The Prodromal Phase of First-Episode Psychosis: Past and Current Conceptualizations

by Alison R. Yung and Patrick D. McGorry

Abstract

The initial prodrome in psychosis is potentially important for early intervention, identification of biological markers, and understanding the process of becoming psychotic. This article reviews the previous literature on prodrome, including descriptions of symptoms and signs, and patterns and durations of prodromes in both schizophrenic and affective psychoses. Early detailed descriptions, achieved through mainly anecdotal reports, are compared with current conceptualizations, such as the *DSM–III–R* checklist of mainly behavioral items, which seeks to enhance reliability of measurement but at the expense of adequately describing the full range of phenomena. Current confusion about the nature of prodromal features and concerns regarding the reliability of their measurement are highlighted. This article proposes an alternative model for conceptualizing prodromal changes (the hybrid/interactive model) and discusses the different ways to view this phase. The need for a more systematic evaluation of the prodromal phase in first-episode psychosis is emphasized.

Schizophrenia Bulletin, 22(2): 353–370, 1996.

Defining the Term "Prodrome"

The term "prodrome" is derived from the Greek word *prodromos* meaning the forerunner of an event (Fava and Kellner 1991). In clinical medicine, a prodrome refers to the early symptoms and signs of an illness that precede the characteristic manifestations of the acute, fully developed illness. For example, measles is described as having a prodrome of 3 to 4 days characterized by fever, coryzal symptoms, conjunctivitis, and cough. This is followed by the specific rash, making definitive diagnosis possible (Yung and Stanley 1989). Prodrome in psychotic disorders is similarly defined. For example, Keith and Matthews (1991) defined it as "a heterogeneous group of behaviors temporally related to the onset of psychosis" (p. 53). The definition used by Loebel et al. (1992) was the time interval from onset of unusual behavioral symptoms to onset of psychotic symptoms. And Beiser et al. (1993) defined it as the period from first noticeable symptoms to first prominent psychotic symptoms. Essentially, the term refers to a period of prepsychotic disturbance, representing a deviation from a person's previous experience and behavior. As in clinical medicine, prodrome is a retrospective concept, diagnosed only after the development of definitive symptoms and signs.

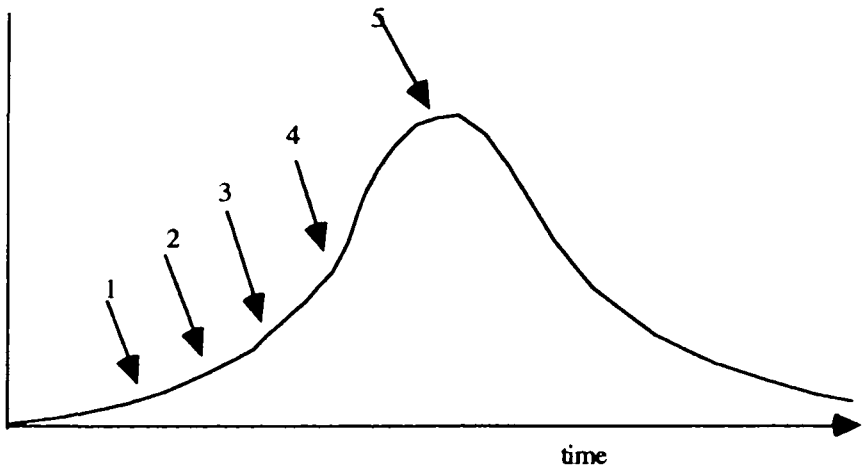
The term "prodrome" has been used by some authors to denote the prepsychotic period before a relapse in those patients with established psychotic illnesses (Herz and Melville 1980; Birchwood et al. 1989; Malla and Norman 1994). This "relapse prodrome" should be distinguished from the prepsychotic period preceding the first onset of a psychotic illness, the "initial pro-

Reprint requests should be sent to Dr. A.R. Yung, Early Psychosis Prevention and Intervention Centre, 35 Poplar Rd., Parkville, Victoria 3052, Australia.

drome." In this article, the term "prodrome" is sometimes used instead of the longer "initial prodrome."

Initial prodrome is defined as the period of time from the first change in a person until development of the first frank psychotic symptoms. Figure 1 illustrates some of the difficulties with accurately defining this period of time. The y-axis represents the severity of symptoms or change in functioning of a hypothetical patient who has developed a psychosis and then recovered. The x-axis shows the time scale. The arrows indicate points of change as noted by the patient or informants:

Figure 1. Development of psychosis over time, with arrows indicating points of change noted by the patient or informants



Arrow points: 1 = patient first notices some change in self, 2 = family or friends first notice some change in patient, 3 = patient first notices psychotic symptoms in self, 4 = family or friends first notice psychotic symptoms in patient, 5 = first psychotic intervention. See text for amplification.

Arrow 1 indicates the point when the patient first noticed some change in himself, but not symptoms that would be called psychotic. For example, he may have noticed that he was not coping with stress as well as he usually would or may have noticed vague depressive feelings or uneasiness; he may remember feeling more disinhibited and saying what he was thinking more often. Changes may have been subtle, so that only the person and not his acquaintances noticed.

Arrow 2 indicates the point when the patient's family or friends noticed some change in the person, but not changes indicative of frank psychosis. For example, they may have found him more moody or irritable, anxious, or doing some things out of character, such as spending a lot of money. They may have put it down to "a phase he was going through" (particularly in the case of adolescents) or thought it was worries at work.

Arrow 3 indicates the point when the patient first noticed changes that would be described as psychotic. For example, he might describe having heard voices or having had the belief that external agencies were controlling his mind.

Arrow 4 indicates the point when the family or others first noticed changes that are attributed to psychosis, such as the patient accusing others of reading his mind or claiming to have great powers.

Arrow 5 indicates the point of first psychiatric intervention, such as community team involvement or admission into a hospital. The symptom severity then decreased following effective intervention.

This is of course a hypothetical sequence, and in a given individual, informants may note changes in the patient before the patient does.

So, what defines the prodrome? In this hypothetical case, it could be defined as the time period between Arrow 1 and Arrow 3, using the patient's information. It could also be defined as the period between Arrow 2 and Arrow 4, using the informants' information. Alternatively a combination of information could be used, for instance defining the prodrome as being between Arrow 1 and Arrow 4. This consensus method was used by Loebel et al. (1992):

> First we asked patients and their family members when the patient (or the family member) first experienced (or noticed) behavioral changes which, in retrospect, appear to have been related to the patient's becoming ill. Second, after explaining psychosis in clear language, we asked when the patient (or the family member) first experienced (or noticed) psychotic symptoms. When differences be-

> tween patients' and family members' responses occurred, a consensus decision was made by the research staff. [p. 1184]

In essence, the prodrome is the period between the most valid estimates of the onset of change in the person and the onset of psychosis.

The points represented by these arrows are rough estimates of times as given by the patient or his family (or friends) in retrospect. They are not discrete points but represent periods of days or weeks, or sometimes even months. Changes generally occur gradually, and the point of departure from the patient's normal level of functioning (Arrow 1 or 2)—the *onset* of the prodrome—may be difficult to pinpoint for both patient and informant. The point when changes could be called "psychotic" (Arrow 3 or 4)—the *offset* of the prodrome and onset of psychosis—may also be difficult to accurately define. The boundary between "different but not psychotic" (or "prepsychotic") and "frankly psychotic" is blurred.

Because of the retrospectivity inherent in the prodrome concept, the accuracy of recall is an issue. Recall may be affected by a long delay between changes first occurring and obvious psychotic symptoms developing (Fava and Kellner 1991). It may also be influenced by "effort after meaning," which refers to patients and families looking for an event that seemed to start all the changes and dating their histories from that point (Tennant 1985; Henderson 1988; Fava and Kellner 1991; Hirsch et al. 1992). This scenario may not be how things actually evolved. Other factors can also affect accuracy of recall, such as family guilt at not having noticed changes earlier or not having taken action sooner. The family may not have noticed any changes at all until the signs of obvious psychosis were apparent. In addition, when the patient is asked to reflect on his or her experience, the mental state of the patient at the time of interview will affect what is revealed or remembered. The degree of "sealing over" similarly will influence what is recalled (Levy et al. 1975; McGlashan et al. 1975). The patient may not wish to recall this period of his or her life; the family may feel the same. In other words, the coping style of both patients and informants will affect a retrospective description of the prodrome.

Significance of the Prodrome

The psychotic prodrome is potentially important for early diagnosis and management of psychotic disorders, early detection of relapse, prospective studies of high-risk individuals, and prognosis.

Early Diagnosis and Management of Psychotic Disorders. The importance of early detection and treatment of psychotic disorders has been raised in psychiatric literature for some time. Cameron wrote of the need for a preventive approach to schizophrenia (Cameron 1938). He called for "the detection of very early disorder to prevent later serious ill health" (p. 574). More recent authors have also stressed the need for early diagnosis and management in schizophrenia to reduce or prevent the psychological and social disruption that results from psychosis (Falloon 1992; Birchwood and MacMillan 1993).

Delay in treatment of the first episode is a major problem and is associated with poorer outcome. The Northwick Park Study of 253 first-episode patients (Johnstone et al. 1986) found that 26 percent of patients took more than 1 year to get effective treatment. Those taking longer than 1 year to access services revealed a higher relapse rate over the following 2 years than those with a briefer duration of untreated illness. Another study (Loebel et al. 1992) found a mean duration of 52 weeks of psychotic symptoms before initial treatment in a sample of first-episode psychosis patients. It also found poorer outcome associated with such treatment delay: longer illness duration before treatment was associated with longer time to remission of symptoms and a lesser degree of remission.

The connection between the delay in treatment of first-episode psychosis and poorer outcome is understandable. The process of becoming psychotic creates profound psychological changes, almost always disturbing to the patient (Bowers 1965, 1968; Bowers and Freedman 1966; Stein 1967). As well as being frightening and difficult to comprehend, these experiences isolate the person from others. The consequent disruption of social networks, including family and peer relationships and schoolwork and occupation functioning, can be devastating. The timing of onset of psychosis is usually in adolescence or young adulthood, when personality development and identity issues are still being resolved. Deviant behavior during this period of untreated, unrecognized, and misunderstood psychosis may cause potentially life-threatening crises

(Loebel et al. 1992) such as aggressive and suicidal behavior. Increased use of substances may also occur at this time. Effects are felt not only by the individual but by the family as well. Not surprisingly, the Northwick Park Study found that long treatment delay was associated with family difficulties (Johnstone et al. 1986). A theory of toxic effect of psychosis on the brain via pathophysiological changes in nervous tissue has also been suggested (Lieberman et al. 1990; Wyatt 1991).

Clearly, minimizing the delay between onset of psychosis and treatment can reduce this psychological, social, and possibly biological disruption. Intervention at the time of emerging psychosis may also be possible. A detailed characterization of the symptoms and signs of initial psychotic prodrome and a study of the evolution of prodromal symptoms to psychotic symptoms are necessary for early diagnosis and intervention. In particular, specific symptoms heralding a psychotic episode need to be identified.

Early Diagnosis of Relapse. Early diagnosis of psychotic relapse is another area where a detailed knowledge of prodrome could be important. Several researchers have commented on the stability of patterns of prodromal symptoms indicating impending relapse in individual patients (Herz and Melville 1980; Heinrichs and Carpenter 1985; Molnar et al. 1988; Birchwood et al. 1989; Birchwood 1992). The identification of the same sequential pattern of symptoms in patients each time they relapse, termed "relapse signature" (Birchwood 1992), would be of great importance to the psychiatrist planning a treatment strategy. The pattern holds implications for targeting medication and psychoeducation for both families and patients. The idea of relapse signature, however, has not been examined critically in relation to prodromal symptoms occurring early in the course of illness. For example, it is not known whether the prodrome of the relapse resembles the prodrome that preceded the first episode of psychosis or not. One avenue of study would be to accurately describe first prodromes in a series of patients and then follow up to determine if relapse prodromes (if in fact the patients do relapse) are similar. If specific features heralding the imminent onset of psychosis could be identified, then opportunity for early treatment exists.

Development of Neurobiological and Phenomenological Theories of Psychosis. More accurate characterization of the prodrome can help identify high-risk individuals when they first manifest subtle changes in mental state suggestive of impending psychosis. Such people could then be studied with neuropsychological and biological investigations to identify any abnormalities in these areas before the development of acute psychotic symptoms. The results will aid the investigation into the pathogenesis of psychosis and the definition of markers to predict psychosis. In addition, detailed study on the subjective experiences leading to psychosis can map the evolution of psychotic symptoms from preceding, nonpsychotic symptoms, leading to theories about the development of psychotic symptoms such as delusions. Further study could identify primary and secondary abnormalities. Much has been written on the process of delusion formation. A recent review of the literature (Roberts 1992) revealed a need for more systematic data collection and methodologically sound investigation of the issue.

Prognostic Significance. The presence and duration of prodromal symptoms may predict outcome in schizophrenia, that is, long duration of prodromal symptoms may be indicative of poor prognosis (Chapman et al. 1961; Vaillant 1962, 1964*a*, 1964*b*; Fenton and McGlashan 1987). This connection has led to various hypotheses about subtypes of schizophrenia (e.g., process and reactive) with differing prognoses (Langfeldt 1969). The accurate characterization of prodrome therefore has diagnostic and prognostic significance.

There is growing interest in researching first-episode psychosis (Kirch et al. 1992; Lieberman et al. 1992) and an increasing emphasis on early intervention and prevention of psychotic disorders (Birchwood and MacMillan 1993; McGorry and Singh 1995). Following is a review of the available literature on the initial prodrome in psychosis, examining current knowledge of this phase's symptoms and signs, patterns of change over time, and duration and considering ways the prodrome may be conceptualized.

Past Conceptualizations of Psychotic Prodrome

Diagnoses are considerably unstable from a first episode of psychosis to subsequent episodes in those patients who do relapse

(McGorry 1994). Therefore, descriptions of prodromes in both schizophrenic and affective psychoses require examination. However, many authors discussed prodrome in relation to either schizophrenia or affective psychoses, rather than considering all psychotic disorders as a whole. Thus, the following review is divided along diagnostic lines also, beginning with a consideration of the literature on prodrome in schizophrenia, which forms the bulk of previous work, and then on prodrome in affective psychoses.

Prodrome in Schizophrenia.

Methodologies and phenomena described. Methodologies employed in the past to investigate the prodromal phase of schizophrenia include the following:

1. *Detailed, retrospective reconstruction from patient and information interviews and other information sources of changes from the patient's previous personality, through the first prodromal symptoms to frank psychosis.* This method was used by Bleuler (1911/1950), Kraepelin (1919/1921); Conrad (1958), Meares (1959), Bowers (Bowers and Freedman 1966, Bowers 1968), Stein (1967), Fish (1976), Docherty (Docherty et al. 1978), Huber (Huber et al. 1980), and more recently Häfner's groups (Häfner et al. 1992*a*, 1992*b*, 1993, 1994; Hambrecht et al. 1994), and Beiser (Beiser et al. 1993). Patients are interviewed after recovery from psychosis, but with variable lengths of time between the psychosis and the interview. Problems of recall and effort after meaning arise and are particularly exacerbated by the variable time interval between the prodrome and the interview. The Häfner studies used an instrument designed for the systematic collection of data on onset features (Häfner et al. 1992*a*) and are the most methodologically sound studies of this retrospective type.

2. *Interviews with patients in the early stages of psychosis.* Patients are able to describe their symptoms and experiences as they are occurring and for only a short time after the prodrome. One disadvantage is that patients are psychotic at the time of interview, which may affect the procedure and what is recalled. In examples of this method, Chapman et al. (1959), McGhie and Chapman (1961), Chapman (1966), and Varsamis and Adamson (1971) interviewed patients with early and recently diagnosed schizophrenia and obtained collateral information from relatives and friends. Freedman and Chapman (1973) developed a structured interview schedule for patients with early and recently diagnosed schizophrenia. This study was narrow, describing mainly the subjective experience of patients and not observable signs such as deterioration in role functioning and social withdrawal.

3. *In-depth observations of a small number of patients during the development of a psychosis.* This method has the advantage of prospectivity, allowing observation and recording of changes in the individual as they happen. However, it is not possible to predict with any reasonable degree of accuracy who will develop a psychosis, and thus it is difficult to know which individuals to study prospectively. Studies of high-risk individuals, such as children of psychotic parents, have low numbers of cases developing psychotic disorders and are therefore costly (Walker 1991; Häfner et al. 1992*a*). Studies of this type are few and fortuitous, including Pious (1961)—who performed a longitudinal, prospective observation of a patient, initially referred to him for a neurotic illness, who developed schizophrenia—and autobiographical accounts about the experience of developing a psychosis (Anonymous 1950; Bowers 1965).

4. *Using relapse prodrome as a model for the prodrome preceding first psychotic episode.* Generally, the relapse prodrome area has been investigated with a view to early intervention in psychotic relapse. However, some authors (Docherty et al. 1978; Cutting 1985; Keith and Matthews 1991) have inferred that relapse prodromes are the same as initial psychotic prodromes. It has not been established how the signs and symptoms of a relapse prodrome in schizophrenia relate to the prodromal features of a first psychotic episode. Some symptoms may be modified by medication, the fear of relapse and hospitalization, or the family's changing perception of the patient. In fact, in Donlon and Blacker's study (1973), concern about the possibility of relapse is mentioned early as a symptom in patients taken off maintenance medication and observed. Examples of use of this method include Docherty et al. (1978), who reviewed nursing notes on 2 patients with histories of schizophrenia who relapsed while in the hospital; Herz and Melville (1980), who used retrospective interviewing of patients and families regarding symptoms and signs leading up to psychotic relapse in patients with histories of schizophrenia; and a prospective study done by Donlon and Blacker (1973) who took schiz-

ophrenia patients off medication and recorded subjective symptoms and behavioral changes as they relapsed. Other prospective studies include Heinrichs and Carpenter (1985), Subotnik and Nuechterlein (1988), Birchwood (Birchwood et al. 1989; Birchwood 1992), and Tarrier et al. (1991).

In summary, previous works on the initial psychotic prodrome (in contrast to relapse prodrome) are largely anecdotal in nature. The most methodologically sound studies focus on describing the range of prodromal features, those of Varsamis and Adamson (1971), Häfner et al. (1992*a*, 1992*b*, 1993, 1994), and Hambrecht et al. (1994). Ranking frequency of symptoms described in these first-episode studies showed the same phenomena reported consistently. These features are shown in table 1 in descending order of frequency and are notably nonspecific. Table 2 summarizes the subjective symptoms and observable behavioral changes described in the literature as occurring during the prodromal phase of schizophrenia. Some of these studies do not describe the range of phenomena, but comment on the presence of certain features (Offenkrantz 1962; Bowers and Freedman 1966) or focus on only one aspect of the prodrome, such as subjective experiences (Offenkrantz 1962; Bowers and Freedman 1966; Stein 1967; Freedman and Chapman 1973).

Table 1. Prodromal features in first-episode psychosis most commonly described in first-episode studies (in descending order of frequency)

Reduced concentration, attention
Reduced drive and motivation, anergia
Depressed mood
Sleep disturbance
Anxiety
Social withdrawal
Suspiciousness
Deterioration in role functioning
Irritability

Patterns of changes. In addition to the range of subjective symptoms and observable behavioral changes in the schizophrenic prodrome, the sequence of such changes over time is also important. The prodrome is a process, involving changes in experiences and behavior over time, rather than a simple list of symptoms at any one point (Bleuler 1911/1950; Kraepelin 1919/1921; Conrad 1958; Meares 1959; Bowers and Freedman 1966; Chapman 1966; Kubie 1967; Stein 1967; Bowers 1968; Varsamis and Adamson 1971; Donlon and Blacker 1973; Fish 1976; Docherty et al. 1978; Huber et al. 1980; Häfner et al. 1992*a*; Hambrecht et al. 1994). Docherty et al. (1978) described the process as "a moment to moment march of psychological changes" (p. 420). Previous authors have generally fallen into two schools of thought, or variations of them, regarding the sequence of changes that leads to psychosis.

Pattern 1: Nonspecific changes, followed by specific prepsychotic symptoms, then psychosis. Most authors consider the prodrome to consist of nonspecific neurotic-type symptoms, followed by more marked deviations from normal, eventually leading to frank psychosis (see figure 2) (Cameron 1938; Meares 1959; Kubie 1967; Stein 1967; Bowers 1968; Donlon and Blacker 1973; Docherty et al. 1978; Herz and Melville 1980; Cutting 1985; Heinrichs and Carpenter 1985). Subjective symptoms are usually accompanied by some deterioration in role functioning and other behavioral changes. Cameron (1938) described two patterns of nonspecific changes in the schizophrenic prodrome: "changes of hypofunction" and "changes of hyperfunction." The hypofunction pattern is characterized by seclusive, quiet, and withdrawn behavior. The hyperfunction pattern is characterized by complaints of nervousness, restlessness, tenseness, unease, apprehension, and anxiety. Cameron described these nonspecific symptoms as lasting weeks to years before the onset of the "specific" symptoms heralding impending psychosis. These are "symptoms of a clinically recognizable schizophrenic nature" (p. 569) and consist of suspiciousness, feelings ". . . that their external environment had lost its feeling of familiarity," and feeling "dazed" or "confused" (p. 570). These symptoms would seem to be attenuated forms of frank psychotic phenomena. Cameron believed that these early specific changes often persisted for months to years before the person came to the attention of psychiatric services.

Pattern 2: Early specific changes, with neurotic symptoms as a reaction to these, then psychosis. Chapman suggested an alternative view on the pattern of changes (McGhie and Chapman 1961; Chapman 1966). His theory is that specific subjective changes occur first and are followed by apparent neurotic symptoms and behavioral change (see figure 3). Chapman's putative phenomena consist of the following:

Table 2. Studies of prodromal symptoms and signs in schizophrenia

Symptoms and sign in the prodrome	Described by
"Neurotic" symptoms	
Anxiety	Cameron (1938), Meares (1959), Bowers and Freedman (1966), Chapman (1966), Varsamis and Adamson (1971), Donlon and Blacker (1973),[1] Fish (1976), Docherty et al. (1978),[1] Herz and Melville (1980),[1] Huber et al. (1980),[1] Heinrichs and Carpenter (1985),[1] Subotnik and Nuechterlein (1988),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Restlessness	Chapman (1966), Fish (1976), Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Anger, irritability	Bleuler (1911/1950), Cameron (1938), Chapman (1966), Varsamis and Adamson (1971), Docherty et al. (1978),[1] Heinrichs and Carpenter (1985),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Mood-related symptoms	
Depression	Cameron (1938), Conrad (1958), Chapman (1966), Varsamis and Adamson (1971), Donlon and Blacker (1973),[1] Fish (1976), Herz and Melville (1980),[1] Huber et al. (1980), Heinrichs and Carpenter (1985),[1] Subotnik and Nuechterlein (1988),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Anhedonia	Chapman (1966), Fish (1976), Docherty et al. (1978),[1] Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Guilt	Cameron (1938), Subotnik and Nuechterlein (1988),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Suicidal ideas	Chapman (1966), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Mood swings	Cameron (1938), Bowers and Freedman (1966), Bowers (1968)
Changes in volition	
Apathy, loss of drive	Cameron (1938), Chapman (1966), Varsamis and Adamson (1971), Docherty et al. (1978),[1] Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Boredom, loss of interest	Cameron (1938), Chapman (1966), Docherty et al. (1978),[1] Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Fatigue, loss of energy	Cameron (1938), Docherty et al. (1978),[1] Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Cognitive changes	
Disturbance of attention, inability to concentrate	Cameron (1938), Chapman (1966), Varsamis and Adamson (1971), Donlon and Blacker (1973),[1] Fish (1976), Herz and Melville (1980),[1] Huber et al. (1980), Heinrichs and Carpenter (1985),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Preoccupation, daydreaming	Cameron (1938), Chapman (1966), Herz and Melville (1980),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Thought blocking	Bleuler (1911/1950), Kraepelin (1919/1921), Pious (1961), Chapman (1966)

Table 2. Studies of prodromal symptoms and signs in schizophrenia—*Continued*

Symptoms and signs in the prodrome	Described by
Reduced abstraction	Meares (1959)
Physical symptoms	
Somatic complaints	Bleuler (1911/1950), Cameron (1938), Meares (1959), Offenkrantz (1962), Chapman (1966), Varsamis and Adamson (1971), Donlon and Blacker (1973),[1] Fish (1976), Herz and Melville (1980),[1] Huber et al. (1980), Heinrichs and Carpenter (1985),[1] Subotnik and Nuechterlein (1988),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Loss of weight	Birchwood et al. (1989)[1]
Poor appetite	Cameron (1938), Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Sleep disturbance	Cameron (1938), Bowers and Freedman (1966), Bowers (1968), Donlon and Blacker (1973),[1] Huber et al. (1980), Heinrichs and Carpenter (1985),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Other symptoms	
Obsessive compulsive phenomena	Bleuler (1911/1950), Pious (1961), Chapman (1966), Donlon and Blacker (1973),[1] Docherty et al. (1978),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Dissociative phenomena	Docherty et al. (1978)[1]
Increased interpersonal sensitivity	Subotnik and Nuechterlein (1988),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Change in sense of self, others, or the world	Cameron (1938), Meares (1959), Bowers and Freedman (1966), Chapman (1966), Stein (1967), Bowers (1968), Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Change in motility	Meares (1959), Pious (1961), Chapman (1966), Donlon and Blacker (1973),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Speech abnormalities	Chapman (1966), Cutting (1985), Häfner et al. (1992*a*), Hambrecht et al. (1994)
Perceptual abnormalities	Pious (1961), Bowers and Freedman (1966), Chapman (1966), Bowers (1968), Varsamis and Adamson (1971), Huber et al. (1980), Cutting (1985), Subotnik and Nuechterlein (1988),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Suspiciousness	Conrad (1958), Stein (1967), Varsamis and Adamson (1971), Heinrichs and Carpenter (1985),[1] Subotnik and Nuechterlein (1988),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Change in affect	Meares (1959), Varsamis and Adamson (1971)
Behavioral changes	
Deterioration in school, work, or other role functioning	Bleuler (1911/1950), Kraepelin (1919/1921), Chapman (1966), Varsamis and Adamson (1971), Huber et al. (1980), Häfner et al. (1992*a*), Hambrecht et al. (1994)

Table 2. Studies of prodromal symptoms and signs in schizophrenia—*Continued*

Symptoms and signs in the prodrome	Described by
Social withdrawal	Cameron (1938), Meares (1959), Chapman (1966), Donlon and Blacker (1973),[1] Docherty et al. (1978),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)
Impulsivity	Docherty et al. (1978)[1]
Odd behavior	Conrad (1958), Meares (1959), Birchwood et al. (1989)[1]
Aggressive, disruptive behavior	Cameron (1938), Meares (1959), Varsamis and Adamson (1971), Heinrichs and Carpenter (1985),[1] Subotnik and Nuechterlein (1988),[1] Birchwood et al. (1989),[1] Häfner et al. (1992*a*), Hambrecht et al. (1994)

[1]Investigated relapse prodromes only.

1. Disturbances in attention. Chapman saw this as a fundamental symptom in early schizophrenia and the underlying mechanism for some subsequent symptoms and behaviors. The chief abnormality in attention was the inability to filter out irrelevant stimuli, a disturbance of the ability to *selectively* attend to information. The patient is distracted by multiple events and feels overwhelmed, resulting in information overload and finally a total disruption in attention.

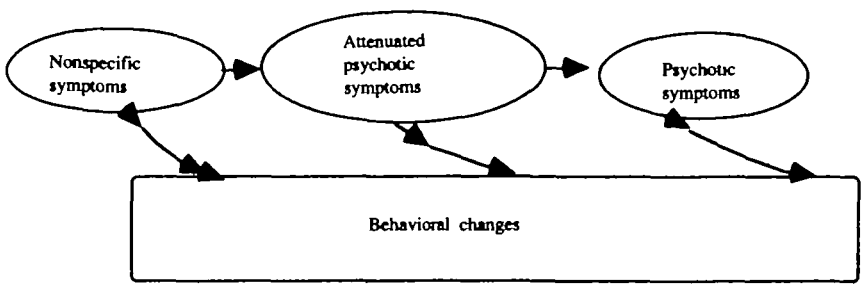
2. Disturbances in perception. Chapman described these as intermittent, transient, but occasionally severe. Included were abnormalities in visual perception, such as seeing objects as altered in size, shape, color, brightness, movement, and distance away from the observer. He also described the patient's inability in some cases to perceive objects as a whole, being diverted to inspecting parts of the whole instead, resulting in an inability to see the overall Gestalt of the image—which relates back to the disorder of selective attention.

3. Blocking phenomena. This term refers to sudden disruptions in attention, thought, perception, memory, speech, and motility. The patient is aware of intermittent "blank spells" or "trances," which have also has been described by other investigators (see table 2). These blocking phenomena may be caused by defects in selective attention. As the patient becomes more and more distracted by multiple sensory experiences, he would then switch suddenly to being unable to attend at all. With increasing volumes of information that he is unable to process, the patient finally reaches a point where his consciousness is disturbed.

4. Disturbances in speech production. These are described as intermittent and include disturbances in the production of speech as well as in the ability to understand speech. They are secondary to a disorder of selective attention.

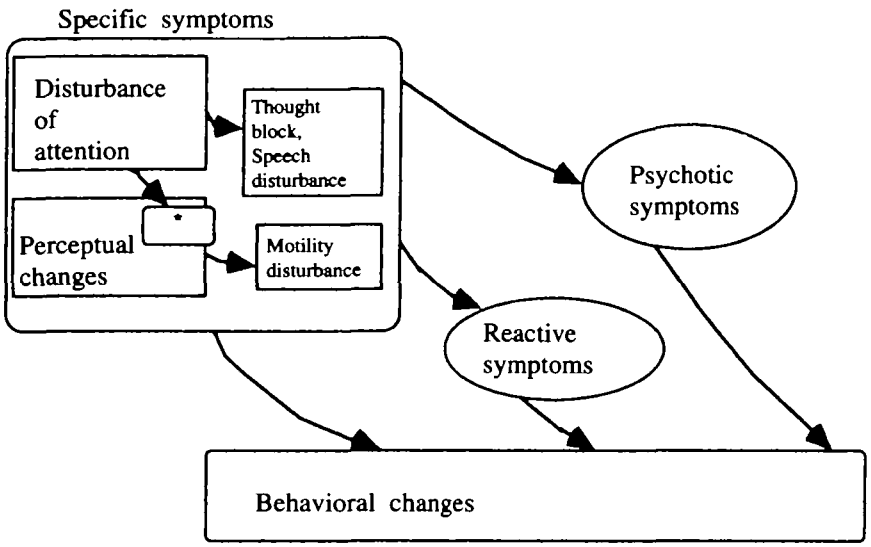
5. Disturbances in motor function. This includes loss of spontaneous movements and coordination. Disorders of motility are

Figure 2. Pattern 1 model of prodromal changes



Nonspecific changes occur first, followed by more frank deviations from normal that are precursors to psychosis. Behavioral changes can result from nonspecific prodromal symptoms, attenuated psychotic symptoms, and psychotic symptoms themselves.

Figure 3. Pattern 2 model of prodromal changes



Specific changes in attention and perception occur primarily. Some perceptual changes also occur secondary to attention disturbance (*). Attention and perceptual changes lead to the other specific features of changes in speech and motility and thought block. Specific symptoms precede psychosis and are accompanied by nonspecific reactive symptoms. Behavioral changes can result from specific prodromal symptoms, nonspecific prodromal symptoms, and psychotic symptoms themselves.

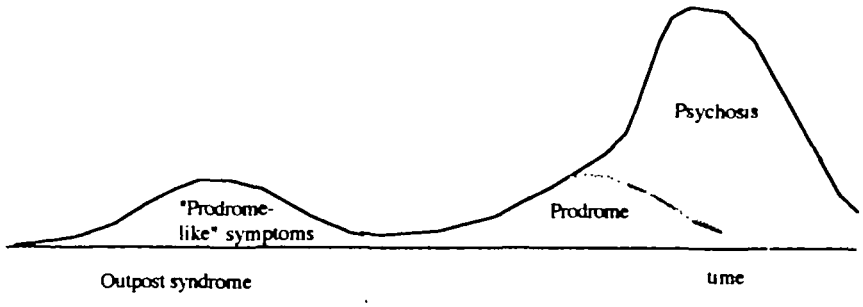
secondary to disturbances of both attention and perception, for example, having to stop moving because of certain visual or auditory sensations. "Motility and perceptions are intimately linked, motility being dependent upon the stability of the perceptual field" (McGhie and Chapman 1961, p. 107).

Chapman felt that patients may experience disturbances of attention, perception, thought, speech, and motility subjectively before signs of established disease appear overtly and long before the patient actually complains to others of symptoms. To support this contention, he compiled the symptoms that each patient first reported to his or her doctor or that were first noticed by relatives. He found "every kind of neurotic symptom." Anxiety was almost invariable and depression also common. When Chapman compared this information with data on patients' subjective experiences, he concluded that these neurotic symptoms *followed* subjective changes and were but superficial indications of disturbance in the patient, essentially reactions to the underlying primary disturbances of attention and perception. He suggested that many delusions similarly arose from preexisting disturbances in cognition and perception and served as a way for patients to explain the phenomena they were experiencing. Malla and Norman (1994) have also suggested that nonpsychotic prodromal symptoms such as depression and anxiety may actually be reactions to early, but often hidden, psychotic symptoms.

Outpost syndromes. These are a variant of the patterns of change in the evolution of psychosis. Outpost syndromes are clusters of symptoms and behaviors that cross-sectionally appear to resemble prodromes but that resolve spontaneously without immediately progressing to psychosis (see figure 4) (Huber et al. 1980). Such episodes were described by Huber (Huber et al. 1980), Koehler and Sauer (1984), and Conrad (1958). Huber et al. described the symptomatology of outpost syndromes as resembling a defect or residual state in chronic schizophrenia and coined the term "basic symptoms" for such phenomena. The basic symptoms have been summarized in a article by Koehler and Sauer (1984) and consist of subjective complaints of impairments in cognitive, emotional, motor, and autonomic functioning, as well as in bodily sensation, energy, external perception, and tolerance to normal stress. The concept of an outpost syndrome is illustrated in figure 4.

The hybrid/interactive model. Instead of following one certain pattern of changes, psychotic prodromes can be a combination of patterns 1 and 2 above and also incorporate the outpost syndrome. In this hybrid/interactive model (see figure 5), people move in and out of symptomatic periods of both the nonspecific type and the attenuated psychosis type. Both types of symptoms may precede psychosis, and either may occur primarily. Reactive symptoms, such

Figure 4. Outpost syndrome model of prodromal changes



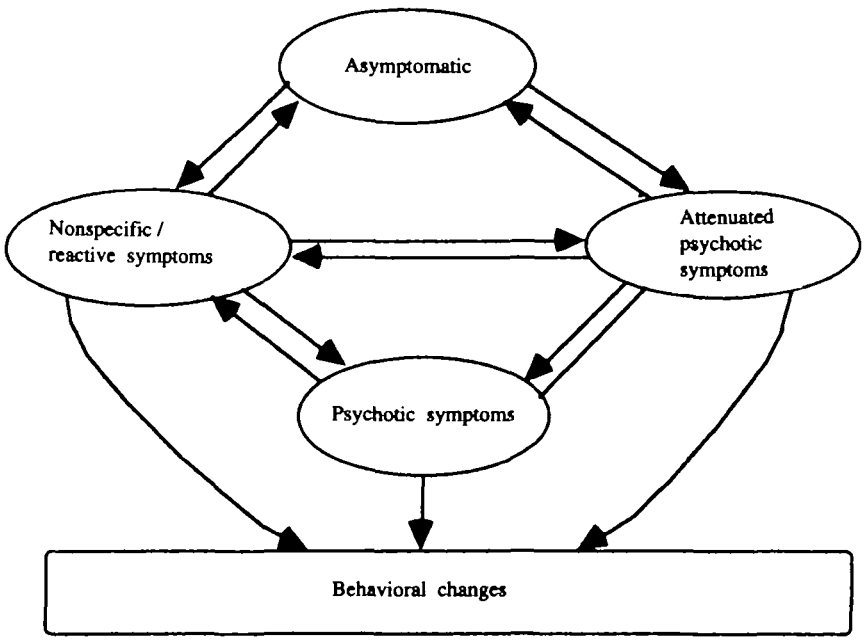
An outpost syndrome may resemble a prodrome cross-sectionally but does not proceed to psychosis.

as anxiety, can occur in response to prodromal and psychotic symptoms, and behavioral changes may occur in response to any of these symptoms.

Duration of the schizophrenic prodrome. Conrad (1958) reported that virtually all patients experience a prodromal phase, which varies in duration from a very brief period to several years. Findings of Varsamis and Adamson (1971) were not as absolute regarding the invariable presence of a prodrome, more in keeping with Cameron's report that 17 of his 100 patients had experienced no premonitory symptoms at all (Cameron 1938). Varsamis and Adamson (1971) found a tendency for the duration of the prodromal phase to be bimodal in distribution: for some patients it was less than 1 year and for others more than 4½ years. Cameron (1938) noted that prodromal symptoms could persist for varying periods from days to years. Beiser et al. (1993), in their study of 141 first-episode psychosis patients, found that the prodromal period was highly variable in length, from none at all to 20 years duration. The median prodrome length in schizophrenia was 52.7 weeks. Loebel et al. (1992) found that the time interval from the onset of prodromal symptoms to the onset of psychotic symptoms lasts a mean of 98.5 weeks. This time interval was not significantly different for the schizophrenia and schizoaffective subjects, and there was no significant gender difference.

Research findings suggest that the prodrome before the first episode of psychosis in schizophrenia is often prolonged, often lasting many months and up to several years. In contrast, the literature describes shorter durations of prodromes preceding psychotic relapse. In Herz and Melville's study (1980) over half the patients had a relapse prodrome of less than 1 month with a median between 2 and 4 weeks. Tarrier et al. (1991) reported prodromal changes within 1 month of relapse in their pro-

Figure 5. Hybrid/Interactive model of prodromal changes



Patients can move in and out of symptomatic periods, both of nonspecific and attenuated psychosis types. Both types of symptoms may precede psychosis, and either may occur primarily. Reactive symptoms can occur in response to prodromal and psychotic symptoms, and behavioral changes may occur in response to any of these symptoms.

spective study. Birchwood et al. (1989) observed that 75 percent of relatives noticed changes from 2 to 4 weeks before relapse. The focus of these studies was to ensure that relapse prodromes were long enough to be useful in early intervention. If prodromes of relapse were only hours to a few days long, detection by relatives or mental health professionals would be less likely, and the relapse prodrome concept would be much less useful in determining treatment strategies. As a result, early intervention studies do not focus on longer durations, unlike the studies of first prodromes. Also, the patients in such studies are likely to be on medication, and medication is likely to be increased or started earlier on evidence of relapse, unlike first presentation patients in whom treatment is often delayed (Johnstone et al. 1986; McGorry and Singh 1995). Other factors also confound the examination of prodromes in this relapse group, such as the presence of residual symptoms and the fear of relapse, making these syndromes admixtures of different factors in many patients. Nonetheless, relapse prodromes seem considerably shorter than first psychotic prodromes. Other reasons for this might be an increased vulnerability to psychotic decompensation once a first episode is experienced, or a reduced threshold for manifesting psychotic symptoms after the onset of a psychotic disorder.

Prodrome in Affective Psychoses. In contrast to the amount of literature on prodrome in schizophrenia, relatively little is written about prodromal features of affective psychoses. There are no studies specifically examining prodromes in first-episode patients with affective disorders, and studies tend to focus on nonpsychotic affective disorder. The literature on bipolar disorder and unipolar depression is considered in turn.

Bipolar disorder. Mania is usually considered to have an acute onset, that is, a short duration of prodrome. For example Kraepelin (1919/1921) in discussing acute mania stated: "The beginning of the illness is always very sudden; at most headaches, weariness, lack of pleasure in work or a great busyness [sic], irritability, sleeplessness, precede by some days or weeks the outbreak of more violent manifestations" (p. 61). He thus contrasted this type of rapid onset contrasts with the more insidious onset of dementia praecox (schizophrenia).

Winokur (1976) retrospectively studied modes of onset in a long series of patients with affective disorders, but not necessarily first presentations. He defined *onset* as "the time at which the patient suffers a change in his life until the time he is admitted to hospital" (p. 87). Thus, the endpoint used by Winokur in his study is admission to the hospital, not development of psychotic symptoms. He found that episodes of mania were much more likely to have acute onset, less than 1 month, than were episodes of depression.

Carlson and Goodwin (1973) studied retrospectively the progression of symptoms during acute manic episodes in 20 patients with known bipolar disorder. They noted that patients passed through different phases before relapsing and becoming acutely psychotic. The initial phases were characterized by increased activity, increased talking and rate of speech, irritability, lability of mood, and sometimes euphoria and overconfidence. Thought content changed, with preoccupation with sexual and religious themes quite common. Some patients were aware of these changes and described themselves as "going high." The authors described acute onset, with rate of progression from normal to psychotic varying between hours to a few days.

Molnar et al. (1988) investigated prodromal symptoms and onset features of bipolar episodes, both manic and depressive. They asked 20 subjects with known bipolar disorder to recall events leading up to each of their episodes. They defined the prodrome as the interval from the time that the first symptom was recognized to the time when the symptoms reached maximum severity. Increased activity, elevated mood, decreased need for sleep, racing thoughts, feeling more talkative, increased self-worth, distractibility, and irritability were the frequently reported symptoms leading up to a manic episode. Depressed mood, loss of energy and interest in things, poor concentration, decreased sleep, and morbid thoughts were the most frequently recalled symptoms leading up to a depressive episode. Unlike previous studies, manic prodromes were found to be considerably longer than depressive prodromes, an average 20.50 days and 10.96 days, respectively. The average duration of illness was more than 14 years, and thus patients were having to recall events from quite long ago, particularly their first episode. Accuracy of recall is therefore a concern. Most of the data obtained in this study relate to prodromal features of relapse

rather than first episode. Another finding from this study was the large variation in symptoms and duration of prodrome between individuals, but the consistency of the prodromal picture within individuals, both according to patients and relatives. This therefore lends further weight to the theory of relapse signature (Birchwood 1992), the belief that patients have their own distinctive pattern of relapse.

Beiser et al.'s study (1993) found evidence of a prolonged prodromal phase in affective psychoses through data on the prodromal phases of a group of 141 patients presenting for the first time. A mean duration of prodrome of 103 weeks was found in psychotic depression, and of 129.4 weeks in bipolar disorder. The study did not give prominence to actually describing the prodromal symptoms experienced by patients or changes noted by informants in this phase. The only "first noticeable symptoms" recorded were "lost his/her drive," "became sad," "up all night and slept all day," and "developed strange ideas." Symptoms were not compared across diagnostic groups.

Unipolar depression. Unipolar depression is not a unitary phenomenon, which must be borne in mind when reviewing studies on any aspect of this group of disorders. Furthermore, the articles discussed below varied in their endpoints in relation to prodrome and onset issues, some taking development of the full depressive syndrome as the end of the prodromal period rather than the development of psychotic features, which did not invariably occur. Because of the paucity of literature available on the prodrome in affective disorders, these articles are briefly reviewed, although their relevance to psychotic prodrome may be doubtful.

Hays (1964) studied prodromal symptoms in 81 patients with endogenous depression by retrospective case note review. The endpoint of his period of onset was hospital admission and treatment (usually with electroconvulsive therapy). Although some patients had psychotic symptoms, this was not so in all cases. He found four patterns of onset: (1) sudden, (2) gradual, (3) neurotic, and (4) fluctuating. The sudden onset cases had prodromes of "a few weeks or less." They generally had melancholic features, good response to treatment, and a high rate of affective disorders, including bipolar disorders, in the family history. These patients were probably presenting with the depressed phase of manic depression. "Gradual onset" referred to a prodrome of several months and were the majority in this study. Neurotic onset cases were those in which "psychotic depression is preceded by a state phenomenologically indistinguishable from a neurotic state, in which anxiety and its elaborations form the central symptoms without evidence of depression" (p. 783). This is therefore similar to some conceptualizations of the prodrome in schizophrenia. The fluctuating onset depressions referred to those in which symptoms showed marked fluctuations in severity "before reaching their full force." Such cases occurred infrequently.

Winokur (1976) found that patients with depressive spectrum disorder (those with first-degree relatives with alcoholism or antisocial personalities) were much less likely to have an abrupt onset than were other depressive patients (pure depressive disease).

Fava and Kellner (1991) investigated psychiatric symptoms present 6 months before onset of depressed mood in 15 outpatients presenting with their first episode of major depression. Generalized anxiety was present in 13 cases and irritability was present in 9. Other symptoms commonly described were fatigue, impaired work performance, reduced initiative, and sleep disturbance.

The Stirling County study, a longitudinal investigation of psychiatric epidemiology in a general population, suggested that unipolar depression has a prolonged prodrome (Murphy et al. 1989). The population was assessed in 1952 and (16 years later) in 1968. At first assessment, subjects were divided into three groups: (1) individuals who were symptom free, (2) cases, and (3) subthreshold individuals. At followup 16 years later, the researchers found that the subthreshold group had a significantly higher incidence of depression and anxiety than the symptom-free group ($p < 0.001$). The authors suggested that subjects who were assessed as subthreshold in 1952 were actually showing prodromal signs warning of impending depression or anxiety, which then tended to develop insidiously. Symptoms found in this subthreshold phase were not described.

Current Conceptualizations of Psychotic Prodrome

Current Diagnostic Systems. The bulk of the previously mentioned literature, particularly in relation to schizophrenia, comes from the

1960s and 1970s or earlier. Most of this work used anecdotal reports of patients and families, nonstandardized interview techniques, and other problematic methods. Consequently, much of this phenomenological work is lost in modern perspectives of psychotic prodromes. For example, the *DSM–III–R* (American Psychiatric Association 1987) focuses mainly on observable behavioral changes in its description of the prodromal features of schizophrenia. It provides a list of nine symptoms in its operationalized criteria for schizophrenic prodrome: (1) marked social isolation or withdrawal; (2) marked impairment in role functioning; (3) markedly peculiar behavior; (4) marked impairment in personal hygiene and grooming; (5) blunted or inappropriate affect; (6) digressive, vague, overelaborate, or circumstantial speech, or poverty of speech, or poverty of content of speech; (7) odd beliefs or magical thinking; (8) unusual perceptual experiences; and (9) marked lack of initiative, interests, or energy. Items 1 to 6 are based on observable behavioral changes. Item 7, although requiring the presence of unusual thought content, also requires this to influence behavior, and so an observable element is again necessary. Inclusion of mainly observable phenomena in this description of prodrome intends to increase the reliability of the diagnosis. However, some items such as odd or bizarre ideation or markedly peculiar behavior cannot be reliably measured at all (Jackson et al. 1994). In addition, whether these items give a valid description of the initial prodromal period is not known. Concerns such as these have led to this list of criteria being dropped from the *DSM–IV* (American Psychiatric Association 1994). A prodrome is not even described in relation to mood disorders in the *DSM–III–R* or *DSM–IV*. Although ICD–10 (World Health Organization 1994) acknowledges a prodrome as part of the schizophrenic syndrome, prodromal symptoms are not included in its description of schizophrenia because they cannot be reliably measured and are too nonspecific (Keith and Matthews 1991).

Thus, some confusion about the nature and specificity of prodromal features and about the reliability of their measurement still exists. Past descriptions, with their emphasis on subjective experience and a broad range of often nonspecific symptoms, seem to have been overlooked. The meaning and significance of the prodromal period in psychosis must be addressed, and given its potential importance in early intervention, it must be systematically evaluated with a preventive approach to psychotic disorders in mind.

Reexamining the Initial Psychotic Prodrome and Its Significance for Early Intervention. Psychotic prodrome may be thought of in two ways. The first is as the earliest form of a psychotic disorder. For example, a person with symptoms such as those described by Chapman (1966)—possibly disordered attention and perceptual abnormalities accompanied by anxiety related to these changes—would be thought of as having early schizophrenia. This person is not yet psychotic but would be thought of as having prepsychotic schizophrenia. Early intervention would result in prevention of psychotic symptoms and hence reduction in severity of the disorder, but not the primary prevention of schizophrenia. This model is often used clinically in mood disorders, where a patient may be seen with hypomania, and intervention such as medication prevents a full-blown mania. The conceptualization of the prodrome implies that, in the absence of intervention, a prodromal syndrome would be inevitably followed by psychosis.

The second way to envision the prodrome in psychosis is as a syndrome that confers a heightened vulnerability to becoming psychotic but does not inevitably lead to psychosis. This was the view of Huber et al. (1980) with their outpost syndrome concept. Thus, the prodrome is seen as a state (as opposed to a trait) risk factor for psychosis. This model implies that a person with certain features, such as attention and perception defects accompanied by anxiety, may or may not develop a psychosis. In this case, the term "prodrome" is misleading, as it implies that the psychosis is inevitable (prodrome being a retrospective concept). "At-risk mental state" has been suggested as a more accurate term (McGorry and Singh 1995).

The second model of prodrome, or at-risk mental state, has several important implications for clinical practice and research. Identification of an at-risk mental state enables prospective studies of vulnerable individuals and "close-in" followups. This sequential screening study design, described by Bell (1992), involves combining risk factors to enhance the true positive pickup rate from a prospective study and to shorten the likely followup period required to observe the transition to frank psychosis. Thus, an at-risk mental

state can be combined with other known risk factors for the development of psychosis, such as the trait risk factor of family history, and vulnerable individuals can be prospectively followed up.

From a clinical point of view, any intervention at this period of time, before the development of any psychotic disorder, would be primary prevention. Clinical features that best predict the subsequent development of psychosis could be studied; neuropsychological and biological investigations could determine if there are any abnormalities in these areas before the development of acute psychotic symptoms; and potential biological markers could be explored. Such a study has recently been funded and will take place in a special clinic designed to identify individuals with multiple risk factors and at-risk mental states (Yung et al. 1995).

The danger in such a prospective investigation is that psychiatric attention and intervention could occur in people who will not go on to develop psychotic disorders (false positives). Mental state changes that seem to resemble a prodrome cross-sectionally may or may not progress to psychosis for two reasons. First, the mental state changes may not represent a vulnerable state at all but might indicate a different underlying pathology—an incipient anxiety, a depressive disorder, or a situational crisis. Second, the mental state changes might indicate a potentially prepsychotic at-risk mental state, but factors such as enhanced coping, increase in social support, or some other change in circumstance could prevent, delay, or modify the progression to psychosis. Thus, the person may be described as having an outpost syndrome (Huber et al. 1980).

Researchers need to be aware of the ethical aspects involved in a prospective study. Warning the individual of the risk of developing a psychosis must be balanced with the potentially stigmatizing and anxiety-provoking effect of such information. Other interventions, such as commencing neuroleptic medication, should proceed only with caution and only when it becomes obvious that the patient really does have an early psychosis. Such warnings were made as long ago as 1938, by Harry Stack Sullivan in his reply to Cameron's urging for preventive interventions in early schizophrenia (Cameron 1938). Sullivan emphasized the lack of specificity of early signs of "incipient schizophrenia" and pointed out the dangers of unnecessary intervention in those who may not become ill. Early treatment of such syndromes may be unnecessarily interventionist according to a study by Falloon (1992): Individuals suspected of having "prodromal schizophrenia" were treated with education about schizophrenia, stress management, and, in some cases, low-dose neuroleptic medication. Falloon himself acknowledged the difficulty with such a strategy: "Inevitably some persons who would not develop any significant disorder will receive stress management and drugs that they do not need. They may also worry needlessly about the possibility of developing schizophrenia in the future" (p. 13).

Discussion

The prodrome in psychosis is an area of potential early intervention. If prepsychotic states could be recognized and if the person could receive help at this early stage, then the psychosis, with all its psychologically and socially disruptive effects, could be prevented or at least minimized (Sullivan 1927/1994; Cameron 1938; Meares 1959). However, previous research, necessarily retrospective, has highlighted the variable and usually nonspecific nature of the prodromal phenomena, raising the issue of false positives. The wide range of durations of prodromes contributes further to the difficulty of predicting if and when a person will make the transition from an at-risk mental state to a psychotic episode.

The different theories on sequence of changes in the schizophrenic prodrome need consideration to delineate the primary features of the disorder. Chapman's hypothesis (1966) is that disturbances in selective attention and perceptual changes occur primarily and lead to psychosis as well as reactive neurotic symptoms. Others see the neurotic symptoms as occurring first, followed by specific attenuated psychotic symptoms such as change in the sense of self and the world (delusional mood) (Bowers and Freedman 1966; Stein 1967; Bowers 1968) and suspiciousness (Cameron 1938; Conrad 1958; Heinrichs and Carpenter 1985), and then evolving into psychosis. However, no testing of these different hypotheses has taken place.

Little research has been done about prodromes of first episodes of affective disorders; most of the studies focused on patients with known affective disorders in relation to their relapse prodromes. The duration of prodrome in affec-

tive psychoses has been described as brief (a matter of days) by most authors but has been questioned in later literature describing prodromes as lasting weeks to even years. Hypomanic features such as increased activity, irritability, and sleeplessness are characteristically described in the manic prodrome, and depressed mood, anxiety, and reduced energy noted in the unipolar depression prodrome.

Conclusion

The relative paucity of methodologically sound research on initial psychotic prodromes, both schizophrenic and affective, together with the confusion regarding current diagnostic systems, highlights the need for ongoing work in this area. Rigorous and systematic data collection of first-episode psychosis is needed, with focus on the prepsychotic period and a wide and inclusive coverage of symptomatology. This foundation would lead to investigation of high-risk individuals; specification of symptoms that lead to the development of psychosis; and deeper understanding of the neurobiology of the onset of psychotic disorder.

References

American Psychiatric Association. *DSM–III–R: Diagnostic and Statistical Manual of Mental Disorders.* 3rd ed., revised. Washington, DC: The Association, 1987

American Psychiatric Association. *DSM–IV: Diagnostic and Statistical Manual of Mental Disorders.* 4th ed. Washington, DC: The Association, 1994.

Anonymous. An autobiography of a schizophrenic experience. *Journal of Abnormal and Social Psychology,* 51:677–680, 1950.

Beiser, M.; Erickson, D.; Fleming, J.A.E.; and Iacono, W.G. Establishing the onset of psychotic illness. *American Journal of Psychiatry,* 150:1349–1354, 1993.

Bell, R.Q. Multiple-risk cohorts and segmenting risk as solutions to the problem of false positives in risk for the major psychoses. *Psychiatry,* 55:370–381, 1992.

Birchwood, M. Early intervention in schizophrenia: Theoretical background and clinical strategies. *British Journal of Clinical Psychology,* 31:257–278, 1992.

Birchwood, M., and MacMillan, J.F. Early intervention in schizophrenia. *Australian and New Zealand Journal of Psychiatry,* 27:374–378, 1993.

Birchwood, M.; Smith, J.; MacMillan, J.F.; Hogg, B.; Prasad, R.; Harvey, C.; and Bering, S. Predicting relapse in schizophrenia: The development and implementation of an early signs monitoring system using patients and families as observers: A preliminary investigation. *Psychological Medicine,* 19:649–656, 1989.

Bleuler, E. *Dementia Praecox or the Group of Schizophrenias.* [1911] Translated by J. Zinkin. New York, NY: International Universities Press, 1950.

Bowers, M.B. The onset of psychosis—A diary account. *Psychiatry,* 28:346–358, 1965.

Bowers, M.B. Pathogenesis of acute schizophrenic psychosis. *Archives of General Psychiatry,* 19:348–355, 1968.

Bowers, M.B., and Freedman, D.X. "Psychedelic" experiences in acute psychoses. *Archives of General Psychiatry,* 15:240–248, 1966.

Cameron, D.E. Early schizophrenia. *American Journal of Psychiatry,* 95:567–578, 1938.

Carlson, G.A., and Goodwin, F.K. The stages of mania. *Archives of General Psychiatry,* 28:221–228, 1973.

Chapman, J.P. The early symptoms of schizophrenia. *British Journal of Psychiatry,* 112:225–251, 1966.

Chapman, J.P.; Freeman, T.F.; and McGhie, A. Clinical research in schizophrenia—The psychotherapeutic approach. *British Journal of Medical Psychology,* 32:2–16, 1959.

Chapman, L.J.; Day, D.; and Burstein, A. The process-reactive distinction and prognosis in schizophrenia. *Journal of Nervous and Mental Disease,* 133:383–391, 1961.

Conrad, K., ed. *Die beginnende Schizophrenie.* Stuttgart, Germany: Georg Thieme Verlag, 1958.

Cutting, J. *The Psychology of Schizophrenia.* London, England: Churchill Livingstone, 1985.

Docherty, J.P.; van Kammen, D.P.; Siris, S.G.; and Marder, S.R. Stages of onset of schizophrenic psychosis. *American Journal of Psychiatry,* 135:420–426, 1978.

Donlon, P.T.; and Blacker, K.H. Stages of schizophrenic decompensation and reintegration. *Journal of Nervous and Mental Disease,* 157:200–209, 1973.

Falloon, I.R.H. Early intervention for first episodes of schizophrenia: A preliminary exploration. *Psychiatry,* 55:4–15, 1992.

Fava, G.A., and Kellner, R. Prodromal symptoms in affective disor-

ders. *American Journal of Psychiatry*, 148:823–830, 1991.

Fenton, W.S., and McGlashan, T.H. Prognostic scale for chronic schizophrenia. *Schizophrenia Bulletin*, 13(2):277–286, 1987.

Fish, F.J. *Fish's Schizophrenia*. Bristol, England: Wright and Sons, 1976.

Freedman, B., and Chapman, L.J. Early subjective experience in schizophrenic episodes. *Journal of Abnormal Psychology*, 82:46–54, 1973.

Häfner, H.; Maurer, K.; Löffler, W.; Fätkenheuer, B.; van der Heiden, W.; Riecher-Rössler, A.; Behrens, S.; and Gattaz, W.F. The epidemiology of early schizophrenia: Influence of age and gender on onset and early course. *British Journal of Psychiatry*, 164(Suppl. 23):29–38, 1994.

Häfner, H.; Maurer, K.; Löffler, W.; and Riecher-Rössler, A. The influence of age and sex on the onset and early course of schizophrenia. *British Journal of Psychiatry*, 162:80–86, 1993.

Häfner, H.; Riecher-Rössler, A.; Hambrecht, M.; Maurer, K.; Meissner, S.; Schmidtke, A.; Fätkenheuer, B.; Löffler, W.; and van der Heiden, W. IRAOS: An instrument for the assessment of onset and early course of schizophrenia. *Schizophrenia Research*, 6:209–223, 1992*a*.

Häfner, H.; Riecher-Rössler, A.; Maurer, K.; Fätkenheuer, B.; and Löffler, W. First onset and early symptomatology of schizophrenia: A chapter of epidemiological and neurobiological research into age and sex differences. *European Archives of Psychiatry and Clinical Neurosciences*, 242:109–118, 1992*b*.

Hambrecht, M.; Häfner, H.; and Löffler, W. Beginning schizophrenia observed by significant others. *Social Psychiatry and Psychiatric Epidemiology*, 29:53–60, 1994.

Hays, P. Modes of onset of psychotic depression. *British Medical Journal*, 2:779–784, 1964.

Heinrichs, D.W., and Carpenter, W.T., Jr. Prospective study of prodromal symptoms in schizophrenic relapse. *American Journal of Psychiatry*, 142:371–373, 1985.

Henderson, A.S. *An Introduction to Social Psychiatry*. Oxford, England: Oxford University Press, 1988.

Herz, M.I., and Melville, C. Relapse in schizophrenia. *American Journal of Psychiatry*, 137:801–805, 1980.

Hirsch, S.; Cramer, P.; and Bowen, J. The triggering hypothesis of the role of life events in schizophrenia. *British Journal of Psychiatry*, 161(Suppl. 18):84–87, 1992.

Huber, G.; Gross, G.; Schüttler, R.; and Linz, M. Longitudinal studies of schizophrenic patients. *Schizophrenia Bulletin*, 6(4):592–605, 1980.

Jackson, H.J.; McGorry, P.D.; and McKenzie, D. The reliability of *DSM–III* prodromal symptoms in first episode psychotic patients. *Acta Psychiatrica Scandinavica*, 90:375–378, 1994.

Johnstone, E.C.; Crow, T.J.; Johnson, A.L.; and MacMillan, J.F. The Northwick Park Study of first episode schizophrenia: I. Presentation of the illness and problems relating to admission. *British Journal of Psychiatry*, 148:115–120, 1986.

Keith, S.J., and Matthews, S.M. The diagnosis of schizophrenia: A review of onset and duration issues. *Schizophrenia Bulletin*, 17(1):51–67, 1991.

Kirch, D.G.; Lieberman, J.A.; and Matthews, S.M. First-episode psychosis: Part I. Editors' introduction. *Schizophrenia Bulletin*, 18(2):177–178, 1992.

Koehler, K., and Sauer, H. Huber's basic symptoms: Another approach to negative psychopathology in schizophrenia. *Comprehensive Psychiatry*, 25:174–182, 1984.

Kraepelin, E. *Manic Depressive Insanity and Paranoia*. [1919] Translated by R.M. Barclay. Edinburgh, Scotland: E. and S. Livingstone, 1921.

Kubie, L.S. The relation of psychotic disorganization to the neurotic process. *Journal of the American Psychoanalytic Association*, 15:626–640, 1967.

Langfeldt, G. Schizophrenia: Diagnosis and prognosis. *Behavioral Science*, 14:173–182, 1969.

Levy, S.T.; McGlashan, T.H.; and Carpenter, W.T., Jr. Integration and sealing over as recovery styles from acute psychosis. *Journal of Nervous and Mental Disease*, 161:307–312, 1975.

Lieberman, J.A.; Kinon, B.J.; and Loebel, A.D. Dopaminergic mechanisms in idiopathic and drug-induced psychoses. *Schizophrenia Bulletin*, 16(1):97–110, 1990.

Lieberman, J.A.; Matthews, S.M.; and Kirch, D.G. First-episode psychosis: Part I. Editors' introduction. *Schizophrenia Bulletin*, 18(3):349–350, 1992.

Loebel, A.D.; Lieberman, J.A.; Alvir, J.M.J.; Mayerhoff, D.I.; Geisler, S.H.; and Szymanski, S.R. Duration of psychosis and outcome in first-episode schizophrenia. *American Journal of Psychiatry*, 149(9):1183–1188, 1992.

Malla, A.K., and Norman, R.M. Prodromal symptoms in schizophrenia. *British Journal of Psychiatry*, 164:487–493, 1994.

McGhie, A., and Chapman, J. Disorders of attention and perception in early schizophrenia. *British Journal of Medical Psychology*, 34:103–115, 1961.

McGlashan, T.H.; Levy, S.T.; and Carpenter, W.T., Jr. Integration and sealing over: Clinically distinct recovery styles from schizophrenia. *Archives of General Psychiatry*, 32:1269–1272, 1975.

McGorry, P.D. The influence of illness duration on syndrome clarity and stability in functional psychosis: Does the diagnosis emerge and stabilize with time? *Australian and New Zealand Journal of Psychiatry*, 28:607–619, 1994.

McGorry, P.D., and Singh, B.S. Schizophrenia: Risk and possibility. In: Raphael, B., and Burrows, G.D., eds. *Handbook of Preventive Psychiatry*. New York, NY: Elsevier, 1995. pp. 492–514.

Meares, A. The diagnosis of prepsychotic schizophrenia. *Lancet*, I:55–59, 1959.

Molnar, G.; Feeney, M.G.; and Fava, G.A. Duration and symptoms of bipolar prodromes. *American Journal of Psychiatry*, 145:1576–1578, 1988.

Murphy, J.M.; Sobol, A.M.; Olivier, D.C.; Monson, R.R.; Leighton, A.H.; and Pratt, L.A. Prodromes of depression and anxiety: The Stirling County Study. *British Journal of Psychiatry*, 155:490–495, 1989.

Offenkrantz, W. Multiple somatic complaints as a precursor of schizophrenia. *American Journal of Psychiatry*, 119:258–259, 1962.

Pious, W.L. A hypothesis about the nature of schizophrenic behavior. In: Burton, A., ed. *Psychotherapy of the Psychoses*. New York, NY: Basic Books, 1961. pp. 43–68.

Roberts, G. The origins of delusion. *British Journal of Psychiatry*, 161:298–308, 1992.

Stein, W.J. The sense of becoming psychotic. *Psychiatry*, 30:262–275, 1967.

Subotnik, K.L., and Nuechterlein, K.H. Prodromal signs and symptoms of schizophrenic relapse. *Journal of Abnormal Psychology*, 97:405–412, 1988.

Sullivan, H.S. Discussion. *American Journal of Psychiatry*, 95:567–578, 1938.

Sullivan, H.S. The onset of schizophrenia. [1927] *American Journal of Psychiatry*, 151(Suppl. 6):135–139, 1994.

Tarrier, N.; Barrowclough, C.; and Bamrah, J.S. Prodromal signs of relapse in schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, 26:157–161, 1991.

Tennant, C.C. Stress and schizophrenia. *Integrative Psychiatry*, 3:248–261, 1985.

Vaillant, G.E. The prediction of recovery in schizophrenia. *Journal of Nervous and Mental Disease*, 135:945–952, 1962.

Vaillant, G.E. An historical review of the remitting schizophrenias. *Journal of Nervous and Mental Disease*, 138:48–56, 1964*a*.

Vaillant, G.E. Prospective prediction of schizophrenic remission. *Archives of General Psychiatry*, 11:509–518, 1964*b*.

Varsamis, J., and Adamson, J.D. Early schizophrenia. *Canadian Psychiatric Association Journal*, 16:487–497, 1971.

Walker, E.F. *Schizophrenia: A Life Course Developmental Perspective*. San Diego, CA: Academic Press, 1991.

Winokur, G. Duration of illness prior to hospitalization (onset) in the affective disorders. *Neuropsychobiology*, 2:87–93, 1976.

World Health Organization. *Manual of the International Classification of Diseases, Injuries, and Causes of Death*. 10th rev. Geneva, Switzerland: The Organization, 1994.

Wyatt, R.J. Neuroleptics and the natural course of schizophrenia. *Schizophrenia Bulletin*, 17(2):325–351, 1991.

Yung, A.R.; McGorry, P.D.; McFarlane, C.A.; and Patton, G. The PACE Clinic: Development of a clinical service for young people at high risk of psychosis. *Australasian Psychiatry*, 3:345–349, 1995.

Yung, A.P., and Stanley, P.A. Fever and maculopapular rash. In: Kincaid-Smith, P.; Larkins, R.; and Whelan, G., eds. *Problems in Clinical Medicine*. Sydney, Australia: MacLennan and Petty, 1989. pp. 335–340.

The Authors

Alison R. Yung, M.B.B.S., M.P.M., F.R.A.N.Z.C.P., is Consultant Psychiatrist, Early Psychosis Prevention and Intervention Centre (EPPIC), and Lecturer, Department of Psychiatry, University of Melbourne, Parkville, Victoria, Australia. Patrick D. McGorry, M.B.B.S., Ph.D., M.R.C.P. (U.K.), F.R.A.N.Z.C.P., is Associate Professor, Department of Psychiatry, University of Melbourne, and Director, EPPIC, Parkville, Victoria, Australia.