination in a young child.

HISTORY

Interest in childhood psychosis can be traced to the nineteenth century, when Maudsley first wrote a description of the ''insanity of early life'' in 1874 in his textbook, *Physiology and Pathology of Mind* (4). He took a developmental approach by noting that the mental faculty of children was not organized, and hence the insanity in children must be of the simplest kind, influenced more by ''reason of bad descent or of baneful influences during uterine life.'' However, De Sanctis may be credited first with setting out childhood schizophrenia as different from mental deficiency and from certain neurologic disorders, such as epilepsy or postinfectious encephalopathy (5). It was not until 1919, that Kraeplin introduced the concept of *dementia praecox* and noted its onset in late childhood and adolescence (6). Given the insidious onset of the disorder, Kraeplin cautiously suggested that 3.5% of patients with schizophrenia had the onset of their illness before the age of 10 years. This led to an increased interest in understanding the developmental aspects of psychosis. Historically, despite this early description of the syndrome by Kraeplin that is now recognized as schizophrenia, other diagnostic terms were put forward as well. These included *dementia praecossima* (5) and *dementia infantilis* (7). Potter offered clearer descriptions of schizophrenia, with consideration of the child's developmental age, and offered specific diagnostic criteria for children (8).

Despite efforts to recognize childhood schizophrenia as a distinct clinical entity, during the decades between 1920 and 1970, the term *childhood psychosis* comprised all forms of severe mental disorders in children, including schizophrenia and autism. Kanner's description of early infantile autism catalyzed an alternative view of the conceptualization of these disorders.

Beginning with the works of Loretta Bender (9), Leo Kanner (10), and others (11), all considered childhood schizophrenia to fall under the broader category of childhood psychoses. Nevertheless, there came an acknowledgment and new awareness of major developmental differences in the perception of reality (12) and that developmentally or culturally appropriate beliefs (e.g., imaginary playmates and fantasy figures) did not, of themselves, suggest psychosis. This cluster of syndromes, including infantile autism, was defined by developmental lags in the maturation of language, perception, and motility (11). Although psychotic speech and thoughts were initially considered inherent components of childhood schizophrenia, hallucinations and delusions were not required criteria (6,13–15). DSM-II adopted this nosology and grouped all childhood psychoses under childhood schizophrenia. As a result of this broad grouping, the literature regarding childhood schizophrenia from this period overlaps with that of autism and does not differentiate autism from other psychotic disorders. With further development of psychiatric taxonomy and elucidation of the phenomenology (course, onset, family history, and associated features), the distinctiveness of the various childhood psychoses and the similarity between child and adult schizophrenia were demonstrated (16,17). This change had a pronounced influence on the nosology of these disorders and led eventually to changes with the DSM-III (18). Schizophrenia arising in childhood and infantile autism came to be recognized as distinct clinical syndromes, each with its unique and distinct psychopathologic phenomenology, theories about causes, and longitudinal course. Research since the advent of DSM-III generally validated this decision (19,20). This distinction has had an impact on how children with these disorders are currently evaluated, managed, and treated.

COGNITIVE ASPECTS

Although children do not describe disorders, they nevertheless may complain of changes in their mental and cognitive states. To these changes, clinicians add signs, based on observations derived from the mental state examination of the children and data obtained from laboratory or cognitive tests. Subsequently, a distinctive pattern may emerge over the course of the child's illness. A collection of symptoms and signs occurring in a certain temporal pattern is then used to categorize the child's problem. Psychotic symptoms can be attributed to distinct mental illnesses (functional psychoses), which are contrasted with the psychotic symptoms that usually result from a demonstrable underlying pathologic mechanism and organic origin (organic psychoses), such as delirium. Cognitive impairments, particularly impaired concentration and ability to focus, usually accompany psychosis in children. However, when the psychosis is secondary to an organic origin, there is often accompanying

impairment in the sensorium presenting as confusion and disorientation, as is typical of delirium.

From a cognitive and developmental standpoint, certain clinical features in children create diagnostic challenges. One problem is distinguishing true psychotic phenomena in children from nonpsychotic idiosyncratic thinking, perceptions caused by developmental delays, exposure to disturbing and traumatic events, and overactive and vivid imaginations. Furthermore, because the onset of childhood schizophrenia is insidious, with a lifelong history of developmental and personality abnormalities, differentiating between the premorbid state and the active psychotic state can be difficult. It has also been suggested that the development of psychotic conditions during childhood may have major adverse effects on development, a feature further complicating diagnostic assessment (21).

Investigators have noted that social withdrawal, ''shyness,'' and disturbances in adaptive social behavior seem to be the first signs of dysfunctional premorbid development. Eggers et al. suggested that these should be considered vulnerability factors, indicative of a risk of psychotic illness (22). Recent work has also pointed to early language deficits and motor impairments as being significant for very early-onset schizophrenia, in children younger than 12 years (23). However, a socially odd child is not usually schizophrenic. In fact, most children who have hallucinations are not schizophrenic (24–26), because they lack the requisite persistence and associated symptoms. Intellectual delays have long been considered as general risk factors for psychopathology and psychosis in children (27). In fact, the estimated rates may be low, because most studies examining psychosis in children exclude patients with mental retardation (28, 29).

CLINICAL AND DEVELOPMENTAL CONSIDERATIONS

Developmental factors influence the detection, form, and context of psychotic symptoms in children. One problem of assessing psychotic disorders in very young children compared with older children is that these symptoms in young children tend to be more fluid and less complex. Isolated hallucinations can occur in acutely anxious but otherwise developmentally intact preschool children. In older children, hallucinations may occur in the absence of other signs of psychosis, but they are usually associated with other psychopathologic conditions, such as depression, severe anxiety, and posttraumatic stress disorder.

Often, there is an underestimation of the subtle differentiation among age-related cognitive preoccupations, pseudohallucinations, and imaginative experiences. Further, it is often too difficult to tease out the physiognomic-animistic interpretations of the inner and outer world on one hand and the first prominent psychotic phenomena such as delusions and hallucinations on the other.

It is critical to avoid rushing to a premature conclusion about unusual behaviors and beliefs in children. Such atypical mental experiences in children can be recognized as prodromal or prepsychotic signs only after the manifestation of frank psychotic symptoms. Odd beliefs and unusual behaviors deserve close observation, but they cannot be ascribed to psychosis without the concomitant presence of a thought disorder.

For example, a young schizophrenic girl lived by the railroad tracks all her life. At age 11 years, about the time when her disorder had its onset, she noted that the sound of the train whistle changed, and she began to wonder why. She came to believe that it had a specific purpose and meaning—that it beckoned her. Until that time, such events were inconsequential and unimportant, but at about age 11 years, she started to attach a different meaning to them. She was uncomfortable with these thoughts and realized that it was not her usual pattern of thinking. Things around her started to have special meaning, her thoughts were ''strange,'' and she was puzzled and bewildered.

This may be considered a *predelusional phenomenon,* idiosyncratic but not yet fixed. Over the next several years, she developed ideas of reference, thought broadcasting, and thought insertion. She believed that the train whistle was sending special messages from God to her. She no longer questioned these perceptions and believed them to be real. By age 14 years, she was diagnosed with childhood-onset schizophrenia.

A formal thought disorder in a child is more ominous and requires careful psychiatric and neurologic evaluation. Distinguishing between the formal thought disorder of schizophrenia and that of developmental disorders, personality disorders, and speech and language disorders also presents diagnostic problems (30). Symptoms such as thought disorder have been noted to arise in persons with pervasive developmental disorders, particularly those with good language skills, such as (often referred to as ''high functioning'') autistic persons and those with Asperger syndrome (31,32).

Although loose associations and incoherence are valid diagnostic signs of early-onset schizophrenia, these symptoms are also sometimes seen in schizotypal children (33). The inclusion criteria of disorganized speech according to DSM-IV (34), rather than a formal thought disorder, presents a particular challenge when assessing children, because disorganized speech is an inherent component of many of the developmental disorders. Clearly, the assessment and ascertainment of delusions, hallucinations, and thought disorder in linguistically impaired children are difficult and complicated.

Therefore, developmental disorders must be considered in the differential diagnosis of a child presenting with psychotic symptoms. The use of comparable criteria across the age span facilitates analyses of progressive symptoms from

childhood to adulthood. However, one of the difficulties in assessing psychotic disorders in very young children is to determine whether nonspecific behavioral disturbances represent an incipient psychosis or are signs of autism or pervasive developmental disorders (35,36).

Further, the conceptualization of psychoses in childhood as a neurodevelopmental disorder has drawn increasing attention, especially as it relates to childhood-onset schizophrenia (37). Therefore, another alternative in the conceptualization of psychotic episodes is a grouping of symptoms that are not part of the formal DSM or International Classification of Diseases (ICD) scheme. For decades, clinicians recognized that a pattern of brief psychotic episodes, affective dysregulation, and poor social abilities occurs in children. Early references on schizophrenia (17) and later writings (38,39) noted the diagnostic problem of children with poor social development and psychosis. Now, the absence of a formal single diagnostic address for this syndrome has produced a wide variety of terms applied to the same phenomena. The older literature suggested that such children may be considered to have "borderline syndrome of childhood" (40), and then later "schizotypal disorder of childhood" was considered (38). In 1986, Cohen et al. suggested the term *multiplex developmental disorder* and proposed that this condition was best understood as a developmental deviation within the group of pervasive developmental disorders (41). Towbin and co-workers offered operational criteria and preliminary validating evidence for the concept and criteria and used the term *multiple complex developmental disorder* (42). Following Cohen et al., the view of Towbin and co-workers was that multiple complex developmental disorder was a higher-functioning type of pervasive developmental spectrum disorder. Rather than pointing to one particular outcome, Towbin and coworkers suggested that multiple complex developmental disorder was a nonspecific risk factor for a poor adaptation in adult life but with a myriad of adult diagnostic outcomes such as schizophrenia, bipolar illness, or any of the more severe unstable personality disorders. Further elaboration of these criteria have shown support for the concept and validated that children with pervasive developmental disorder not otherwise specified and autism can be meaningfully separated from those with multiple complex developmental disorder (43). Further exploration of the concept of multiple complex developmental disorder has received support from neurophysiologic studies as well (44).

The National Institute of Mental Health (NIMH) project on early schizophrenia culled children for a study of clozapine. The most common referrals were children whose symptoms closely resembled those of multiple complex developmental disorder. The NIMH group suggested the term *multidimensionally impaired* (45,46) and offered criteria that were analogous to those described by Towbin and co-workers. However, despite findings that many of these children met partial criteria for pervasive developmental disorder not otherwise specified, the NIMH group preferred to consider the constellation a *forme fruste* of schizophrenia (46). Yet longitudinal studies suggested that the constellation remains stable and does not progress to schizophrenia (46). Other work reporting on similar children has used terms like such as "pervasive developmental disorder plus bipolar" (47) or "obsessive difficult temperament" (48). As further exploration now points to "high rates of speech and language, motor, and social impairments in patients with childhood-onset schizophrenia," the association with pervasive developmental spectrum disorders is drawn even closer for this very early-onset subgroup (23).

In addition to the developmental factors and disorders described earlier, the other differential diagnoses of childhood psychoses can be classified as described in the following sections.

Functional Psychoses

Childhood-Onset Schizophrenia

Schizophrenic psychoses with onset before age 11 years are rare. The prevalence in this age group is about 0.01 to 0.05 per 1,000. In addition, developmental status can affect the expression of the disorder. The earliest descriptions by DeSanctis (5), Bleuler (49), and Kraeplin (6) reported the onset and occurrence during childhood and considered schizophrenic psychoses to be an early onset of the same disease, which appeared to be on a continuum phenomenologically, that they observed in adolescents and adults. Furthermore, it has been shown that schizophrenic psychoses can be diagnosed reliably in children using the same criteria as for adults (20,36,50,51). Very few studies to date have dealt with the long-term outcome in childhood-onset schizophrenia. Most studies have followed children for between 1 and 5 years (52). Because of methodologic difficulties, there is a striking absence of data before the age of 11 years on the long-term course of psychosis. Asarnow emphasized the "crucial importance" of long-term follow-up data for establishing the validity of psychotic symptoms manifested in early childhood (53). This is especially important because children often describe "hearing voices," especially in clinical populations. An astute clinician will delve into this symptom in greater depth, to obtain a qualitative appreciation of these "voices." Often, the child will describe this "voice" inside his head as if hearing his own voice or that of an adult in his life. He most likely will not hear this voice through his ears and seems affectively not to be too troubled by it. Conversely, a child experiencing true auditory hallucinations is frightened, puzzled, and unable to be reassured. This differentiation is especially important because management of these youngsters often includes the use of psychotropic medications, which, in and of themselves, require serious consideration because of their long-term adverse effects. If the phenomenology of these so-called psychotic

symptoms is not clarified, many youngsters with pseudohallucinations will be prescribed psychotropic medication needlessly. In addition, they will wrongly be labeled with a psychotic disorder.

Premorbid developmental peculiarities have been reported in children with childhood-onset schizophrenia who have been followed into their thirties. These peculiarities are primarily internalizing such as shyness, isolatory behaviors, lack of interest, awkwardness, being fickle with peculiar facial expression, aggression, paranoia, anxious thoughts, and being mistrustful of others, along with symptoms of depression. These signs have been reported to be much more common than externalizing, acting-out behaviors such as temper tantrums, aggression, opposition, and hostility (22). From a developmental standpoint, the age of first manifestation of nonpsychotic symptoms is younger than the age of onset of schizophrenic symptoms (53–56). However, the predictive relevance in prepsychotic symptoms in children seems to be extremely uncertain because of the high variability of developmental peculiarities.

The nature of the diagnostic subtypes varies markedly across the course of the illness. In patients with continuous predominantly catatonic symptoms, the outcome is poor. Eggers et al. suggested that detailed case description helps to illuminate the heterogeneous psychopathology of childhood-onset schizophrenia (22). These investigators found that various temporary premorbid behavioral peculiarities were precursors of childhood-onset schizophrenia. Children with early-onset schizophrenic psychosis develop a phenomenology of positive and negative psychotic symptoms that are similar to those seen in adult patients with schizophrenia, and the course variability is perhaps even greater than in adult patients. Their findings contradicted the assumption that childhood-onset schizophrenia is characterized only by negative symptoms, because a differentiation between premorbid and prodromal signs proved to be arbitrary.

Since Kraeplin's first description of *dementia praecox* in 1889, the onset and course of schizophrenia relied heavily on first admission data and on the subsequent course of the disease. However, Hafner et al. argued that items taken from the preadmission phase of the disease were often incorrectly used as premorbid characteristics (57). In an attempt systematically to account for the age and gender distribution of the true onset and the symptoms and pattern of the early and later course, Hafner et al. developed an Interview for the Retrospective Assessment of the Onset of Schizophrenia (IRAOS) (57). This instrument allows an objective, reliable, and valid assessment of the symptoms, psychological impairments, demographic and social characteristics, and the referring points in time of the early course of psychosis. Their findings suggested that the IRAOS provides information on the earliest course of the disease and enables them to separate premorbid characteristics, possibly the most powerful predictors of the later course and outcome, from contamination with symptoms and deficits belonging to the early phase of the disease. The influence of certain life events on the early course is also made accessible to empiric research. Other instruments that have been used for assessing psychotic symptoms in youngsters have been the Interview Schedule for Children (58), the Diagnostic Interview Schedule for Children (59), the Schedule for Affective Disorders and Schizophrenia for School-Aged Children (60, 61).

Several nonspecific and nondiagnostic neurobiological abnormalities have been reported in patients with schizophrenia. These include deficits in smooth pursuit eye movements and autonomic responsivity (62,63). Neuroimaging findings include a progressive increase in ventricular size and a fourfold greater decrease in cortical gray matter volume during adolescence, with the greatest differences occurring in the frontal and temporal regions (64–67). Others findings reported in the literature are a smaller total cerebral volume, correlated with negative symptoms (37), and frontal lobe dysfunction (68).

Schizophrenia with childhood onset is usually a severe and chronic disorder with a more guarded prognosis and poorer therapeutic response to neuroleptic agents than schizophrenia with adolescent or adult onset. New research and data will help to clarify the origin and pathogenesis of schizophrenia in children. Subsequently, development of more effective treatments and preventive measures may reduce its severity.

Mood Disorders

Mood disorders such as major depression and acute mania can often be accompanied by psychotic symptoms. Over the past several decades, the prevalence of mood disorders appears to have been increasing (69). Although information on the epidemiology of psychotic depression in children is limited, Chambers et al. described the occurrence of psychotic depression in children (61). The psychotic symptoms usually are mood congruent, but at times they can be quite like those seen in childhood schizophrenia (20,70–72). This overlap in symptoms increases the likelihood of incorrect diagnosis, especially at the time of onset. Sometimes, the negative symptoms of schizophrenia in children can be mistaken for those of depression. However, it has been shown that children with schizophrenia have poorer premorbid adjustments, lower IQs, and more chronic dysfunction, when compared with children who suffer from a depressive disorder (50). It is therefore prudent to make only a tentative diagnosis at the outset that must be confirmed longitudinally. Careful follow-up of psychotic patients is needed to detect diagnostic errors. This issue can be compounded, however, if the symptoms resolve with antipsychotic medications. It becomes unclear whether the child improves because of treatment or spontaneous remission. Approximately one-half of adolescents with bipolar disorder may

be originally diagnosed as having schizophrenia (20,70). Therefore, it is extremely important that longitudinal reassessment is needed to ensure accuracy of the diagnosis. Despite an increased family history of depression in schizophrenic youth (20), family psychiatric history can be an extremely helpful differentiating factors. However, the opposite is not true, that is, an increased family history of schizophrenia in depressed or bipolar youngsters. Often, the rule of thumb is first to rule out mood disorder in a child or adolescent before the diagnosis of schizophrenia is more strongly considered.

Even though there is an overlap of the quality of psychotic symptoms in children with mood disorders and childhood-onset schizophrenia, often with careful examination, some of the mood-congruent symptoms can be ascertained. As clinicians, it is important that we ascertain chronologically what came first, that is, a change in mood and then the onset of delusions or hallucinations, or a disturbance in thought followed by a change in mood. For example, the child who first starts to have "strange thoughts" and to hear voices over time becomes puzzled, fearful, distraught, and depressed. This is quite different from the child who first starts to lose interest in activities, to feel irritable or depressed, to not want to play with friends, and who demonstrates neurovegetative symptoms, such as a decrease in appetite, sleep disturbance, and lethargy. Subsequently, the child starts to think he is a bad and evil person and then hears a voice that tells him he is a bad boy and that he should kill himself. The phenomenology in this instance is quite different. However, it is not always this clear, and there is a high rate of misdiagnosis in both directions (72, 73).

Psychotic symptoms during a manic episode have been recognized for many years, although misdiagnoses of schizophrenia were, and remain, relatively common (74). Bipolar disorder eventually develops in a minority of children initially hospitalized for major depression (1). This is particularly so if the child has a positive family history of bipolar disorder, psychomotor retardation, rapid onset of symptoms, mood-congruent psychotic symptoms, or pharmacologically induced mania or hypomania. The characteristics of the delusions and hallucinations are often mood congruent (expansiveness, grandiosity, and euphoria). Therefore, a child experiencing mania may have delusions of being "superman" with special powers, of being able to fly and leap from high places. Conversely, the child may believe that he or she has special skills playing baseball, even though the child perhaps may have problems with gross motor skills and is clumsy and uncoordinated. Similarly, the child may hear voices, the content of which are mood congruent, with the altered state in mood (i.e., grandeur), and may believe that the voice is saying that he or she is superior and can do anything.

Brief Reactive Psychosis

Occasionally, children and adolescents suddenly develop psychotic symptoms that can last from a few hours or days. The child experiences these symptoms when under tremendous stress, such as after a death in the family, witnessed acts of violence or destruction, or physical or sexual abuse. The *acute psychotic symptoms* often resolve quickly, with total recovery in a few days. These youngsters may suddenly become disorganized, confused, agitated, or withdrawn. At times, their speech becomes nonsensical and incomprehensible. They may also experience delusions and hallucinations. These, too, are usually short-lived.

Anxiety Disorders

Children who experience *acute anxiety* or who have a history of maltreatment, abuse or neglect report significantly higher rates of psychotic symptoms when compared with controls (75). Several studies have documented psychotic-like symptoms in children with *posttraumatic stress disorder*. In such instances, the psychotic symptoms actually represent intrusive thoughts or worries regarding the traumatic event (73, 76,77). Mental status examination usually reveals the lack of a formal thought disorder, and the psychotic-like symptoms are more akin to derealization or depersonalization, as is often observed in traumatized children. Furthermore, there is often a qualitative difference in the way children with anxiety disorders and those with childhood-onset schizophrenia relate. The former have better-developed relationship and prosocial skills compared with the socially isolated, awkward, and odd behaviors of a child with schizophrenia. An identifiable traumatic event, abuse, or neglect in the child's history, in and of itself, does not necessarily rule out a psychotic disorder, because children with both schizophrenia and mood disorders may have had such experiences (73).

Organic Psychoses

Neurologic Conditions

Seizure Disorder

Children with *seizure disorders* can experience hallucinations as part of the seizure activity. Complex partial seizures, especially those with a temporal focus, may be associated with interictal psychotic symptoms of delusions, hallucinations, and unusual preoccupations. Caplan and co-workers described a formal thought disorder in children with partial complex seizures (78,79), although their way of defining thought disorder makes it intertwine closely with language organization deficits. However, they did emphasize that these epileptic children usually do not display negative symptoms such as those seen in schizophrenia. Hallucinations in children with epilepsy typically are brief. Therefore, these children experience mainly positive symptoms, which

are often short-lived. Caplan and co-workers also described a higher incidence of formal thought disorder in those children who have lower IQs, earlier onset of the seizure disorder, and poor seizure control. They postulated that these symptoms may either reflect the underlying neuropathology that produces the seizures or result from the ''kindling phenomenon'' as a secondary effect of the seizure activity.

Deteriorative Neurologic Disorders

Psychotic symptoms have been described in children who have a *deteriorative and degenerative neurologic disorders* such as subacute sclerosing panencephalitis (80). Other disorders include Wilson disease, lipid storage disorders, and Huntington chorea. These are usually differentiated from childhood-onset schizophrenia by the presence of neurologic findings on physical examination of the child, further corroborated by abnormal findings on laboratory testing. Children suffering from such neurologic deterioration often have a gradual, persistent, but global decline in their neurologic condition.

Central Nervous System Lesions

These conditions include brain tumors, congenital malformations, and head trauma.

Metabolic and Hormonal Disturbances

Various *metabolic and hormonal conditions* can be responsible for psychotic symptoms in children. Endocrinopathies may include disorders of the adrenal, thyroid, or parathyroid glands. Exogenous metabolic disturbances leading to psychotic symptoms can include exposure to heavy metals.

Toxic Psychoses

Toxic psychosis or delirium usually occurs secondary to bacterial or viral infections, high fevers, and exogenous toxins including medications, illicit drugs, alcohol, and poisonings. Unlike childhood schizophrenia or other psychotic disorders, in which impaired thinking and communication are the most salient symptoms, toxic psychosis is more likely to cause vivid, disturbing visual or tactile hallucinations and other perceptual problems. Auditory hallucinations can also occur, but their content is qualitatively different from those experienced in childhood schizophrenia or mood disorders. These sensory experiences may be extremely frightening and may be accompanied by agitation or by uncontrolled or even aggressive behaviors. Children and adolescents often describe the experience as ''losing their mind''—a frightening concept, and they can become disoriented, unable to orient to person or place, or comprehend why they are behaving in an unusual manner. They may also experience fluctuating levels of alertness.

In children, infections (bacterial or viral) can cause encephalitis, meningitis, and human immunodeficiency virus–related syndromes, which can result in delirious states. High fevers, regardless of origin, have been known to cause delirious states with perceptual disturbances. In addition, chronic liver and kidney disease may cause delirious states associated with psychotic symptoms in children, manifested by states of confusion, distortions in perceptions, and frank hallucinations.

The best example of medication-induced psychosis is that resulting from high doses of stimulants (the most commonly prescribed group of medications in this age group). In young children, normal doses of common medications, such as over-the-counter antihistamines and decongestants, can induce similar symptoms. Some of the other medications that can have a similar result are steroids, which can cause not only a disturbance in mood (depression and manic symptoms), but also delirium. Children prescribed anticholinergic drugs are also vulnerable to developing delirium, presenting with psychotic symptoms.

Other causes, especially in older children and adolescents, are alcohol intoxication, amphetamine-like drugs (''speed'' and cocaine), hallucinogenic drugs (LSD and psilocybin), solvents, and cannabis. Most children who develop drug-induced psychosis recover once the drugs are out of their system.

The psychotic symptoms sometimes experienced by patients after anesthesia should be included in the category of toxic psychoses. Although usually short-lived, this phenomenon is reported by patients to be a very frightening experience. Support, reassurance, and ensuring safety at the time are usually sufficient in the management of patients after anesthesia.

MANAGEMENT AND TREATMENT

Assessment

Effective treatment requires knowledge of the psychotic disorders, diagnostic criteria, symptoms, and longitudinal course, in addition to an understanding of the youngster's developmental, social, educational, and psychological needs. Treatment strategies therefore need to focus on the clinical symptoms and morbidity of the underlying disorder, while also addressing any comorbid disorders or biopsychosocial stressors. The physician must prioritize symptoms and diagnoses, so a reasonable treatment plan addresses multiple problems. A clinician examining a child for psychoses must first ascertain whether the child comprehends the clinician's question about delusions and hallucinations and whether the child endorses the psychotic symptoms only to please the interviewer or to get attention. In addition, it is important to determine whether the child acts on the basis of the delusional or hallucinatory perceptions—associated with an affective response of fear, dread, avoidance, or elation.

The assessment of the child with psychotic symptoms should include a careful, comprehensive, and thoughtful

evaluation. The history is often obtained from multiple informants, and several sessions may be required to gain accurate assessment of the child's mental status. The assessment should include a detailed evaluation of the symptom presentation, course of illness, and phenomenology. A developmental history of the child and a detailed family psychiatric history are invaluable components of the evaluation and assessment. A positive family history, especially for an affective disorder or schizophrenia because these disorders tend to run in families, often helps the clinician with the differential diagnosis in the child.

Once it is determined that the child is experiencing psychotic symptoms, it is important foremost to ascertain the cause of such symptoms. This will, in large part, determine the management and treatment of the child presenting with psychosis. A thorough physical examination is essential, and pertinent tests and procedures may be necessary, as clinically indicated. These may include imaging studies, an electroencephalogram, toxicology screens, and renal and liver function tests. Some children may require consultation with other pediatric specialists.

Psychological and projective testing are not indicated as a method of diagnosing specific disorders causing the psychosis. However, they can be helpful for intellectual assessment and to determine developmental delays, because these deficits may influence the presentation or interpretation of symptoms. Routine use of adaptive function measures is important for understanding actual function in social, daily living, and communication domains. These can be quite helpful in planning and maintaining developmentally relevant treatment goals. Similarly, speech and language evaluations are often helpful, especially with a child who appears to have linguistic impairments on examination.

Treatment

If it is deemed that the cause is organic, then the first step is to diagnose and treat the underling cause of the psychotic symptoms. This may include treating a partial complex seizure disorder, managing a metabolic imbalance, or treating an underlying infection or reducing a fever. Conversely, if it is determined that there is no medical cause for the psychotic symptoms, then the next step is to ascertain whether the psychosis is functional. If so, is it secondary to severe depression or acute mania with psychotic symptoms or secondary to a schizophrenic illness?

Adequate treatment requires a combination of pharmacotherapy and various psychosocial interventions that target the child's specific difficulties. Some of this depends on the phase of the underlying illness (81):

Stage 1 (prodromal phase): The child may experience some period of deteriorating function, which may include social isolation, idiosyncratic preoccupations and behaviors, and academic difficulties.

Stage 2 (acute phase): This is usually the time when the child comes to the attention of a mental health professional, when the clinical picture is dominated by frank delusions and hallucinations and other positive symptoms such as a formal thought disorder or strange and idiosyncratic behaviors.

Stage 3 (recovery phase): The symptoms usually begin to remit and dissipate. However, often there may still be the presence of some psychotic symptoms, although they are less disturbing to the child. In this phase, the child may continue to experience some levels of confusion, disorganization, or lability in mood.

Stage 4 (residual phase): The positive symptoms continue to subside, but the child continues to experience apathy, lack of motivation, withdrawal, and restricted or flat affect.

Unfortunately, some children remain symptomatic and chronically impaired, despite what would be considered adequate treatment. Usually, such impairment is characterized by persistent symptoms, which occur especially if the psychosis is secondary to a schizophrenic illness, rather than the result of depression or mania.

Psychosocial interventions should include working with both the parents and the child. Interventions targeted at improving family functioning, problem solving, communication skills, and relapse prevention have been shown to decrease relapse rates in adults (82). Children may benefit from social skills training and may require specialized educational programs, academic adjustments, and support at school. Ongoing illness teaching and medication education, are important to promote compliance with treatment and to help in coping with the daily and sometimes long-term implications of the child's illness. Every effort should be made for the child to be maintained in the least restrictive setting, such as home. However, in some cases, the severity and chronicity of the underlying illness may warrant long-term placement in a hospital or residential facility.

Pharmacotherapy is instituted in an attempt to treat the underlying cause of the psychosis, or for symptom control, in those children who have psychotic symptoms secondary to a known origin. Informed consent from the parents or guardian should be obtained before treatment with psychopharmacologic agents is instituted.

It is not in the purview of this chapter to discuss each medication in detail. For the treatment of major depression, the following antidepressants have been used in children:

Tricycle antidepressants (nortriptyline, imipramine, desipramine)

Selective serotonergic reuptake inhibitors (fluoxetine, paroxetine, sertraline, fluvoxamine, citalopram)

Nonselective serotonergic reuptake inhibitors (nefazodone, mirtazapine)

Monoamine oxidase inhibitors (phenelzine, tranylcypromine) (seldom used currently)

Others: bupropion, venlafaxine

Mood stabilizers that have been used for the treatment of manic-depressive illness in children include the following:

Anticonvulsants (divalproex sodium, carbamazepine, gabapentin)
Lithium

Often, the use of antipsychotic medications in addition to the use of antidepressants or mood stabilizers is indicated in functional psychosis.

If the suspicion is that of early-onset schizophrenia, then antipsychotics are first-line medications. Although children may metabolize neuroleptics more rapidly than adolescents and adults, optimum doses for children are typically less than those required in adolescents and adults.

First-line agents include traditional neuroleptic medications that block dopamine receptors or the atypical antipsychotic medications that have a variety of effects including antagonism of serotonergic receptors. The atypical antipsychotic medications are reported to be at least as effective for positive symptoms and may even be more helpful for negative symptoms. Further, there is some suggestion that they have fewer adverse effects. Except for clozapine, the novel agents also appear to produce tardive dyskinesia. Experience with novel antipsychotic agents is too scant to determine whether the risk of tardive dyskinesia is equal to or less than with the older antipsychotics. Newer antipsychotic medications that have been used in children are risperidone and olanzapine. They may be less sedating than the traditional neuroleptic agents such as haloperidol, fluphenazine, thioridazine, and chlorpromazine. There have been some case reports in the literature of the use of clozapine for children and adolescents with schizophrenia in whom normally adequate treatment with other traditional antipsychotic medications has failed.

For a child suffering from acute reactive psychosis, support and safety are the two primary considerations. If the child is extremely stressed and acutely ill, hospitalization may be necessary to provide a safe and structured environment. Brief treatment with antipsychotic mediations has often been effective for the alleviation of psychotic symptoms in some children. However, medications will not eliminate the problem that originally caused the brief psychosis. Thus, psychotherapy is often helpful in helping the child learn to cope with the emotional trauma that may have precipitated the episode.

Toxic psychosis requires immediate medical intervention to identify the cause and to provide appropriate treatment. Identifying the cause may include laboratory tests such as serum electrolytes, liver function tests, toxicology screens, blood alcohol level, serum levels of prescribed medications including theophylline, tricyclic antidepressants (nortriptyline, amitriptyline, imipramine, desipramine), or mood stabilizers (valproic acid, lithium, carbamazepine). Neuroleptics, because of their common usage, comprise another important group of medications that needs to be considered in the psychiatric population. The rare but possible development of *neuroleptic malignant syndrome,* manifesting as a disturbance of sensorium, fever, rigidity, and high blood pressure, should be considered. A history of treatment with neuroleptics and an elevated creatinine phosphokinase usually enable one to determine this cause (83). Most children who develop drug-induced psychosis recover once the drugs are discontinued and out of their system. The gravest danger occurs during the psychotic episode, when a child may cause serious harm to himself or herself or to others, because judgment is impaired. Some children may need brief hospitalization until the cause is determined and the psychotic symptoms dissipate. Except for the presence of neuroleptic malignant syndrome as the cause, brief treatment with antipsychotic medications may be necessary to decrease the child's agitation and to control the distorted perceptions.

In addition to the foregoing treatment strategies, other interventions and services may be needed to address either comorbid conditions or associated sequelae of the underlying disorder causing the psychosis, such as substance abuse, depression, and suicidal tendencies.

CONCLUSIONS

From the clinical perspective, the rapid change and development of childhood have immediate implications for diagnosis and intervention. When one is treating children, it is important to maintain diagnostic fluidity and to tolerate the pressure of uncertainty.

In the realm of childhood-onset psychopathology, we have a great deal to learn from the psychoses. The stability of a diagnostic category over time is usually considered to be one measure of the construct validity of that category. One possibility is that lack of stability of a diagnosis during childhood implies that it lacks validity. This is only important if one is trying to establish a unique direct link with later-onset disorders and to apply the same terminology. However, another possibility is that some childhood diagnoses are only risk factors for development of more enduring adult conditions, such as the relationship between conduct disorder and antisocial personality disorder. Variability of normal and psychopathologic development and the heavy influence of environmental features and familial functioning during childhood make it difficult to be certain about diagnoses in children. Although categoric classification has its advantages and at times is necessary (34), dimensional perspectives can be important for understanding these phenomena as well.

It is useful to recognize the close, reciprocal relationship between diagnostic classification and biological or genetic advances. Advances in genetic and imaging studies should open the way to a different classification system that links

symptoms, neural circuitry, and biological (genetic) markers more closely than any current system. We should not be too surprised to discover that conditions once considered to be quite distinct are now closely linked, as has been found for Tourette syndrome, obsessive-compulsive disorder, and attention-deficit/hyperactivity disorder (84). ''Diagnostic stability'' may refer to the stability of these biological features, rather than the stability of clinical signs and symptoms. One could expect that developments in molecular biology would shed light on the natural history, protective factors, and risk factors for a specific biological risk. However, these developments will depend on increasingly reliable, reproducible diagnoses. The success of these strategies demands that probands or cohorts have been reliably diagnosed according to the most valid criteria at the time. Thus, the diagnoses inform the biological work, and the biological work, in turn, influences our classification and criteria. This process fosters a more accurate understanding of the natural history, pathophysiology, and etiology of disorders and the relationships among disorders. It will inform us about prenatal psychoneurohormonal factors that influence development, sexual differentiation, and maturation of the central nervous system. In time, we stand to gain a much clearer understanding of the complex, diverse contributions to the development and maintenance of psychotic disorders. We look forward to developing treatments that will offer more comfort and better functioning to the patients and families afflicted with these chronic conditions. There is, in addition, a real prospect of finding protective factors and preventive interventions that can avert the worst manifestations of these disorders.

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