occasionally be long-term effects. Toxic interactions have been repo between lithium and antipsychotic drugs such as haloperidol and thioridazine. Lithium toxicity is characterised by diarrhoea, vomiting, increased tremor, dysarthria (**1078**), drowsiness, and ataxia (**1063**) and in the most severe cases by restlessness, confusion, nystagmus, fits, delirium and eventually death.[78]

Combining lithium with other drugs

Haloperidol is commonly combined with lithium, the former providing immediate control of symptoms while the effects of lithium build up to the point where the antipsychotic medication can be withdrawn.[79] However, according to Kendell, there is no evidence that lithium and haloperidol are more effective in the control of severe mania than haloperidol alone. Furthermore, "there are reports of patients developing an acute brain syndrome, followed in some cases by lasting extrapyramidal and cognitive deficits, on large doses of the two drugs together."[80]

CARBAMAZEPINE

In cases of resistant mania or bipolar affective disorder, carbamazepine (CBZ) is sometimes used instead of, or in conjunction with, lithium. It may also be used as a prophylactic although one study showed that while lithium doubled the mean time in remission, carbamazepine only increased it by 50 per cent.[81] Because it may depress the white cell count, regular checks on this are necessary, particularly early on during treatment. The drug is available as Carbamazepine (tablets), Tegretol (tablets, liquid, suppositories), and Tegretol Retard (tablets). The BNF guideline dose is 400mg initially, increased until the symptoms are controlled, with a usual range of 400–600mg daily and a maximum of 1600mg. Common adverse effects include mild leukopenia, nausea and vomiting. Carbamazepine decreases blood levels of haloperidol and tricyclic antidepressants and suppresses circulating levels of T_3 and T_4 (**1298**).

CALCIUM CHANNEL BLOCKERS

Calcium channel blockers such as verapamil and nifedipine, which are usually prescribed for heart conditions such as angina, have also been used to treat mania and they may act by blocking serotonin receptors.

ELECTROCONVULSIVE THERAPY (ECT)

ECT has a role for patients with severe manic illnesses which do not respond to medication (**1132**). One recent trial demonstrated that bilateral ECT given three times a week was more effective than lithium.[82]

78 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.208.

79 J. Biederman, *et al.*, "Combination of lithium carbonate and haloperidol in schizo-affective disorder" *Archives of General Psychiatry* (1979) 36, 327–333; M. Lader and R. Herrington, *Biological treatments in psychiatry, supra*, p.203.

80 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), pp.448–449.

81 S.E. Watkins, *et al.*, "The effect of carbamazepine and lithium on remission from affective illness" *British Journal of Psychiatry* (1987) 150, 180–182; M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.210.

82 J.G. Small, *et al.*," Electroconvulsive treatment compared with lithium in the management of manic states" *Archives of General Psychiatry* (1988) 45, 727–732.

23. Schizophrenia and related psychoses

INTRODUCTION

The majority of people detained under the Mental Health Act 1983 are diagnosed as suffering from a form of mental illness known as schizophrenia. Schizophrenia is commonly thought of as a psychiatric term for a range of experiences which the majority of the population describe as "madness." For this reason, to be diagnosed as having schizophrenia carries a stigma which other diagnoses do not. Beyond the public perception, what schizophrenia is is difficult to define. Innumerable definitions and models have been suggested but it is impossible to point to any single defining pathology, symptom or cluster of symptoms, common to all people so diagnosed. It is therefore important to realise at the outset that schizophrenia is a model, an organisational concept the purpose of which is to make it easier to comprehend the variegated phenomena of illness than it would otherwise be.[1] Whether the various presentations collectively classified as forms of schizophrenia do indeed share a particular unifying pathology, and are homogenous at some fundamental level, or instead represent several different kinds of illness or disease process, has still to be established. For the moment, the description of schizophrenia given in the International Classification of Diseases gives an idea of the broad range of experiences associated with the diagnosis[2] —

> "The schizophrenic disorders are characterised in general by fundamental and characteristic distortions of thinking and perception, and by inappropriate or blunted affect ... The most intimate thoughts, feelings, and acts are often felt to be known to or shared by others, and explanatory delusions may develop, to the effect that natural or supernatural forces are at work to influence the afflicted individual's thoughts and actions in ways that are often bizarre. The individual may see himself or herself as the pivot of all that happens. Hallucinations, especially auditory, are common and may comment on the individual's behaviour or thoughts ... Perplexity is also common early on and frequently leads to a belief that everyday situations possess a special, usually sinister, meaning intended uniquely for the individual. In the characteristic schizophrenic disturbance of thinking ... thinking becomes vague, elliptical, and obscure, and its expression in speech sometimes incomprehensible. Breaks and interpolations in the train of thought are frequent, and thoughts may seem to be withdrawn by some outside agency. Mood is characteristically shallow, capricious, or incongruous. Ambivalence and disturbance of volition may appear as inertia, negativism, or stupor. Catatonia may be present."

1 R.E. Kendell, "Diagnosis and classification" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 1993), p.278. Janzarik once described the history of schizophrenia as a history not of medical discoveries but of intellectual models on which the orientation of psychiatry is based.

2 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.86–87.

ASSESSMENT, DIAGNOSIS AND CLASSIFICATION

When a patient is examined prior to admission, or immediately following admission, the first task is to establish the kind of disorder (if any) which is troubling him or others so that, having identified it, conclusions can be reached about its causes, probable course and treatment. Assessment is the process of collecting information relevant to the diagnosis, management, and treatment of a patient's clinical condition; including, therefore, this process of distinguishing the presence of a particular syndrome, such as schizophrenia, from the existence of a characteristic pattern of symptoms. A diagnosis is a "short-hand way of describing what is wrong with the patient"[3] and it involves assigning the patient's case to a predesignated diagnostic class according to a reliable medical classification of abnormal mental phenomena.

International Classification of Mental Disorders (ICD–10)

The classification of mental disorders in official usage in England and Wales is the World Health Organisation's International Classification of Diseases, now in its tenth revision (ICD–10); and, more particularly, that part of it dealing with mental and behavioural disorders. One section or "block" of the classification is concerned with schizophrenia and similar disorders (Block F20–F29). Within this block, each type and sub-type of mental disorder is separately listed and coded. Schizophrenia is given the code F20, and a further digit is used to record various sub-types such as paranoid schizophrenia (F20.0) and catatonic schizophrenia (F20.2). Inevitably, the classification involves "compromises between scientists with the most influential theories and the practice of senior clinicians at national and international level."[4]

Operational definitions (diagnostic guidelines)

Every symptom seen in cases of schizophrenia may also be present in some other type of mental disorder. For example, symptoms such as elation, flight of ideas and grandiose ideas are quite common in both schizophrenia and mania. Operational definitions (diagnostic guidelines or criteria) are used to specify which combinations of symptoms are adequate to substantiate a diagnosis. They define what a clinician means when he uses the term "schizophrenia" and represent an attempt to standardise clinical practice and understanding.

Other classifications

The ICD–10 classification, and the diagnostic guidelines which form part of it, are but one of many medical classifications of mental disorder. Over the past quarter of a century there has been a multiplication of diagnostic criteria, reflecting the many different ideas held by psychiatrists about schizophrenia. At least 20 have been published since 1972.[5] Kendell notes that the co-existence of alternative definitions at least serves the purpose of being a reminder that all definitions are arbitrary. None of the competing definitions can be said to be right or wrong since there is as yet no external criterion of validity. It is impossible to decide which is the most valid because this would involve determining which of several different ways of defining the syndrome of schizophrenia most accurately picks out patients possessing an

3 J.M. Pfeffer and G. Waldron, *Psychiatric Differential Diagnoses* (Churchill Livingstone, 1987), p.4.

4 J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.17.

5 C. Thompson, *The Instruments of Psychiatric Research* (John Wiley & Sons, 1989), p.4.

underlying abnormality which has yet to be identified.[6] Although a core of typical patients meet all definitions, there are significant differences in the populations of patients covered by each of them. Each operational definition generates different values for the incidence of a disorder, its heritability, its responsiveness to therapeutic agents, and its prognosis. Various studies have demonstrated poor agreement between clinicians about who merited the diagnosis[7] and the concordance between the different sets of operational criteria for schizophrenia is "not impressive; in other words the different criteria tend to diagnose different people as schizophrenic."[8] Similarly, statistical techniques have not yielded convincing evidence either of a naturally occurring group of correlated psychotic traits or of discrete groups of individuals who share a common set of schizophrenic symptoms.[9] It is therefore important to realise that a patient who meets the very inclusive criteria for a diagnosis of schizophrenia in the ICD–10 classification may not satisfy the more tightly-drawn operational criteria of another classification. It is also the case that a considerable minority of apparently well-adjusted people have reported schizophrenic-like experiences and behaviour.[10]

SYMPTOMS AND SIGNS

The idea that schizophrenia is a distinct type of disease carries with it an expectation that certain characteristic symptoms or symptom-patterns will be found in the vast majority of patients diagnosed as having the condition. These symptoms will fit together in some fashion because of the common underlying disease process. However, the symptoms of people diagnosed as having the condition do not conjoin in this fashion whatever operational definition is used: "disjunction is its essence and any one symptom is capable of replacing another in the descriptive term 'schizophrenia.'"[11] No symptom has been found to be "pathognomonic"; that is, there is no symptom the existence of which establishes the diagnosis.

6 R.E. Kendell, "Schizophrenia: A Medical View of a Medical Concept" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.63.

7 R.P. Bentall, "The classification of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.24; K. Blashfield, *The Classification of Psychopathology: Neo-Kraepelinian and Quantitative Approaches* (Plenum, 1984).

8 R.P. Bentall, "The classification of schizophrenia," *supra*, p.25; I.F. Brockington, *et al.*, "Definitions of schizophrenia: Concordance and prediction of outcome" *Psychological Medicine* (1978) 8, 399–412.

9 R.P. Bentall, "The classification of schizophrenia," *supra*, p.25; K. Blashfield, *The Classification of Psychopathology: Neo-Kraepelinian and Quantitative Approaches*, *supra*; P.D. Slade and R. Cooper, "Some conceptual difficulties with the term 'schizophrenia': an alternative model" Brit. J. Soc. Clin. Psychol. (1979) 18, 309–317; B.S. Everitt, *et al.*, "An attempt at validation of traditional psychiatric symptoms by cluster analysis" *British Journal of Psychiatry* (1971) 119, 399–342; R.E. Kendell and J.A. Gourlay, "The clinical distinction between the affective psychoses and schizophrenia" *British Journal of Psychiatry* (1970) 117, 261–266; I.F. Brockington and R.S. Wainwright, "Depressed patients with schizophrenic or paranoid symptoms" *Psychological Medicine* (1980) 10, 665–675; R.E. Kendell and I.F. Brockington, "The identification of disease entities and the relationship between schizophrenic and affective psychoses" *British Journal of Psychiatry* (1980) 137, 324–331. Bentall summarises the position by stating that, taken together, the studies cast doubt on the existence of a unique schizophrenia syndrome.

10 The relevant studies are referred to by Bentall in R.P. Bentall, "The classification of schizophrenia," *supra*, p.32.

11 "... One is left with the hope that a lesion in the brain will either be discerned or excluded. It seems that only if disease is validated by such discernment can we hope to appreciate the linkages within the variety of symptoms, and the distinctions between those symptoms, that are pathognomonic of the disorder and those that are pathoplastic to the individual and his situation." P.R. McHugh, "Schizophrenia and the Disease Model" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.77.

The form and content of the experience

Jung once noted that "in our dreams we are all schizophrenic" by which he meant that just as the symbolism of dreams is not random and meaningless so the perceptions and ideas of persons with that diagnosis are pointers to the root conflict which the mental illness addresses. A carefully taken history often reveals the nature of this conflict between the individual and his environment and why it became so intense that the impasse could seemingly only be resolved by acquiescence and self-destruction or by some reconstruction of beliefs and perceptions capable of bridging the chasm between objective reality and subjective need. Listening to a client's views offers the professional a window through which he can perceive, if at times only dimly, the individual's predicament and the constellation of internal conflicts which have given rise to the symptoms. However, while such an approach is essential if progress is to be made, it is nevertheless only part of the picture, and psychiatry traditionally distinguishes between the content of a person's subjective experiences and their form. Thus, Kendell writes that the content of an idea may "be meaningful and understandable. But it is even more significant that the idea is a delusion, and not merely an overvalued idea; that the hallucination is occurring in a setting in which other people do not experience false perceptions; and that the patient's difficulty in expressing himself coherently is not explicable in terms of limited vocabulary or education, or emotional arousal."[12]

Front-rank symptoms

Certain symptoms are sometimes referred to as "front-rank" symptoms because of the diagnostic significance attributed to them by Schneider.

SCHNEIDER'S FRONT-RANK SYMPTOMS

Front-rank symptoms	*Second-rank symptoms*
▪ Audible thoughts	▪ Other disorders of perception
▪ Voices arguing or discussing or both	▪ Sudden delusional ideas
▪ Voices commenting	▪ Perplexity
▪ Somatic passivity experiences	▪ Depressive and euphoric mood changes
▪ Thought withdrawal and other experiences of influenced thought	▪ Feelings of emotional impoverishment
▪ Thought broadcasting	▪ Various others
▪ Delusional perceptions	
▪ All other experiences involving volition, made affects, and made impulses	

12 R.E. Kendell, "Schizophrenia: A Medical View of a Medical Concept" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.69.

Positive and negative sympto.

A further distinction which is often made is to describe certain symptoms of schizophrenia as being positive or negative. Positive symptoms are those which appear to reflect an excess or distortion of normal functions, whereas negative symptoms reflect a diminution or loss of normal functions and are mainly behavioural.[13] Positive symptoms include distortions or exaggerations of inferential thinking (delusions), perception (hallucinations), language and communication (disorganised speech).[14] They are most clearly recognised when an articulate patient is describing his inner experiences.[15] Negative symptoms consist of restrictions in the range and intensity of emotional expression (emotional blunting/affective flattening), in the fluency and productivity of thought and speech, and in the initiation of goal-directed behaviour. Conversation is restricted, speech and movement are slow. There is a lack of motivation and initiative, a loss of interest in the patient's immediate environment and the wider world, and a withdrawal from social contacts.[16] Social withdrawal may lead to a worsening of positive as well as negative symptoms. Patients commonly report that their auditory hallucinations recede when they are engaged in workshop activities[17] and they occur less frequently when the person is in the presence of an interviewer than when alone.[18] The picture is seen in a wide range of psychiatric conditions, including dementia and mood disorders, and is well-known to neurologists.[19] Patients who are discharged from hospital free of positive symptoms often retain negative symptoms for between one and two years after discharge.[20]

Negative symptoms and institutionalism

It is unclear to what extent negative symptoms are induced by a deprived social environment, as opposed to being an integral part of the schizophrenic process.[21] Wing and Brown demonstrated wide variations between three psychiatric hospitals in the amount of activity provided for patients and commensurate differences in the prevalence of negative symptoms.[22]

Negative symptoms the natural consequence of positive symptoms

Care must be taken to distinguish between true emotional indifference about one's situation and mere indifference about communicating one's ideas and feelings to

13 *Diagnostic and Statistical Manual of Mental Disorders, Fourth Revision (DSM–IV)* (American Psychiatric Association, 1994), p.274.

14 *Ibid.*, pp.274–275.

15 J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.9.

16 *Diagnostic and Statistical Manual of Mental Disorders, Fourth Revision (DSM–IV), supra*, p.275; J. Leff, "Schizophrenia: social influences on onset and relapse" in *Community Psychiatry: The Principles* (ed. D.H. Bennett and H.L. Freeman, Churchill Livingstone, 1991), p.208.

17 *Ibid.*, p.210.

18 9 per cent. of the time, compared with 55 per cent., according to Cooklin. See R. Cooklin, *et al.*, "The relationship between auditory hallucinations and spontaneous fluctuations of skin conductance in schizophrenia" *British Journal of Psychiatry* (1983) 142, 47–52. The observation is important in the context of tribunal hearings because some patients may appear to be free of such phenomena when their attention is engaged at the hearing or when interviewed prior to the hearing.

19 J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.6.

20 J. Leff, "Schizophrenia: social influences on onset and relapse" in *Community Psychiatry: The Principles* (ed. D.H. Bennett & H.L. Freeman, Churchill Livingstone, 1991), p.209.

21 *Ibid.*

22 J.K. Wing and G.W. Brown, *Institutionalism and schizophrenia* (Cambridge University Press, 1970).

others. Prolonged failure to establish any rapport with others about ___eriences which dominate a person's life inevitably leads eventually to a withdrawal from further social contact with them. Communication becomes futile and emotionally unrewarding, so that the patient's withdrawal is the natural final consequence of his long-standing positive symptoms, such as hallucinations and delusions.

Measuring the severity of symptoms

The severity of a symptom can be rated on a number of different criteria, such as frequency, intensity, duration or degree of incapacitation or tolerability.[23] Various rating scales, such as the Present State Examination (PSE), are commonly used to assess schizophrenic phenomena.

ICD–10 DIAGNOSTIC GUIDELINES FOR SCHIZOPHRENIA

The ICD–10 classification divides symptoms of special diagnostic importance into nine groups of symptoms which often occur together. The table on page 1234 lists these symptom groups with an explanation of the meaning of medical terms.[24] It will be seen that where one "very clear" symptom from a certain number of first-rank symptoms has endured for a period of one month or more then its presence alone establishes the diagnosis. Thus, while acknowledging that "no strictly pathognomonic symptoms can be identified," the classification nevertheless comes close to establishing them.

SYMPTOMS OF LESS THAN ONE MONTH'S DURATION

One of the diagnostic guidelines for schizophrenia is that the symptoms listed in the table have been present for a minimum period of one month. However, some people become acutely psychotic without any obvious organic cause for this, such as dementia, delirium, or intoxication by drugs or alcohol. Acute onset is defined as a change during a period of a fortnight or less from a state without psychotic features to an obviously abnormal psychotic state. Such psychotic states may prove transient or persist for a month or longer and the presentation may include schizophrenia-type symptoms. If the psychotic symptoms are comparatively stable and fulfil the criteria for schizophrenia but have lasted for less than one month, the diagnosis made is that of an "acute schizophrenia-like psychotic disorder (F23.2)." If the schizophrenic symptoms then persist for more than one month, the diagnosis is changed to schizophrenia.[25]

Highly variable and changeable mental state

Acute polymorphic psychotic disorders are a further type of acute psychotic episode. "Polymorphic" means "having many forms", and these disorders are characterised

[23] See R. Manchanda, *et al.*, "A Review of rating scales for measuring symptom changes in schizophrenia research" in *The Instruments of Psychiatric Research* (ed. C. Thompson, John Wiley & Sons., 1989), p.61.

[24] More detailed explanations of some of the terms will be found in chapter 18.

[25] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.103.

by their rapidly changing and ...riable state. Several types of hallucinations, delusions, and perceptual disturbances are obvious but markedly variable, changing from day to day or from hour to hour. The patient's emotional state is similarly changeable, and perplexity, preoccupation, and inattention are often present. There is usually an abrupt onset (within 48 hours) followed by a rapid resolution of symptoms. If symptoms fulfilling the criteria for schizophrenia have been present for the majority of the time since an obviously psychotic state developed, and these then persist for more than one month, the diagnosis is changed to schizophrenia.[26]

Outcome of acute psychotic episodes

There is some evidence that acute onset is associated with a good outcome, and it may be that the more abrupt the onset, the better the outcome. Abrupt onset is defined as within 48 hours or less. Complete recovery usually occurs within two to three months, often within a few weeks or even days, and only a small proportion of patients with these disorders develop persistent and disabling states.[27]

BORDERLINE AND MIXED MENTAL STATES

In practice, many patients do not conform to stereotypes and the diagnosis is not always clear cut. Some borderline states may be suggestive of a schizophrenic-type process but no more than that. Other patients may have some features indicative of a personality or mood disorder but also some symptoms commonly found in schizophrenia. Following an explanation of the diagnostic guidelines for schizophrenia and its three historical sub-types (**1239**), the following topics are therefore briefly considered —

- schizophrenia and personality disorders (**1243**)
- schizophrenia and borderline states (**1244**)
- schizophrenia and mood disorders (**1247**)

Summary

- A diagnosis of schizophrenia may be appropriate if a certain symptom or symptoms have been present for one month or more.
- In acute cases where the symptoms have not endured for that period, a diagnosis of acute schizophrenia-like psychotic disorder is made or, if the patient's mental state is highly variable and changeable, one of acute polymorphic psychotic disorder.
- In borderline cases, consideration must be given to whether the patient's disorder represents a disorder of the personality and or an amalgam of schizophrenia and a mood disorder.

[26] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.101–102.

[27] *Ibid.*, pp.99–100.

- The normal requirement is that a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any of the groups (a) to (d) below, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of one month or more.
- Conditions meeting these symptomatic requirements but of a duration less than one month (whether treated or not) should initially be diagnosed as acute schizophrenic-like psychotic disorder (**1232**) and reclassified as schizophrenia if the symptoms persist for longer periods. The one-month duration criterion applies only to the specified symptoms and not to any prodromal non-psychotic phase.
- Schizophrenia should not be diagnosed in the presence of overt brain disease or during states of drug intoxication or withdrawal.
- The diagnosis of schizophrenia should not be made in the presence of extensive depressive or manic symptoms unless it is clear that schizophrenic symptoms antedated the affective disturbance.

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SYMPTOMS WHICH IF CLEAR-CUT MAY ALONE ESTABLISH THE DIAGNOSIS

(a) *thought echo, thought insertion or withdrawal, and thought broadcasting;*

The individual's thoughts are being repeated or echoed, but not spoken aloud, within his head (*thought echo*) or they are being broadcast to the outside world (*thought broadcasting*). Some other person, persons or outside forces are placing thoughts in his mind (*thought insertion*) or withdrawing his thoughts from his mind (*thought withdrawal*).

(b) *delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;*

The individual believes that his feelings, impulses, thoughts, sensations, actions or bodily movements are being controlled or influenced by some other person, persons or outside forces (*delusions of influence or control*). He is the passive object of these active outside influences (*passivity phenomena*).

(c) *hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;*

The individual hears imaginary voices commenting on his behaviour or discussing him or hears voices which seem to emanate from somewhere within his body.

(d) *persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world)*

The individual holds some belief which is bizarre, not true to fact, cannot be corrected by an appeal to reason, and is out of harmony with his educational or cultural background (a delusion). The central theme may, *inter alia,* be some absurd exaggeration of his own importance, power, knowledge, or identity (*grandiose delusion*); a belief that events and the actions of others refer to him in some special way, *e.g.* a belief that programmes on the radio are being broadcast to him especially (*delusion of reference*); a belief that he or someone else is being attacked, harassed, cheated, persecuted, or conspired against (*persecutory/paranoid delusion*); or relate to the way his body functions, *e.g.* a false belief that one is pregnant despite being post-menopausal (*somatic delusion*). Delusional beliefs may be fleeting, changeable and unconnected with each other (*unsystematised*) or form part of a logical fixed system of such beliefs (*systematised*).

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OTHER SYMPTOMS

(e) *persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end*

The individual experiences a sensory perception in the absence of any external stimulation of the relevant sensory organ (hallucination). The hallucination may relate to sounds or voices (*auditory hallucination*); sight (*visual hallucination*); taste (*gustatory hallucination*); smell (*olfactory hallucination*); touch (*tactile/haptic hallucination*), or to the perception of a physical experience within the body (*somatic hallucination*), such as the muscles or joints (*kinaesthetic hallucination*) or an internal organ (*visceral hallucination*). An overvalued idea is an irrational belief or idea which is not as firmly held as a delusion.

(f) *breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms*

The patient's stream of thought, and therefore speech, suddenly stops and he is unable to account for this stoppage (thought blocking). He may invent new words (neologisms), which have a known meaning for him and are often an amalgam of real words, *e.g.* "bancid" = "bad" and "rancid." Where the association between successive thoughts is disturbed and successive sentences or topics are only obliquely related (*loosening of associations*), speech becomes inexact, vague, diffused or unfocused. In severe cases, there may be a lack of logical or meaningful connection between words, phrases, or sentences (*incoherence*).

Other symptoms of schizophrenia—cont.

(g) *catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor*

The patient may voluntarily assume some inappropriate or bizarre posture, often held for a long period of time, during which neither expression nor bodily position changes (*cataxtonic posturing*). The muscles of the limbs may be maintained in a semi-rigid position and can be moulded into any position by an examiner, as if made of pliable wax (*catatonic waxy flexibility*). Although conscious, the individual may not respond to external stimuli (*catatonic stupor*) or resist all instructions or attempts to be moved, perhaps doing the opposite of what is asked (*catatonic negativism*). He may be mute. In other cases, there is excited and apparently purposeless motor activity not influenced by external stimuli (*catatonic excitement*).

(h) *"negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication*

Certain symptoms of schizophrenia are sometimes distinguished as being positive or negative. Positive symptoms (such as delusions, hallucinations and disorganised speech) are said to reflect an excess or distortion of normal functions. In contrast, negative symptoms (such as low motivation, lack of initiative, loss of interest, social withdrawal, restricted fluency and productivity of thought and speech, and blunting of affect) appear to reflect a diminution or loss of normal functions. There may be a lack of feeling, emotion, interest or concern (*apathy*) and limited use of speech (*paucity of speech*). Emotional responses may be incongruous.

(i) *a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.*

This category overlaps considerably with that immediately above. A preoccupation with one's own, often overbearing, internal experiences or fantasies will generally lead to a corresponding lack of engagement with the outside world.

Source: Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines (World Health Organisation, 1992), pp.87–88.

THE SUB-TYPES OF SCHIZOPHRENIA

Kraepelin recognised three main sub-types of schizophrenia: catatonic, hebephrenic and paranoid.[28] Paranoid schizophrenia aside, the sub-types have been found to be unstable and heterogeneous over time both with respect to symptom content and outcome. In other words, the persons assigned to each of the three categories show a marked variability both in terms of their symptoms and outcomes.[29] The sub-types of schizophrenia recognised in the ICD–10 classification are listed and described below. Brief notes then follow on the three main sub-types: paranoid, hebephrenic and catatonic schizophrenia. Residual schizophrenia is referred to later in the section on the course and outcome of schizophrenic disorders (**1252**); simple schizophrenia, schizoid personality disorder, and schizotypal disorder in the section on personality and schizophrenia (**1244**); and post-schizophrenic depression in the section on mood and schizophrenia (**1248**).

Schizophrenia : Main sub-types (ICD-10)

F20.6	***Simple Schizophrenia***	A disorder in which there is an insidious but progressive development of oddities of conduct, inability to meet the demands of society, and decline in total performance. The characteristic negative features of residual schizophrenia develop without being preceded by overt psychotic symptoms.
F20.0	***Paranoid Schizophrenia***	Paranoid schizophrenia is dominated by relatively stable, often paranoid delusions, usually accompanied by hallucinations, particularly of the auditory variety, and perceptual disturbances. Disturbances of affect, volition and speech, and catatonic symptoms, are absent or relatively inconspicuous.
F20.1	***Hebephrenic Schizophrenia***	A form of schizophrenia in which affective changes are prominent, delusions and hallucinations fleeting and fragmentary, behaviour irresponsible and unpredictable, and mannerisms common. The mood is shallow and inappropriate, thought is disorganised, and speech is incoherent. There is a tendency to social isolation. Hebephrenia should normally be diagnosed only in adolescents or young adults.

[28] E. Kraepelin, *Textbook of Psychiatry* (MacMillan, 1907).

[29] K.S. Kendler, *et al.*, "Sub-type stability in schizophrenia" *American Journal of Psychiatry* (1985) 142, 827–832; R.E. Kendell, *et al.*, *Prognostic implications of six different definitions of schizophrenia* Arch. Gen. Psych. (1979) 36, 25–31.

F20.2	***Catatonic Schizophrenia***	Catatonic schizophrenia is dominated by prominent psychomotor disturbances that may alternate between extremes such as hyperkinesis and stupor, or automatic obedience and negativism. Constrained attitudes and postures may be maintained for long periods. Episodes of violent excitement may be a striking feature.
F20.5	***Residual Schizophrenia***	A chronic stage in the development of a schizophrenic illness in which there has been a clear progression from an early stage to a later stage characterised by long-term, though not necessarily irreversible, "negative" symptoms, *e.g.* psychomotor slowing; underactivity; blunting of affect; passivity and lack of initiative; poverty of quantity or content of speech; poor non-verbal communication by facial expression, eye contact, and posture; poor self-care and social performance.
F20.4	***Post-Schizophrenic Depression***	A depressive episode, which may be prolonged, arising in the aftermath of a schizophrenic illness. Some schizophrenic symptoms, either "positive" or "negative," must still be present but no longer dominate the clinical picture. These depressive states are associated with an increased risk of suicide.

Disorders resembling or possibly associated with schizophrenia

F21	***Schizotypal disorder***	A disorder characterised by eccentric behaviour and anomalies of thinking and affect which resemble those seen in schizophrenia, though no definite and characteristic schizophrenic anomalies occur at any stage.
F60.1	***Schizoid personality disorder***	A personality disorder characterised by emotional coldness and detachment; limited capacity to express warmth; preference for solitary activities; excessive preoccupation with fantasy and introspection; lack of confiding relationships; marked insensitivity to prevailing social norms and conventions.

PARANOID SCHIZOPHRENIA (F20.0)

Paranoid schizophrenia is the sub-type of schizophrenia most commonly encountered in tribunal proceedings. According to Kraepelin, paranoid schizophrenia is characterised by suspiciousness and well-organised delusions, usually of persecutory or grandiose content.[30]

Clinical picture

The ICD–10 classification describes the clinical picture as dominated by relatively stable, often paranoid, delusions, usually accompanied by hallucinations, particularly of the auditory variety, and perceptual disturbances. Disturbances of affect, volition, and speech, and catatonic symptoms, are not prominent. Thought disorder may be obvious in acute states but does not prevent the typical delusions or hallucinations from being described clearly. Mood disturbances such as irritability, sudden anger, fearfulness, and suspicion are common.[31] Examples of the most common paranoid symptoms are:

- delusions of persecution, reference, exalted birth, special mission, bodily change, or jealousy;
- hallucinatory voices that threaten the patient or give commands, or auditory hallucinations without verbal form, such as whistling, humming, or laughing;
- hallucinations of smell or taste, or of sexual or other bodily sensations; visual hallucinations may occur but are rarely predominant.[32]

Onset and course

The onset tends to be later than in the hebephrenic and catatonic forms.[33] The course of paranoid schizophrenia may be episodic, with partial or complete remissions, or chronic. In chronic cases, the florid symptoms persist over years and it is difficult to distinguish discrete episodes.

Diagnostic guidelines

The diagnostic guidelines are as follows —

- The general criteria for a diagnosis of schizophrenia must be satisfied (**1234**).
- In addition, hallucinations and/or delusions must be prominent, and disturbances of affect, volition and speech, and catatonic symptoms must be relatively inconspicuous.

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30 R.P. Bentall, The classification of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.29.

31 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.89–90.

32 *Ibid.*, p.89.

33 *Ibid.*, pp.89–90.

- The hallucinations will usually be delusions of control, influence or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception; hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body.
- Delusions can be of almost any kind but delusions of control, influence, or passivity, and persecutory beliefs of various kinds are the most characteristic.[34]
- It is important to exclude epileptic and drug-induced psychoses, and to remember that persecutory delusions might carry little diagnostic weight in people from certain countries or cultures.[35]

Delusional disorders (F22.0)

Paranoid schizophrenia is distinguished from paranoid personality disorder (**1185**) and also from paranoid delusional disorders. Delusional disorders are characterised by the development of a single delusion or set of related delusions which are usually persistent and sometimes lifelong. The delusions are often persecutory, hypochondriacal, or grandiose. They may be concerned with litigation or jealousy or a belief that other people think the individual smells or is homosexual. The content of the delusion, and the timing of its emergence, can often be related to the individual's life situation. Onset is commonly in middle age. Depressive symptoms may be present intermittently, and olfactory and tactile hallucinations may develop in some cases. Clear and persistent auditory hallucinations, schizophrenic symptoms such as delusions of control and marked blunting of affect, and definite evidence of brain disease, are all incompatible with the diagnosis. The diagnostic guidelines specify that the delusions must constitute the only or most conspicuous clinical characteristic, have been present for at least three months, and clearly be personal rather than sub-cultural.[36] When the central delusion has a persecutory theme, the disorder is sometimes referred to as paranoia, paranoid psychosis, or a paranoid state. If a paranoid delusional disorder develops in old age, sometimes following loss or deterioration of hearing or eyesight, the term paraphrenia may be used. If paranoid delusions are accompanied by symptoms satisfying the criteria for a diagnosis of schizophrenia, the diagnosis will be one of paranoid schizophrenia (**1239**).

HEBEPHRENIC SCHIZOPHRENIA (F20.1)

According to Kraepelin, hebephrenic schizophrenia was characterised by over-scrupulousness about trivial matters, emotional indifference, laughing and immature speech. Although Schneider did not consider that the condition represented a distinct sub-type, recent research indicates a move backwards to regarding hebephrenia with its preponderantly negative symptoms as a separate disorder.[37]

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34 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.90.

35 *Ibid.*

36 *Ibid.*, pp.97–98.

37 See R.P. Bentall, The classification of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.29.

Clinical picture

The ICD–10 classification describes hebephrenic schizophrenia as "a form of schizophrenia in which affective changes are prominent, delusions and hallucinations fleeting and fragmentary, behaviour irresponsible and unpredictable, and mannerisms common. The disturbances of affect, volition, and thought disorder are usually prominent but, when present, not hallucinations and delusions. The mood is shallow and inappropriate and often accompanied by giggling or self-satisfied, self-absorbed smiling, or by a lofty manner, grimaces, mannerisms, pranks, hypochondriacal complaints, and reiterated phrases. Thought is disorganised and speech rambling and incoherent. A superficial and manneristic preoccupation with religion, philosophy, and other abstract themes may add to the listener's difficulty in following the train of thought. There is a tendency to remain solitary and behaviour seems empty of purpose and feeling.[38]

Onset and course

The form of schizophrenia usually starts between the ages of 15 and 25 years. Hebephrenic schizophrenia tends to have a poor prognosis because of the rapid development of negative symptoms, particularly flattening of affect and loss of volition. Drive and determination are lost and goals abandoned, so that the patient's behaviour becomes characteristically aimless and empty of purpose.[39]

Diagnostic guidelines

The diagnostic guidelines are as follows—

- The general criteria for a diagnosis of schizophrenia (**1234**) must be satisfied.
- Hebephrenia should normally be diagnosed for the first time only in adolescents or young adults.
- The premorbid personality is characteristically, but not necessarily, rather shy and solitary.
- For a confident diagnosis of hebephrenia, a period of two or three months of continuous observation is usually necessary, in order to ensure that the characteristic behaviour is sustained.[40]

CATATONIC SCHIZOPHRENIA (F20.2)

In 1874, Kahlbaum described catatonia as a severe motor disorder consisting of strange attitudes, odd movements and postures, together with stupor and mental deterioration. According to Kraepelin, who believed that some cases of catatonia represented a distinct sub-type of the condition now known as schizophrenia, catatonic schizophrenia is characterised by pronounced motor symptoms and swings from stupor to extreme excitement.

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38 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.90–91.

39 *Ibid.*

40 *Ibid.*, p.91.

Clinical picture

According to the ICD–10 classification, prominent psychomotor disturbances are essential and dominant features and may alternate between extremes such as hyperkinesis and stupor, or automatic obedience and negativism. Constrained attitudes and postures may be maintained for long periods. Episodes of violent excitement may be a striking feature of the condition. These catatonic phenomena may be combined with a dream-like (oneiroid) state with vivid scenic hallucinations.[41]

Onset and course

There is some evidence that catatonic symptoms may be more common in developing countries and also that the condition has become much less common in Europe during the course of this century.[42]

Diagnostic guidelines

- The general criteria for a diagnosis of schizophrenia must be satisfied (**1234**).
- Transitory and isolated catatonic symptoms may occur in the context of any other subtype of schizophrenia but for a diagnosis of catatonic schizophrenia one or more of the following behaviours should dominate the clinical picture:

  a. stupor (marked decrease in reactivity to the environment and in spontaneous movements and activity) or mutism;

  b. excitement (apparently purposeless motor activity, not influenced by external stimuli);

  c. posturing (voluntary assumption and maintenance of inappropriate or bizarre postures);

  d. negativism (an apparently motiveless resistance to all instructions or attempts to be moved, or movement in the opposite direction);

  e. rigidity (maintenance of a rigid posture against efforts to be moved);

  f. waxy flexibility (maintenance of limbs and body in externally imposed positions); and

  g. other symptoms such as command automatism (automatic compliance with instructions), and perseveration of words and phrases.[43]

41 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.91.

42 In one survey of 172 long-term attenders at psychiatric day care units serving a district in South East London, only one person had signs of catatonia, notwithstanding that the patients had an average of 15 years in contact with services. See T.S. Brugha, *et al.*, "The problems of people in long-term psychiatric day care" *Psychological Medicine* (1988) 18, 443–456.

43 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10), supra, pp.91–92.*

Differential diagnoses

Catatonic phenomena are not limited to schizophrenic psychoses but may be associated with organic cerebral disease (*e.g.* encephalitis), other physical disease, metabolic disturbances, alcohol or drugs, and affective illness. Indeed, Wing states that "nowadays, in psychiatric practice, catatonic symptoms are more often observed in people with disorders in the autistic spectrum than in people with schizophrenia."[44] In uncommunicative patients with behavioural manifestations of catatonic disorder, the diagnosis of schizophrenia may have to be provisional until adequate evidence of the presence of other symptoms is obtained.

SCHIZOPHRENIA, PERSONALITY AND MOOD

Many patients to not conform to stereotypes and their conditions do not neatly correspond to the descriptions found in medical textbooks. In some cases, the onset of schizophrenia-type symptoms may be acute or even abrupt and they may then resolve with similar rapidity. Because schizophrenia was originally formulated as an insidious and progressive disease, it is uncertain whether these short-lived conditions represent a form of acute schizophrenia — the onset of schizophrenia in a person whose body is able to deal with it rapidly and effectively — or represent a process which is fundamentally different at some level. Similarly, it is not yet established whether a person can have schizophrenia and yet be symptom-free ("sub-clinical disease"). In other cases, experiences associated with, or suggestive of, schizophrenia may be present but it be unclear whether they are the early "prodromal features" of a developing illness or indicative of a personality disorder. Finally, in the case of people who are obviously psychotic there may exist both symptoms commonly found in schizophrenia and others typical of a mood disorder. Thus, the presentation is often highly complex and many different ideas have been formulated, and terms invented, to describe these borderline and mixed states.

PERSONALITY AND SCHIZOPHRENIA

What constitutes personality and a disorder of the personality has already been considered (**1025, 1175**). Briefly, and by way of recap, personality represents the sum of a person's traits, habits and experiences; the whole system of relatively permanent tendencies, physical and mental, which are distinctive of a given individual.[45] Certain forms of mental disorder are conceived of as disorders of the personality and both legal and medical classifications generally distinguish between personality disorders and mental illnesses. In the International Classification of Diseases, the different types of personality disorder are grouped together in one block (F60-69). However, the dividing line between personality disorders and mental illness may well be arbitrary. The notion of personality describes the tendency of the brain to function in certain habitual ways so that, in many cases, a particular type of personality predisposes the individual to becoming mentally ill in a particular way. For example, a person with a paranoid personality will be more prone to developing the paranoid form of schizophrenia.

44 J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.13.

45 K. Schneider, *Clinical Psychopathology* (5th ed., trans. M.W. Hamilton, Grune & Stratton, 1958).

Schizoid personality disorders (F60.1)

Kretschmer described the "schizoid personality,"[46] by which he meant people with a rich inner life and, consequently, difficulties in making emotional contact with others. A preoccupation with internal fantasies, and a corresponding lack of engagement with the external world, may give rise to unconventional behaviour not far removed from that sometimes seen in cases of schizophrenia. Nevertheless, that behaviour is sometimes interpreted as an expression of the individual's normal — albeit, compared with other people, abnormal — personality, rather than as the consequence of a schizophrenic illness overlying and distorting that personality. The person is often described as having a schizoid personality, and diagnosed as suffering from a schizoid personality disorder. The diagnostic guidelines for schizoid personality disorder are summarised in the table on page 1246.[47]

BORDERLINE STATES (SCHIZOTYPAL DISORDER)

It may sometimes seem improbable that the bizarre beliefs and conduct of an individual who does not meet the criteria for schizophrenia can be accounted for solely in terms of his personality. There is a suspicion that some kind of illness or disease process is contributing to the presentation. When viewed retrospectively, "it may be clear that a prodromal phase in which symptoms and behaviour, such as loss of interest in work, social activities, and personal appearance and hygiene, together with generalised anxiety and mild degrees of depression and preoccupation, preceded the onset of psychotic symptoms by weeks or even months."[48] Many diagnostic terms have been used to describe such borderline states: borderline schizophrenia, latent schizophrenia, latent schizophrenic reaction, pre-psychotic schizophrenia, prodromal schizophrenia, pseudoneurotic schizophrenia, and schizotypal disorder. If no definite and characteristic schizophrenic anomalies have occurred, the latter is the diagnostic term currently used in ICD–10 to describe a disorder characterised by eccentric behaviour and anomalies of thinking and affect which resemble those seen in schizophrenia. There is "no dominant or typical disturbance"[49] but the picture is more common in individuals related to sufferers of schizophrenia and so is believed to be part of the genetic "spectrum"' of schizophrenia. Schizotypal disorders are thought to run a chronic course with fluctuations of intensity — much like a personality disorder in this respect — although occasionally evolving into overt schizophrenia. The diagnostic guidelines for schizotypal disorder are summarised in the table on page 1246.[50] It should, how- ever, be noted that although the diagnostic category is used in the ICD–10 classification, its general use is not recommended because it is not clearly demarcated from simple schizophrenia or from schizoid or paranoid personality disorders.

SIMPLE SCHIZOPHRENIA (F20.6)

Another diagnosis used to describe conditions which do not fit into any of the established sub-types of schizophrenia (paranoid, catatonic and hebephrenic) is that

[46] E. Kretschmer, *Medizinische psychologie* (G. Thieme, 1956).
[47] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.203.
[48] *Ibid.*, p.88.
[49] *Ibid., p.95.*
[50] *Ibid.*, p.203.

of "simple schizophrenia" (*schizophrenia simplex*).[51] This is described in the ICD–10 classification as "an uncommon disorder in which there is an insidious but progressive development of oddities of conduct, inability to meet the demands of society, and decline in total performance. Delusions and hallucinations are not evident, and the disorder is less obviously psychotic than the hebephrenic, paranoid, and catatonic subtypes. The characteristic "negative" features of residual schizophrenia (*e.g.* blunting of affect, loss of volition) develop without being preceded by any overt psychotic symptoms. With increasing social impoverishment, vagrancy may ensue and the individual may then become self-absorbed, idle, and aimless."[52] The ICD–10 classification states that simple schizophrenia is a difficult diagnosis to make with any confidence. This is because it depends on establishing the slowly progressive development of the characteristic "negative" symptoms of residual schizophrenia[53] manifest as a marked loss of interest, idleness, and social withdrawal but without any history of hallucinations, delusions, or other manifestations of an earlier psychotic episode.[54]

SUMMARY

It can be seen from the table on the following page that there is a considerable overlap in the phenomena described in the ICD–10 classification guidelines as constituting the features of schizoid personality disorder, schizotypal disorder, and simple schizophrenia. Indeed, as drafted, the guidelines for diagnosing a schizotypal disorder are arguably more stringent than those set down for simple schizophrenia. Part of the difficulty arises from the very loose criteria adopted for schizophrenia itself, which allow simple schizophrenia to be diagnosed if there is marked social withdrawal but an absence of the positive symptoms associated with the paranoid and catatonic sub-types. In particular, the diagnostic guidelines for schizophrenia are satisfied if there is evidence of the existence for more than one month of symptoms referred to in paragraphs (h) and (i) —

- (h) "negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication
- (i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

As can be seen, social withdrawal and loss of interest are referred to in both paragraphs and their lack of mutual exclusivity means that if a person's behaviour is marked by persistent social withdrawal and emotional introspection it is somewhat arbitrary which diagnosis is used. Perhaps all that can honestly be said is that the diagnostic categories are not mutually exclusive, the product of drafting by committee, and a somewhat unsatisfactory basis for depriving a citizen of his liberty.

[51] The category of simple schizophrenia was added by Bleuler to describe mixed psychotic symptoms which did not fit into any of the three sub-types propounded by Kraepelin: paranoid, catatonic and hebephrenic schizophrenia.
[52] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines, supra,* p.95.
[53] See page 1252.
[54] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines, supra,* p.95.

	Schizoid personality disorder	Schizotypal disorder	Simple Schizophrenia
General behaviour	Marked insensitivity to prevailing social norms and conventions.	Behaviour or appearance that is odd, eccentric, or peculiar.	Insidious but progressive development of oddities of conduct, inability to meet the demands of society, and decline in total performance. There are significant changes in personal behaviour.
Affect	Emotional coldness, detachment or flattened affectivity; few, if any, activities provide pleasure.	Inappropriate or constricted affect. The individual appears cold and aloof.	Blunting of affect, marked loss of interest, idleness.
Rapport	Almost invariable preference for solitary activities. Lack of close friends or confiding relationships and of desire for such relationships.	Poor rapport with others. Tendency to social withdrawal.	Social withdrawal.
Form of thought	No disorder in the form of thought	Vague, circumstantial, metaphorical, overelaborate, or stereotyped thinking, manifested by odd speech or in other ways, without gross incoherence.	No obvious psychotic thought processes.
Content of thought	Excessive preoccupation with fantasy and introspection.	Odd beliefs or magical thinking; suspiciousness or paranoid ideas; obsessive ruminations, often with dysmorphophobic, sexual or aggressive contents; occasional transient quasi-psychotic episodes with delusion-like ideas.	No history of delusions.
Perception	No perceptual disturbances	Unusual perceptual experiences including somatosensory (bodily) or other illusions, depersonalisation or derealisation. Occasional transient quasi-psychotic episodes with intense illusions, auditory or other hallucinations	Hallucinations are not evident.
Notes	A personality disorder.	No definite, characteristic, schizophrenic anomalies have occurred at any stage. 3 or 4 of the above features should have been present, even if only episodically, for at least 2 years. Use of the diagnosis not recommended.	Meets the criteria for schizophrenia set out in the table on pages, *i.e.* symptoms in paras. ((h) and (i) — negative symptoms and social withdrawal.

Some of the patient's symptoms may commonly be present in a schizophrenic illness and others characteristically present in persons suffering from a mood (affective) disorder. Because most psychiatric syndromes shade into one another, psychiatrists are forced to resort to employing terms such as schizoaffective disorder to describe mental states in which are found symptoms characteristic of more than one type of disorder.

Schizoaffective disorders (F25)

According to the ICD–10 classification, schizoaffective disorders are "episodic disorders in which both affective and schizophrenic symptoms are prominent within the same episode of illness." The diagnostic guidelines are that the diagnosis should be made only when both definite schizophrenic and definite affective symptoms are prominent simultaneously, or within a few days of each other, within the same episode of illness and when, as a consequence of this, the episode of illness does not meet criteria for either schizophrenia or a depressive or manic episode. The diagnostic category should not be applied to (a) conditions in which affective symptoms are superimposed upon or form part of a pre-existing schizophrenic illness or (b) to patients who exhibit schizophrenic symptoms and affective symptoms only in different episodes of illness; for example persons suffering from post-schizophrenic depression (**1248**). Three sub-types are recognised, depending upon whether the affective symptoms are those of mania ("schizoaffective disorder, manic type"), or of depression ("schizoaffective disorder, depressive type"), or of both ("schizoaffective disorder, mixed type).[55]

Schizo-affective disorder, manic type (F25.0)

There must be a prominent elevation of mood, or a less obvious elevation of mood combined with increased irritability or excitement. Within the same episode, at least one and preferably two of typically schizophrenic symptoms set out in paragraphs (a)-(d) on page 1234 should be clearly present. Such disorders are usually florid psychoses with an acute onset. Although behaviour is often grossly disturbed, full recovery generally occurs within a few weeks.[56]

Schizoaffective disorder, depressive type (F25.1)

There must be prominent depression, accompanied by at least two of the characteristic depressive symptoms or associated behavioural abnormalities listed for depressive episode (**1204**). In addition, at least one and preferably two of the symptoms typical of schizophrenia (**1234**, paras. (a)-(d)) should be clearly present within the same episode. Schizoaffective episodes of the depressive type are usually less florid and alarming than schizo-affective episodes of the manic type, but tend to last longer and the prognosis is less favourable. Although the majority of patients recover completely, some eventually develop a schizophrenic defect.[57]

[55] *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.105–106.
[56] *Ibid.*, pp.106–107.
[57] *Ibid.*, pp.107–108.

Post-schizophrenic depression (F20.4)

A depressive episode, sometimes prolonged, may arise in the aftermath of a schizophrenic illness and such episodes are associated with an increased risk of suicide.[58] Some schizophrenic symptoms must still be present but no longer dominate the clinical picture. It is uncertain to what extent the depressive symptoms have merely been uncovered by the resolution of earlier psychotic symptoms (rather than being a new development) or are an intrinsic part of schizophrenia (rather than a psychological reaction to it). They are rarely sufficiently severe or extensive to meet criteria for a severe depressive episode and it is often difficult to decide which of the patient's symptoms are due to depression, which to neuroleptic medication, and which to the schizophrenia itself.

EPIDEMIOLOGY, AETIOLOGY AND PATHOLOGY

Once a discrete psychiatric disorder has been identified, evidence may be acquired about its prevalence and distribution (epidemiology), causes (aetiology) and pathology.

EPIDEMIOLOGY

How many people suffer from schizophrenia depends upon how the disorder is defined. The epidemiological findings have been summarised by Kendell.[59] The lifetime risk of developing the disorder is in the region of 0.85–1.00 per cent. The incidence of the disorder (the annual rate of new cases) is approximately 10–15 new cases per 100,000 population. The age of onset of is characteristically between the ages of 15 and 45. Although the disorder is as common in males and females, males are on average first admitted to hospital some four to five years earlier.[60] The disorder is more prevalent among persons in the lower socio-economic groups, a phenomenon which has, not wholly convincingly, been explained in terms of a downward drift in the social scale because of the disabling nature of the disorder.[61] Similarly, it is more common in urban than rural areas, particularly in the centres of large cities. This may again be a result of downward drift and migration to bedsits and hostels rather than a cause of the disorder. There is some evidence to support the propositions that (1) schizophrenia became much commoner towards the end of the eighteenth century and its prevalence increased during the next hundred years;[62] and (2) during the present century, the hebephrenic and catatonic forms have become much less common and paranoid schizophrenia considerably more common. The

58 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), pp.93–94.

59 R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), pp. 406–409.

60 H. Hafner, *et al.*, "How does gender influence age at first hospitalisation for Schizophrenia?" *Psychological Medicine* 19: 903–918.

61 E.M. Goldberg and S.L. Morrison, "Schizophrenia and social class" *British Journal of Psychiatry* (1963) 109: 785–802.

62 See R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies, supra,* p.407; E.H. Hare, "Schizophrenia as a recent disease" *British Journal of Psychiatry* (1988) 153: 521–531; J.M. Eagles and L.J. Whalley, "Decline in the diagnosis of schizophrenia among first admissions to Scottish mental hospitals from 1969–78" *British Journal of Psychiatry* (1985) 146: 151–154. As to possible explanations, see J.K. Wing, "Differential diagnosis of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.19.

incidence is significantly higher in unmarried persons and sufferers have reduced fertility prior to admission. Research has tended to show that migrants are more likely to suffer from schizophrenia but, within the context of immigration to the United Kingdom, political considerations have made objective discussion of the studies difficult.[63] Persons suffering from schizophrenia are more likely to have been born during the winter months (January to March) and correspondingly less likely to have been born during the summer (July to September). It appears that outcome is more favourable in economically developing countries: "despite the much more extensive follow-up treatment in the industrial countries, a high proportion of their patients had further psychotic episodes, whereas Columbian, Nigerian and Indian patients did not."[64]

AETIOLOGY AND PATHOLOGY

The aetiology of a disease consists of the postulated causes that initiate the disease process, control of which may lead to its prevention. In the case of schizophrenia, the considerable research during the past century "has not produced the discovery of a specific cause. It seems probable that such a cause does not exist."[65] Virtually every variable known to influence human conduct has at one time been implicated as a potential cause of schizophrenia; aetiological hypotheses have included genetic endowment, abnormalities of brain structure and neurochemistry, diet, viral agents, birth complications, the socio-economic environment, unpleasant life events, and family structure.[66]

Neuropathology

The majority of controlled studies have shown some pathological changes in the medial temporal lobe, probably as a result of damage before birth, with abnormalities usually more prominent on the left side of the brain. This may indicate damage before birth and reflect an increased incidence of obstetric complications. It is usually the lower birth weight twin who becomes psychotic, raising the possibility that schizophrenia is a neurodevelopmental disorder. Where one identical twin has developed schizophrenia but not the other, in the vast majority of cases both lateral ventricles were larger, and both hippocampi smaller, in the affected twin. Three-quarters of CT studies have shown modest ventricular enlargement in persons diagnosed as having schizophrenia although this does not then increase, suggesting that any enlargement precedes onset rather than developing as the disorder progresses. There is some evidence that the brains of persons with schizophrenia are shorter and lighter, weighing about six per cent less. There is also some evidence of a reduction in the number of cells in certain parts of the brain and of abnormalities of cerebral blood flow and eye-tracking movements. However, no neurological peculiarities are present in all cases of schizophrenia, either before or after the onset of the illness, and they can also be found in some non-sufferers. None of the abnormalities are therefore universally present, some of them are not specific to schizophrenia, and all of them may be contradicted by later research or susceptible to alternative interpretations.

63 For an analysis of the reliability of the studies, see R.E. Kendell, "Schizophrenia," *supra,* pp. 407–408.

64 *Ibid.*, p.416.

65 M. Bleuler, "The Concept of Schizophrenia in Europe During the Past One Hundred Years" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.7.

66 R.P. Bentall, "The classification of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.24.

Genetics and constitutional factors

While the current evidence indicates a genetically transmitted component in schizophrenia, the concordance rate in identical twins is less than 50 per cent. and this therefore only partially accounts for the disorder's development.[67] The 20–30 year delay before the onset of the psychosis is explained in maturational terms, by the fact that certain key developments in the brain and nervous system are incomplete until or after puberty.[68]

Biochemical factors

It is well established that the ingestion of certain drugs which increase dopaminergic activity, for example amphetamines, can produce a psychotic state which is virtually indistinguishable from that seen in schizophrenia. Conversely, antipsychotic drugs effective in the treatment of schizophrenia block dopamine receptors and reduce dopamine levels. It is therefore likely that there is a biochemical component to the disorder.

Social and environmental factors

Whatever the biological basis of the disorder, "careful investigations over several decades have revealed an important role for social factors, both in the onset and in the relapse of schizophrenia. Hence, there is ample opportunity for appropriate social management to improve the outlook for patients, although preventative measures so far remain elusive."[69] It appears that the role played by life events is as important for the first episode of schizophrenia as it is for subsequent attacks and the crucial period is the three weeks immediately prior to onset.[70] Schizophrenia tends to recur in families and familial factors are therefore involved in its development. There is evidence that prolonged over-dependence on the mother is common as are homes in which the parents live under the same roof but in a state of mutual withdrawal. It is also possible that factors implicit in low socio-economic status, such as poor living conditions, contribute to the aetiology of schizophrenia.[71]

67 Twin studies demonstrate a 50 per cent. concordance for identical (monozygotic) twins and a 17 per cent. concordance for non-identical (dizygotic) twins. The concordance rates for identical twins reared apart is generally similar. This suggests a genetic component, a neurodevelopmental problem specific to identical twins, or the development of particular personality traits and ways of interacting with others within the womb. The principal methods for identifying mode of transmission are known as segregation analysis and genetic linkage analysis. No precise mode of inheritance has been established. A major series of genetic investigations, referred to by Bentall, *supra*, p.32, failed to find evidence that schizophrenia is inherited when only breakdowns leading to hospitalisation are considered. This led to the concept of schizotypal personality disorder being developed, and the suggestion that what is inherited is a polygenically determined vulnerability to schizophrenia which a person may have to a greater or lesser degree.

68 R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), p.414.

69 J. Leff, "Schizophrenia: social influences on onset and relapse" in Community Psychiatry: The Principles (ed. D.H. Bennett & H.L. Freeman, Churchill Livingstone, 1991), p.189.

70 *Ibid.*, p.194.

71 *Ibid.*, p.192.

COU. SE AND OUTCOME

Historically, schizophrenia was believed to run a progressive downhill course while affective disorders relapsed repeatedly but recovered fully each time. However, "it is now clear that this is not so, or perhaps no longer so. Not only is the long-term prognosis much better than we used to believe, the course of the illness is very variable."[72] Although it remains true that patients with affective illnesses are more likely to make a full recovery from their original illness, there is this considerable individual variation.[73] The outcome varies between prolonged recovery, intermittent course, and prolonged psychosis of severe or mild degrees.[74]

DESCRIBING THE LONGITUDINAL COURSE AND OUTCOME

Recovery aside, schizophrenic disorders may be continuous (prominent symptoms are present throughout the observation period) or episodic (the episodes being defined by the re-emergence of prominent psychotic symptoms). The degree of deficit apparent during successive episodes may be stable or progressively worsen. Remission may be natural or a response to treatment. Where the illness is continuous, only partially remits, or there are residual symptoms, it is important to assess whether there are prominent negative symptoms.

PATTERNS OF OUTCOME

Approximately one-third of patients diagnosed as suffering from schizophrenia completely recover from their illnesses, one-third show an intermediate outcome, and in one-third of cases the illness takes the traditional deteriorating course.[75] More specifically, four patterns of outcome can be identified —

- Some resolve completely, with or without treatment, and never recur (Pattern A)
- Some recur repeatedly with full recovery every time (Pattern B)
- Others recur repeatedly but recovery is incomplete; there is a lasting damage to the personality ("persistent defect state") that characteristically becomes more pronounced after each successive relapse (Pattern C)
- Some illnesses pursue a downhill progressive course from the beginning (Pattern D).

The relative frequency of these different outcomes depends a great deal on how schizophrenia is defined. Thus, Kendell observes that if it is defined to exclude patients with prominent affective symptoms, or restricted to patients with a six-month history of schizophrenia, the proportion of patients making a full recovery is

72 R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), p.416.

73 *Ibid.*, p.449.

74 M. Bleuler, "The Concept of Schizophrenia in Europe During the Past One Hundred Years" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.5.

75 M. Bleuler, "The long-term course of schizophrenic psychoses" in *The Nature of Schizophrenia* (ed. L.C. Wynne *et al.*, Wiley, 1978), pp.631–640; L. Ciompi, "Is there really a schizophrenia?; the long-term course of psychotic phenomena" *British Journal of Psychiatry* 145, 636–640.

reduced. The prognosis is relatively good in about 50 per cent. of cases (terms A and B). In patterns C and D, a defect state develops characterised by emotional blunting and apathy, and often accompanied by the faded remnants of previous delusions and hallucinations. On the whole, patients do not deteriorate further after the first 5–10 years.

Residual schizophrenia (F20.5)

The negative symptoms of schizophrenia, which are features of Patterns C and D, include underactivity; blunting of affect; passivity and lack of initiative; poverty of quantity or content of speech; poor non-verbal communication by facial expression, eye contact, voice modulation, and posture; poor self-care and social performance; and psychomotor slowing (1231). They are not necessarily irreversible. When a chronic schizophrenic process develops characterised by such long-term negative symptoms, this may be categorised as residual schizophrenia. The diagnostic guidelines are essentially threefold. There must be historical evidence of at least one clear-cut psychotic episode meeting the diagnostic criteria for schizophrenia; prominent "negative" symptoms present for a period of a year or more, during which the intensity and frequency of florid symptoms, such as delusions and hallucinations, have been minimal or substantially reduced; the negative symptoms cannot be accounted for in terms of chronic depression, institutionalism, or an organic brain disease such as dementia.[76]

PREDICTING THE OUTCOME

Experience shows that no matter how the diagnosis is formulated it never ensures a predictable course and outcome. Nevertheless, Vaillant demonstrated that a simple rating scale based on the presence or absence of seven items predicted outcome with 80 per cent. accuracy.[77] The circumstances of the illness and the patient's premorbid personality tend to determine outcome more than the symptomatology. Illnesses that develop acutely in response to stress have a much better prognosis. Being married and a normal premorbid personality are associated with a good outcome while low intelligence, early age of onset, insidious development, a poor work record, prominent schizoid personality traits, and emotional blunting with a bad outcome.[78] The prognosis for men is worse than for women and patients with enlarged ventricles tend to be male, to have poor premorbid adjustment, early age of onset, poor cognitive performance and poor prognosis.[79] Gelder has very usefully summarised the factors associated with a good and poor prognosis according to research studies.

76 *Classification of Mental and Behavioural Disorders, Tenth Revision (ICD–10): Clinical descriptions and diagnostic guidelines* (World Health Organisation, 1992), p.94.

77 See Manfred Bleuler, "The Concept of Schizophrenia in Europe During the Past One Hundred Years" in *What is Schizophrenia?* (ed. W.F. Flack, *et al.*, Springer-Verlag, 1990), p.5; R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), pp.414–15.

78 J.H. Stephens, *et al.*, "Long term prognosis and follow up in schizophrenia" *Schizophrenia Bulletin* (1978) 4, 25–47; J.A. Lieberman and S.N. Sobel, "Predictors of treatment response in course of schizophrenia" *Current Opinion in Psychiatry* (1993) 6, 63–69; R.E. Kendell, "Schizophrenia," *supra*, p.415.

79 These items are acute onset (in this context within the previous six months); a stressful event or situation at the time of onset; a family history of depressive illness; no family history of schizophrenia; no schizoid traits in the premorbid personality; confusion or perplexity; prominent affective symptoms. See R.E. Kendell, "Schizophrenia," *supra*, p.410.

FACTORS PREDICTING OUTCOME — GELDER ET AL. (1996)

Good prognosis	*Poor prognosis*
▪ Sudden onset	▪ Insidious onset
▪ Short episode	▪ Long episode
▪ No previous psychiatric history	▪ Previous psychiatric history
▪ Prominent affective symptoms	▪ Negative symptoms
▪ Paranoid type of illness	▪ Enlarged lateral ventricles, male gender
▪ Older age at onset	▪ Younger age at onset
▪ Married	▪ Single, separated, widowed, divorced
▪ Good psychosexual adjustment	▪ Poor psychosexual development
▪ Good previous personality	▪ Abnormal previous personality
▪ Good work record	▪ Poor work record
▪ Good social relationships	▪ Social isolation
▪ Good compliance	▪ Poor compliance

Source: M. Gelder, et al, Oxford Textbook of Psychiatry (Oxford University Press, 3rd ed., 1996), p.283.

MANAGEMENT AND TREATMENT

Outcome is affected, for better and worse, by treatment and by social and environmental influences. It is not possible to predict which patients will respond to antipsychotic medication nor to distinguish those patients who will make a natural recovery from those who will require medication in order to improve.[80] It appears that the number of patients receiving medication who relapse within a given period is about half that of patients taking a placebo.[81] Nevertheless, medication probably only postpones rather than prevents relapse.[82] Medication and social intervention appear to produce the best outcome and psychotherapy adds little.[83]

80 J.M. Davis, *et al.*, "Important issues in the drug treatment of schizophrenia" *Schizophrenia Bulletin* (1980) 6, 70–87.

81 G.E. Hogarty and R. Ulrich, "Temporal effects of drug and placebo in delaying relapse in schizophrenic out-patients" *Archives of General Psychiatry* (1977) 34, 297–301; M. Gelder, *et al.*, *Oxford Textbook of Psychiatry* (Oxford University Press, 3rd ed., 1996), p.287.

82 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.230.

83 Quality Assurance Project, "Treatment outlines for the management of schizophrenia" *Australian and New Zealand Journal of Psychiatry* (1984) 18, 19–38. See M. Lader and R. Herrington, *Biological treatments in psychiatry, supra*, p.228.

ANTIPSYCHOTICS

The major therapeutic effects of these drugs are seen when they are used to treat acute psychoses. Their effects include a reduction of positive symptoms such as hallucinations, delusions and thought disorder. There is also a normalisation of psychomotor disturbance (excitement or retardation) and information processing. Although the sedative effects are immediate, the antipsychotic effects take up to three weeks to become evident in the case of schizophrenia.[84] Antipsychotics are also used in the long-term treatment of patients in remission (maintenance therapy).

Efficacy

There is no doubt that antipsychotics have a major effect on the symptoms of acute schizophrenic illnesses but patients with chronic symptoms generally respond less well. In acute cases, the condition is kept in check so that the acute, initial attack is cut short and subsequent relapses minimised.[85] However, none of the drugs has a curative action and perhaps half of all patients with a diagnosis of schizophrenia show little or no response to "typical" antipsychotic drugs.[86]

Long-term benefits

While the long-term course of chronic disorders may be altered, in terms of the time spent in hospital, there is little doubt that the effects on the long-term prognosis are less impressive than the short-term effects. A "disturbingly high proportion still remain chronically handicapped by defect states or recurring hallucinations and delusions and still require repeated admissions to hospital despite long-term drug therapy."[87] The efficacy of antipsychotic medication in chronic schizophrenia is therefore less clear and some trials have failed to demonstrate any drug-placebo difference. Negative, or deficit, symptoms. such as apathy, poverty of speech and social withdrawal, persist over time, even during remissions, and are difficult to treat. It is these symptoms which usually predominate in the chronic stage.[88]

Maintenance therapy

Because some 20–30 per cent. of patients recover from a first attack of a schizophrenic-type illness without any recurrence, the benefits of long-term maintenance medication are less clear-cut in such cases. Thus, 46 per cent. of patients receiving medication and 62 per cent. of patients on placebo in a large Northwick Park study of first episodes of schizophrenia relapsed during the two year period following discharge.[89]

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84 B.K. Puri and P.J. Tyrer, *Sciences Basic to Psychiatry* (Churchill Livingstone, 1992), p.126.

85 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.227.

86 See R.P. Bentall, "The classification of schizophrenia" in *Schizophrenia — An overview and practical handbook* (ed. D.J. Kavanagh, Chapman & Hall, 1992), p.26. As to the efficacy of more recently introduced "atypical" antipsychotics (clozapine, olanzapine, risperidone and sertindole) in cases refractory to treatment with the older, "typical," antipsychotics, see **1256**.

87 R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), p.416.

88 *Ibid.*, p.417.

89 E.C. Johnstone, *et al.*, "The Northwick Park study of first episodes of schizophrenia. I. Presentation of the illness and problems relating to admission" *British Journal of Psychiatry* (1986) 148, 115–120.

ANTIPSYCHOTICS — CHEMICAL GROUPS

Chemical group	*Drug*	*General characteristics*
	Phenothiazines	
▪ *Group 1 — aliphatic phenothiazines*	• Chlorpromazine (Largactil) • Methotrimeprazine • Promazine (Sparine)	Pronounced sedative effects, moderate antimuscarinic and extrapyramidal side-effects.
▪ *Group 2 — piperidines*	• Pericyazine • Pipothiazine • Thioridazine (Melleril)	Moderate sedative effects, marked antimuscarinic effects but fewer extrapyramidal effects than groups 1 and 3.
▪ *Group 3 — piperazines*	• Fluphenazine (Modecate) • Perphenazine • Prochlorperazine • Trifluoperazine (Stelazine)	Fewer sedative effects, fewer antimuscarinic effects but more pronounced extrapyramidal effects than groups 1 and 2.
	Other chemical groups	
▪ *Butryophenones*	• Benperidol • Droperidol • Haloperidol (Haldol, Serenace)	These three groups are similar to Group 3 (the piperazines) in having relatively few sedative and autonomic (antimuscarinic) effects but pronounced extrapyramidal effects.
▪ *Diphenylbutyl-piperidines*	• Fluspirilene • Pimozide (Orap)	
▪ *Thioxanthenes*	• Flupenthixol (Depixol) • Zuclopenthixol (Clopixol)	
▪ *Substituted benzamides*	• Sulpiride	These drugs specifically block D_2 dopamine receptors whereas other antipsychotic drugs block both D_1 and D_2 receptors. It is possible that there may be a reduced risk of tardive dyskinesia and of other adverse effects.
▪ *Dibenzoxazepine*	• Loxapine	Chemically similar to the other antipsychotics but may have a lower incidence of extrapyramidal effects. Also has no endocrine effects.
▪ *Miscellaneous*	• Oxypertine	Oxypertine may be used to treat anxiety.
	Miscellaneous "atypical" antipsychotics	
▪ *Miscellaneous*	• Clozapine	Clozapine is different from other antipsychotic. It blocks serotonin, alpha-adrenergic and histamine receptors with much less dopamine receptor-blocking activity. It may be effective in patients resistant to other compounds.
	• Olanzapine	Olanzapine is a novel antipsychotic which affects dopaminergic, serotonergic, muscarinic and adrenergic activities.
	• Risperidone	Studies suggest that it is less likely than haloperidol to induce extrapyramidal movement disorders.
	• Sertindole	Activity appears to be specific to D_2, 5-HT2 and alpha-1 adrenergic receptors and largely confined to the limbic dopamine system.

Choice of antipsychotic

Which drug is prescribed will depend upon the degree of psychosis, whether sedation is desirable, whether side-effects are tolerable, the degree of compliance, the patient's drug history, the clinician's familiarity with the different drugs, and the age of the patient. Antipsychotics vary significantly both in terms of their pharmacokinetics and pharmacodynamics but there is little evidence of consistent superiority of one compound over another, with the exception of clozapine and possibly risperidone.[90] A patient may respond well to one but badly to another similar drug.

Clozapine

Clozapine is the only drug which has been demonstrated to significantly improve the condition of patients who fail to respond to conventional antipsychotics. About half of the people within this treatment-resistant group respond to the drug. Improvement has been noted in both negative and positive symptoms although patients with paranoid ideation and thought disorder may benefit the most. It is also the case that most of the side-effects associated with the conventional drugs do not occur with clozapine. In particular, it is not known to cause tardive dyskinesia or akathisia. Against this, the drug has a damaging effect on the white blood cells of a small minority of patients.[91] Consequently, all patients taking clozapine must have regular blood tests, initially weekly and then fortnightly. If laboratory results are sufficiently adverse, this leads to the treatment's cessation. Bearing these factors in mind, Cutting has suggested that the general guidelines for prescribing the drug should be as follows: (1) it should only be given to people with schizophrenia if they have not done well with at least three conventional anti-schizophrenic drugs at proper doses; (2) the diagnosis must be quite definite; (3) after an initial period of weaning off the other conventional drugs (about three months), no other anti-schizophrenic drugs are needed; (4) the dose of clozapine can be reduced with time; whether or not a person responds to clozapine is obvious within two months.[92]

Olanzapine

The evidence suggests that olanzapine is superior to haloperidol and is relatively well tolerated.[93] It appears to be significantly more likely to improve negative symptoms, such as affective blunting and apathy.[94] It is reported to be effective in maintaining clinical improvement in patients who have responded to initial treatment.[95] The most common side effects are somnolence and weight gain, but sexual dysfunction may be less likely.

90 M. Gelder, *et al.*, *Oxford Textbook of Psychiatry* (Oxford University Press, 3rd ed., 1996), p.286. The therapeutic advantage of "atypical antipsychotics" has been attributed to alpha-2 adrenergic antagonist effects. D.J. Nutt, "Putting the 'A' in atypical: does alpha-2 adrenoceptor antagonism account for the therapeutic advantage of new antipsychotics?" *Journal of Psychopharmacology* (1994) 8, 193–5.

91 Clozapine was developed in the late 1950s but withdrawn from clinical studies in the 1970s because of a two per cent. incidence of agranulocytosis.

92 J. Cutting, *Open Mind* (December 1993) 66, 28.

93 G.D. Tollefson, *et al.*, "Olanzapine versus haloperidol in the treatment of schizophrenia and schizoaffective and schizophreniform disorders; results of an international collaborative trial" *American Journal of Psychiatry* (1997) 154(4) 457–465; G.D. Tollefson, *et al.*, "Olanzapine versus haloperidol in the treatment of first episode psychosis" *Schizophrenia Research* (1997) 24, Issues 1 and 2).

94 G.D. Tollefson and T.M. Sanger, "Negative Symptoms: a path-analytic approach to a double-blind, placebo and haloperidol-controlled clinical trial with olanzapine" *American Journal of Psychiatry* (1997) 154(4) 466–473

95 *British National Formulary* (British Medical Association and the Royal Pharmaceutical Society of Great Britain, March 1997) 33, 161.

Risperidone

Risperidone is an antipsychotic for patients who have not responded satisfactorily to at least two conventional antipsychotics.[96] It may have an antidyskinetic effect. Although risperidone-induced extrapyramidal reactions have been reported,[97] the drug is less likely to cause extrapyramidal effects than conventional antipsychotics.[98] Efficacy in the treatment of negative symptoms, and the drug's long-term efficacy, have yet to be firmly established.[99] Side effects include sedation, headache, insomnia, anxiety, agitation and extrapyramidal symptoms (approximately 20 per cent. of patients).

Sertindole

Sertindole is licensed for the treatment of acute and chronic schizophrenia and schizoaffective psychoses, including positive and negative symptoms. Its advantages are said to include efficacy in respect of negative as well as positive symptoms, a lack of sedation, and the fact that extrapyramidal symptoms do not exceed those of placebo (thereby improving long-term compliance).[100] Postural hypotension can occur if treatment is initiated too quickly. However, the drug "is associated with QT interval prolongation which may lead to serious ventricular arrhythmias (abnormal heart rhythm)."[101]

Dosage

Individual responses to antipsychotic drugs are very variable and to achieve optimum effect, dosage and dose interval must be titrated according to the patient's response.[102] The correct dosage is that which adequately controls the patient's psychopathological state and behaviour with minimal side-effects.[103] In general terms, a whole series of controlled trials have failed to demonstrate any general advantage in prescribing very high doses — what the Americans call "heroic doses" — and many patients respond to quite low doses.[104] After stabilisation, the long half-life of antipsychotics allows the total daily dose to be given as a single dose in most cases.

96 Chouinard, *et al.*, "A Canadian Multicenter placebo–controlled study of fixed doses of risperidone and haloperidol in the treatment of chronic schizophrenia patients" *Journal of Clinical Psychopharmacology* (1993) 13(1), 25–40; Guy Edwards J., "Risperidone for schizophrenia" *British Medical Journal* (1994) 308,1311–12.

97 T. Mahmood, "Risperidone–induced extrapyramidal reactions" *Lancet* (1995) 346, 1226.

98 *British National Formulary* (British Medical Association and the Royal Pharmaceutical Society of Great Britain, March 1997) 33, 161.

99 G. Robert, *Risperidone for the treatment of refractory schizophrenia* (Research and Development Directorate, 1995)

100 B. Green, *Focus on Sertindole* (Priory Lodge Education, 1997); D.P. Van Kammen, *et. al.*, "A randomised, controlled, dose-ranging trial of sertindole in patients with schizophrenia" *Psychopharmacology* (1996)124, 168–175.

101 *British National Formulary (British Medical Association and the Royal Pharmaceutical Society of Great Britain, March 1997) 33, 161.* European restrictions include ECG monitoring before and during sertindole therapy i.e. at 1–2 weeks, after 4–6 weeks, after six months, and yearly thereafter. The purpose of the pre-treatment ECG being to exclude patients whose QT interval is already prolonged and to avoid prescribing other drugs concurrently which also have this effect, e.g. tricyclic and tetracyclic antidepressants. The drug is contraindicated in patients who have significant cardiac disease.

102 *British National Formulary* (British Medical Association and Royal Pharmaceutical Society of Great Britain , March 1996) 31, 161.

103 M. Lader and R. Herrington, *Biological treatments in psychiatry*, *supra*, p.244.

104 For a summary of these studies, see *ibid.*, pp.244–245.

ANTIPSYCHOTIC DRUGS – NON-DEPOT PREPARATIONS (BNF 4.2.1)

Drug	*Proprietary*	*B.N.F. Indications*	*BNF guideline doses*	*Notes*
Chlorpromazine Hydrochloride (CPZ)	• Chlorpromazine (tablets, oral sol., injection, suppositories) • Largactil (tablets, syrup, suspension, injection)	Schizophrenia and other psychoses, mania, short-term adjunctive management of severe anxiety, psychomotor agitation, excitement, and violent or dangerously impulsive behaviour.	By mouth initially 75mg daily, usual maintenance dose of 75–300mg daily but up to 1g daily may be required in psychoses. By deep IM injection for relief of acute symptoms, 25–50mg every 6–8 hours.	Marked sedative properties with tranquillisation, indifference to surroundings and injuries, lack of temperature control, coupled with retention of mental facilities (orig., "lobotomie pharmacologique"): See Lader and Herrington, 2nd ed., p.217. Extrapyramidal symptoms (**1146**), reversed by dose reduction or antimuscarinic drugs (**1149**).
Benperidol	• Anquil (tablets)	Control of deviant antisocial sexual behaviour.	0.25-1.5 mg. daily adjusted according to response.	Contra-indications and side-effects, see haloperidol.
Clozapine	• Clozaril (tablets)	Schizophrenia in patients unresponsive to, or intolerant of, conventional antipsychotic drugs.	Initial dose of 12.5mg once or twice on first day. If tolerated, slowly increased. Maximum dose 900 mg daily. Usual antipsychotic dose 200–450mg daily. Usual maintenance dose 150–300mg daily.	See **1256**. More sedating than chlorpromazine. Extrapyramidal symptoms may occur less frequently and less likely to cause tardive dyskinesia. High incidence of antimuscarinic symptoms. Other side-effects include neutropenia and agranulocytosis. Only initiated in hospital setting. Special patient registration and monitoring required. Risk of rebound psychosis if abruptly withdrawn.
Droperidol	• Droleptan (tablets, oral liquid, injection)	Tranquillisation and emergency control in mania.	By mouth 5–20mg repeated every 4–8 hours if necessary. By IM injection, up to 10mg repeated every 4–6 hours if necessary. By IV injection, 5–15mg repeated every 4–6 hours if necessary.	Contra-indications and side-effects, see haloperidol.
Flupenthixol	• Depixol (tablets; depot injection see **1263**) • Fluanxol	Schizophrenia and other psychoses, particularly with apathy and withdrawal but not mania or psychomotor hyperactivity.	Initially 3–9mg twice daily adjusted according to response; maximum 18 mg. daily.	Less sedating than chlorpromazine ℔ higher incidence of extrapyramidal symptoms (**1146**) — 25 per cent. of patients. To be avoided in senile confusional states, excitable and overactive patients.

Fluphenazine Hydrochloride	• Moditen (tablets, depot injection see **1263**)	*As for chlorpromazine*	Schizophrenia and other psychoses, mania — by mouth initially 2.5–10mg daily, adjusted according to response to 20mg daily. Daily doses above 20mg "only with special caution."	Less sedating than chlorpromazine and fewer antimuscarinic or hypotensive symptoms. However, high incidence of extrapyramidal symptoms, particularly akathisia and dystonic reactions. To be avoided in depression.
Haloperidol	• Haloperidol (tablets) • Dozic (oral liquid) • Haldol (tablets, oral liquid, injection, depot injection) • Serenace (tablets, capsules, oral liquid, injection)	*As for chlorpromazine*	By mouth initially 1.5–3mg twice or thrice daily; 3–5mg twice or thrice daily in severely affected or resistant patients. In resistant schizophrenia up to 100mg (rarely 200mg) may be needed; adjusted according to response to lowest effective maintenance dose (as low as 5–10mg daily). By IM injection, 2–10mg with subsequent doses every 4–8 hours according to response (up to hourly if necessary) — severely disturbed patients may require initial dose of up to 30mg.	Less sedating than chlorpromazine and fewer antimuscarinic or hypotensive symptoms. However, high incidence of extrapyramidal symptoms, particularly akathisia and dystonic reactions.
Loxapine	• Loxapac (capsules)	Acute and chronic psychoses	Initially 20–50mg daily, increased as necessary over 7–10 days to 60–100mg daily. Maximum 250mg daily, usual maintenance dose of 20–100mg daily.	Side-effects similar to chlorpromazine but no endocrine effects yet reported. Nausea and vomiting, ptosis, hyperpyrexia, paraesthesia have been reported.
Methotrimeprazine	• Nozinan (tablets)	Schizophrenia; as an adjunctive treatment in terminal care.	By mouth, initially 25–50mg (bedpatients 100–200mg) daily, increased as necessary to 1g daily.	More sedating than chlorpromazine. Risk of postural hypotension particularly in patients over 50 years of age.
Olanzapine	• Zyprexa (tablets)	Schizophrenia		See **1256**. Limited experience of its use. May be fewer extrapyramidal side-effects than with CPZ. Said to be effective in maintaining clinical improvement.
Oxypertine	• Oxypertine (tablets, capsules)	*As for chlorpromazine*	Initially 80–120mg daily, adjusted according to response. Maximum 300 mg daily.	Extrapyramidal symptoms may be less frequent than with chlorpromazine. With low doses agitation and hyperactivity may occur and with high doses sedation.
Pericyazine	• Neulactil (tablets, syrup)	*As for chlorpromazine*	*Schizophrenia and other psychoses* — Initially 75mg daily, increased as necessary at weekly intervals. Usual maximum 300 mg daily.	More sedating than chlorpromazine. Hypotension common when treatment initiated.

Perphenazine	• Fentazin (tablets)	*As for chlorpromazine*	Initially 4mg t.d.s., thereafter adjusted according to response. Maximum dose 24mg daily.	Less sedating than CPZ but extrapyramidal symptoms (esp. dystonia) more frequent, particularly at high dosage. Not indicated for agitation and restlessness in the elderly.
Pimozide	• Orap (tablets)	Schizophrenia; monosymptomatic hypochondriacal psychosis; paranoid psychoses; mania, hypomania, short-term adjunctive treatment of excitement and psychomotor agitation.	*Schizophrenia* — Initially 10mg daily in acute conditions, thereafter adjusted according to response to maximum of 20mg daily. Prevention of relapse — initially 2mg daily, range 2–20mg daily. *Paranoid psychoses* — Initially 4mg daily, thereafter adjusted according to response to maximum of 16mg daily.	Highly antipsychotic, long acting, minimal extrapyramidal side-effects; less sedating than CPZ. However, "serious arrhythmias reported ... following reports of sudden unexplained death, Committee on Safety of Medicines recommends ECG before treatment in all patients, periodic ECGs at doses over 16mg daily." CSM further warns that it should not be given with other antipsychotics, tricyclic antidepressants. *BNF*, 34, 167.
Prochlorperazine	• Prochlorperazine (tablets) • Stemetil (tablets, syrups, sachets, injection, suppositories)	Schizophrenia and other psychoses, mania.	By mouth, 12.5mg b.d. for 7 days, thereafter adjusted according to response to usual daily dose of 75–100mg. By deep IM injection, 12.5–25mg twice or thrice daily.	Less sedating than chlorpromazine but extrapyramidal symptoms, particularly dystonia, more frequent.
Promazine Hydrochloride	• Promazine (tablets, injection) • Sparine (suspension)	Short-term adjunctive management of psychomotor agitation; agitation and restlessness in the "elderly."	By mouth, 100–200mg q.d.s. By IM injection, 50mg repeated if necessary after 6–8 hours.	Contra-indications and side-effects, see chlorpromazine.
Risperidone	• Risperdal (tablets)	Acute and chronic psychoses.	Initially 2mg daily increased to 6mg by third day. Usual range 4–8mg daily (maximum 16mg). Doses above 10mg daily only if benefit considered to outweigh risk.	See **1257**. Agitation may occur more frequently than with CPZ. Nausea, anxiety, concentration difficulties, fatigue reported.
Sertindole	• Serdolect (tablets)	Schizophrenia	Initially 4mg daily, increased at intervals of 4/5 days to usual maintenance of 12–20mg as single daily dose. Maximum 24mg daily.	See **1257**. Limited experience of its use. Less sedating than CPZ and extrapyramidal symptoms appear not to exceed placebo. Associated with QT interval prolongation, which may lead to serious ventricular arrhythmias.

Sulpiride	• Dolmatil (tablets) • Sulparax (tablets) • Sulpitil (tablets)	Schizophrenia	200–400mg b.d. Maximum 800 mg daily in patients with predominately negative symptoms; 2400 mg in patients with mainly positive symptoms.	Structurally distinct from, and less sedating than, CPZ. Not associated with jaundice or skin reactions. In high doses controls florid, positive symptoms and in low doses has an alerting effect in apathetic, withdrawn states.
Thioridazine	• Thioridazine (tablets, oral sol.) • Melleril (tablets, suspension, syrup)	*As for chlorpromazine*	Schizophrenia and other psychoses, mania — 150–600mg daily; maximum 800 mg. daily for up to 4 weeks (hospital patients only). Short-term adjunctive management of psychomotor agitation, excitement, violent or dangerously impulsive behaviour — 75–200mg daily.	Less sedating than chlorpromazine. Extrapyramidal symptoms and hypothermia are rare and it is therefore popular for treating the elderly. Sexual dysfunction may occur as may, rarely, pigmentary retinopathy (brownish colouring of vision, impaired night vision).
Trifluoperazine	• Trifluoperazine (tablets, oral sol.) • Stelazine (tablets, spansules, syrup)	*As for chlorpromazine*	By mouth, initially 10mg daily, increased by 5mg after 1 week, then at intervals of 3 days according to response.	Less sedating than chlorpromazine and hypotension, hypothermia, and antimuscarinic symptoms are less frequent. However, the incidence of extrapyramidal symptoms, particularly akathisia and dystonic reactions.
Zuclopenthixol Acetate	• Clopixol Acuphase (injection, oily)	Short-term management of acute psychosis, mania, or exacerbations of chronic psychosis.	By deep IM injection into the gluteal muscle or lateral thigh, 50–150 mg, if necessary repeated after 2–3 days (1 additional dose may be needed 1–2 days after the first injection). Treatment should not exceed 2 weeks — maximum of 4 injections and maximum cumulative dose of 400mg per course.	Contra-indications and side-effects, see chlorpromazine.
Zuclopenthixol Dihydrochloride	• Clopixol (tablets, depot injection see **1263**)	Schizophrenia and other psychoses, particularly when associated with agitated, aggressive, or hostile behaviour.	Initially 20–30mg daily, increasing to a maximum of 150mg daily if necessary. Usual maintenance dose 20–50mg daily.	Contra-indications and side-effects, see chlorpromazine. Should not be used in apathetic or withdrawn states.

Adverse effects

Antipsychotics affect cholinergic, alpha-adrenergic, histaminergic, and serotinergic receptors, while dopamine blockade in the extrapyramidal system causes extrapyramidal side-effects and hypoprolactinaemia. The subsidiary effects may therefore be categorised as sedative, extrapyramidal and autonomic. The meaning of these terms and the most common types of adverse effect have already been summarised (**1146**). However, it is useful to list some of the well-documented adverse effects of chlorpromazine (CPZ) because the side-effect profiles of other drugs are often stated by reference to this commonly prescribed drug. The adverse effects in any particular case may include extrapyramidal symptoms (**1146**), which may sometimes be reversed by dose reduction or antimuscarinic drugs (**1150**); anti-muscarinic symptoms (**1148**), such as a dry mouth, nasal congestion, constipation, difficulty micturating, and blurred vision; occasionally, following prolonged administration, tardive dyskinesia (**1147**); hypothermia (occasionally pyrexia); apathy, depression and, more rarely, agitation; endocrine effects; damage to the eye following prolonged high dosage; skin reactions (photosensitisation is more common than with other antipsychotics).

LONG-ACTING DEPOT PREPARATIONS AND MAINTENANCE

Depot antipsychotics are slow-release long-acting oily preparations administered by way of deep intramuscular injection into the gluteal muscle. The intervals between injections varies between one and four weeks. Pain may occur at the injection site and occasionally erythema, swelling, and nodules. In general, no more than 2–3 mL of oily injection should be administered at any one site.[105] Depot medications may have advantages in terms of convenience and compliance compared with oral preparations but are associated with a higher incidence of extrapyramidal reactions, and also with hypotension and tachycardia. Because the drugs may have undesirable and long-lasting side-effects — it may take a month or more following discontinuance for side-effects to subside — a test dose is generally recommended. Treatment requires careful monitoring both to achieve optimum effect and to control side-effects.

Choice of depot

According to the British National Formulary, all of the drugs are indicated for use in the maintenance of schizophrenia and other psychoses, while an additional indication for clopixol is evidence of aggression and agitation. Depots are contra-indicated in confusional states, parkinsonism, and where there is intolerance to antipsychotics. Brief notes on the drugs given in the table below.

Efficacy

Although maintenance therapy reduces the risk of relapse (**1254**), studies have not established that depot injections have any significant advantages over oral preparations.[106] This may be because patients with poor histories of compliance are

[105] *British National Formulary* (British Medical Association and Royal Pharmaceutical Society of Great Britain, March 1996) 31, 165.

[106] N.R. Schooler, *et al.*, "Prevention of relapse in schizophrenia" *Archives of General Psychiatry* (1980) 37, 16–24; G.E. Hogarty, *et al.*, "Fluphenazine and social therapy in the aftercare of schizophrenic patients: relapse analysis of two year controlled study of fluphenazine decanoate and fluphenazine hydrochloride" *Archives of General Psychiatry* (1979) 36, 1283–1294.

left out of such studies, although voluntary compliance with depot medication may not be greater than compliance with oral medication. A general advantage of injections over oral medicines is certainty about whether or not a the drug has been received as prescribed. Against this, injections are unacceptable for many patients. Consequently, in practice, this clarity may be limited to knowing that the medicine has not been received as prescribed. The real choice is therefore often between compromising on oral medication by consent or compulsory treatment by injection. In the absence of any legal or practical framework allowing indefinite compulsory out-patient treatment, defaulting on injections in due course becomes an option for all discharged patients. In such cases, a consultant's unwillingness to contemplate what he considers to be the second-line treatment may simply lead to no treatment and early relapse.

ANTIPSYCHOTIC DEPOT PREPARATIONS (BNF 4.2.2)

Drug	*Proprietary*	*Notes and BNF guideline doses*
Flupenthixol Decanoate	▪ Depixol ▪ Depixol Conc. ▪ Depixol low volume	Test dose 20mg. Usual maintenance dose range of 50mg every 4 weeks – 300mg every 2 weeks. Maximum 400mg weekly. May have a mood elevating effect but can cause over-excitement in agitated or aggressive patients. Aggression or agitation may necessitate using an alternative antipsychotic. Extrapyramidal symptoms usually appear 1–3 days after administration and continue for about five days but may be delayed.
Fluphenazine Decanoate	▪ Modecate ▪ Modecate Concentrate	Test dose 12.5mg. Thereafter, 12.5–100mg at intervals of 2–5 weeks, adjusted according to response. Contra-indicated in severely depressed states. Extrapyramidal symptoms usually appear a few hours after the dose has been administered and continue for about two days but may be delayed.
Fluspirilene	▪ Redeptin	This drug has been withdrawn.
Haloperidol Decanoate	▪ Haldol Decanoate	Initially 50mg every 4 weeks. Increasing in 50mg steps to 300mg every 4 weeks if necessary, and "higher doses may be needed in some patients." The side-effects are similar to those for chlorpromazine.
Pipothiazine Palmitate	▪ Piportil Depot	Test dose 25mg. Usual maintenance range 50–100mg (maximum 200mg) every 4 weeks. Side-effects similar to chlorpromazine.
Zuclopenthixol Decanoate	▪ Clopixol ▪ Clopixol Conc.	Test dose 100mg. Thereafter increasing to 200–400mg every 2–4 weeks, maximum 600mg weekly. Less sedating that chlorpromazine and may be particularly suitable in cases of aggression and agitation, but it can cause porphyria.

Note: All of the available preparations listed above are oily injections administered by deep intramuscular injection into gluteal muscle (i.e. the buttocks). In each case, the B.N.F. indicator for the drug is the "maintenance in schizophrenia and other psychoses."

ELECTROCONVULSIVE THERAPY (ECT)

Catatonia is generally considered to be a definite indication for ECT. However, following a review of the research studies, Lader and Herrington concluded that the view that ECT is valuable in some cases of schizophrenia is not supported by firm evidence; that it was consistently less effective than either drugs or drugs plus psychotherapy; that any benefits were short-lived; but that it will undoubtedly continue to be used by some psychiatrists in patients with catatonia, affective symptoms, or drug-resistant states.[107] For further information about ECT, see page 1132.

FAMILY THERAPY

During the past quarter of a century, much emphasis has been placed on the significance of the patient's relationship with relatives, in terms both of the occurrence of the disorder and relapse. Schizophrenia tends to recur in families and familial factors are involved in its development. There is considerable evidence that the parents of people with schizophrenia are more often psychiatrically disturbed than are the parents of other children. The fact that a parent has psychiatric problems suggests that the child's subsequent illness has a genetic cause, or that it is attributable to the family environment, or both. It also appears that mothers are more protective towards their children even before the onset of illness.[108] This may lead to the so-called double bind, a term coined by Bateson to refer to the contradictory emotional attitudes which sufferers have to their parents. Children who develop schizophrenia have been found to more often come from homes in which parents live under the same roof but in a state of mutual withdrawal or conflict ("emotional divorce").[109] It should, however, been emphasised that none of these well-substantiated parental and family problems are invariably present.[110]

Relatives and the domestic environment

The literature concerning the family environment has been extensively reviewed by Leff[111] and much of it centres around the concept of "expressed emotion" (EE). The Camberwell Family Interview (CFI) has five principal scales for rating the expression of emotion: critical comments, hostility, over-involvement, warmth and positive remarks. In an early study, Brown "found that in a nine-month period following discharge, a high level of criticism, the presence of hostility, and high over-involvement were each related to relapse of schizophrenia. Conversely, high warmth was related to a good outcome over the same period, and this latter finding is of great importance, since it indicates that relatives can influence the course of schizophrenia

107 M. Lader and R. Herrington, *Biological treatments in psychiatry* (Oxford Medical Publications, 2nd ed., 1990), p.230.

108 P. O'Neal and L.N. Robins, "Childhood patterns predictive of adult schizophrenia: a 30 year follow-up study" *American Journal of Psychiatry* (1958) 115: 385-391; D.F. Ricks and C. Nameche, "Symbiosis, sacrifice and schizophrenia" *Mental Hygiene* (1966) 50: 541-551. This finding is, of course, liable to more than one interpretation because, if a child is vulnerable, a mothers' protectiveness may be well founded rather than overly intrusive.

109 M. Waring and D. Ricks, "Family patterns of children who become adult schizophrenics" *Journal of Nervous & Mental Diseases* (1965) 140: 351-364. See J. Leff, "Schizophrenia: social influences on onset and relapse" in *Community Psychiatry: The Principles* (ed. D.H. Bennett & H.L. Freeman, Churchill Livingstone, 1991), p.190.

110 R.E. Kendell, "Schizophrenia" in *Companion to psychiatric studies* (ed. R.E. Kendell & A.K. Zealley, Churchill Livingstone, 5th ed., 1993), pp.412–413.

111 See J. Leff, "Schizophrenia: social influences on onset and relapse," *supra*.

in a beneficial way."[112] Patients returning to live with high-EE relatives were found by Brown to have a relapse rate of over 50 per cent. over nine months, compared with only 16 per cent. for those in low-EE homes. These findings were almost exactly replicated by Vaughn and Leff.[113] During the two years following discharge, Leff and Vaughn found that the high-EE patients relapsed at almost twice the rate of low-EE patients: after two years, the overall relapse rates were 62 per cent. and 20 per cent. respectively.[114] This association between relatives' expressed emotion and the course of schizophrenia has been found to hold true for a variety of cultural settings and is strongly related to relapse even when there is no disturbed behaviour on the patient's part to mediate the relationship.[115]

Management strategies

In cases where a high level of expressed emotion is problematic, studies by Leff and Vaughn have identified two protective factors: regular maintenance treatment with neuroleptic drugs and low social contact between the relative and patient.[116] Patients who spent less than 35 hours per week in the same room with high-EE relatives were found to have a significantly lower relapse rate than those in high contact. The two protective factors appeared to have an additional effect, with the result that if patients were in low contact and took regular neuroleptic drugs, their relapse rate was lower than if only one protective factor was present. Family-orientated treatments may include a brief educational programme, a relatives' group, and family sessions in which the patient and key relatives in the household are included. Face-to-face contact is reduced by making use of day centres, day hospitals, hostels and classes run by local authority social services.

112 G.W. Brown, J.L.T. Birley, J.K. Wing, "Influence of family life on the course of schizophrenic disorders: a replication" *British Journal of Psychiatry* (1972) 121: 241–258. See J. Leff, "Schizophrenia: social influences on onset and relapse," *supra*, p.195.

113 C.E. Vaughn and J.P. Leff, "The influence of family and social factors on the course of psychiatric illness: a comparison of schizophrenic and depressed neurotic patients" *British Journal of Psychiatry* (1976) 129: 125–137.

114 J.P. Leff and C. Vaughn, "The role of maintenance therapy and relatives' expressed emotion in relapse of schizophrenia: a two year follow-up" *British Journal of Psychiatry* (1981) 139: 102-104.

115 J. Leff, "Schizophrenia: social influences on onset and relapse" in *Community Psychiatry: The Principles* (ed. D.H. Bennett & H.L. Freeman, Churchill Livingstone, 1991), p.196.

116 *Ibid.*