

**PSYCHOPHARMACOLOGY AND THE CLASSIFICATION OF  
FUNCTIONAL PSYCHOSES**

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**PREFACE**

This monograph is based on the controversial contention that a nosological approach to diagnosis is an essential prerequisite for the meaningful study of mental illness. Although the subject of this monograph is restricted to the group of disorders traditionally referred to as "functional psychoses," the same contention applies to "anxiety disorders," traditionally referred to as "neuroses."

The classification proposed in this volume is based on an understanding of all four developmental stages of psychiatric illness. It differs from other classifications by the particular integration of longitudinal-developmental and cross-sectional-psychopathological features and by the shift of emphasis from the interpretation of symptoms to the detection of affected psychopathological structures.

In spite of its historical roots and assumed inner logic, the classification presented here will not be proposed for general use until it is validated in carefully conducted clinical research. To design such studies, it will be important to know to what extent the psychiatric clinical material fits the proposed diagnostic groups in different cultures and to what extent biological homogeneity can be increased by employing the proposed subtyping in the selection of experimental populations in psychiatric research.

The origin of the concepts discussed in this monograph is in the work of Clerambault and Magnan, Kahlbaum and Kraepelin, Wernicke and Kleist, Jaspers and Schneider, and Wimmer. It is hoped that in the course of the presentation no injustice has been done to the contributions of Baruk, Leonhard and Stromgren.

In the preparation of different sections of this monograph publications by Berner, Guze, Fish, Hamilton, Helmchen, Jablensky, Pichot, Robins, Sartorius,, Spitzer and Wing were extremely helpful. The accuracy of some of the information presented was improved through personal communication with Angst, Perris and Winokur.

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INTRODUCTION

Recent progress in epidemiologic and biologic research is responsible for a renewed interest in psychiatric diagnosis and classification. The new trend has received an impetus from the recognition that operationally defined diagnostic criteria are prerequisites for a valid comparison of epidemiological data from different language areas; for the identification of biological markers of disease and for the demonstration of the effectiveness of new psychotropic drugs. In addition to their importance for psychiatric research, diagnosis and classification are "necessary tools" for choosing suitable treatment and providing necessary "care and counselling" to "the psychiatrically ill" (Helmchen, 1980).

#### Multi-Axial Classifications

A rationale for separating "etiology" from "symptomatology" was offered by Essen-Moller (1961). He contended that by assessing patients on two different, independent "axes," a number of combinations of syndromes and etiology would emerge which might not correspond to traditional (syndromatological) psychiatric diagnoses and thereby invalidate some of the old diagnostic hypotheses. By designing a model for a bi-axial system Essen-Moller (1971) opened a new path leading to the development of multi-axial systems of diagnostic classifications in psychiatry (see Appendix I, Table I).

A changing attitude toward psychiatric diagnosis is reflected in the Mental Disorders section of the ninth revision of the International Classification of Diseases (ICD-9) of the World Health Organization (WHO, 1975, 1977). In ICD-8, etiological criteria were mixed with symptomatological, typological and topographic ones as well as with criteria relevant to the course of the disease (WHO, 1965, 1967), whereas in ICD-9, according to Helmchen (1980), there is an attempt to separate "symptomatology" from "etiology." However,

because ICD-9 is a uni-axial classification, many of its diagnostic terms remain a mixture of different elements.

The first models of multi-axial systems of diagnostic classifications in psychiatry were developed independently by Ottosson and Perris (1973) and Helmchen (1975). They entailed four and five axes respectively. The four axes of Ottosson and Perris are "symptomatology," "severity," "etiology," and "course"; and the five axes of Helmchen are "symptomatology," "time," "etiology," "intensity," and "certainty" (see Appendix I, Tables II and III). Other important models of multi-axial classifications are those of Wing et al. (1968) and Strauss (1975). The four axes of Wing et al. are "psychiatric condition," "underlying cause or precipitating factor," "mental subnormality" and "additional physical illness or handicap"; and the five axes of Strauss are "symptoms," "previous duration and course of symptoms," "associated factors," "personal relationships" and "work function" (see Appendix I, Tables IV and V).

A significant, recent contribution to multi-axial psychiatric diagnosis is the third edition of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-III, 1980). By its operationally defined diagnostic criteria and multi-axial system of evaluation DSM-III represents an important step towards a scientific approach to psychiatric diagnosis. Other important contributions in the development of operationalized diagnostic criteria are the St. Louis Criteria of Feighner et al. (1972), the Present State Examination Criteria of Wing, Cooper and Sartorius (1974), the Research Diagnostic Criteria (RDC) of Spitzer, Endicott and Robins (1978a and b), Taylor and Abram's Criteria (Taylor and Abrams, 1978; Taylor Redfield and Abrams, 1981) and the Vienna Research Criteria of Berner and Katschnig (1983).

Empiricistic, Experimental and Nosological Approaches

In spite of the increasing sophistication in the differentiation of diagnostic categories within the traditional framework, research findings which have accumulated during the past decades strongly suggest that the classical nosological groups are only in part homogenous entities. This is reflected in the differential responsiveness within the same diagnostic category to the same psychotropic drug, and in the considerable variation of neurophysiological and biochemical measures within the same diagnostic category.

In the absence of well-identified etiology in most psychiatric disease, there are three approaches employed in differentiating biologically meaningful homogenous psychiatric patient populations: the empiricistic, the experimental and the nosological.

The empiricistic approach is based on the development of an assessment instrument, e.g., rating scale, that is constructed in a manner to include all known manifestations of a psychiatric disease, e.g., depression. It is assumed that by administering such a scale to large, clinically homogenous depressive populations and employing different statistical procedures, e.g., factor analysis, cluster analysis, multiple discriminant function analysis in the treatment of collected data, meaningful subtypes or diagnoses within a group of disorders can be obtained.

An alternative to the empiricistic approach is the experimental approach. It is based on biologic measures, e.g., neurophysiologic, biochemical, neuroendocrine. While it is hoped that some of these measures (biologic markers) will bring about a more meaningful classification of clinical psychopathology, it is commonly held that the meaningfulness of biologic markers is limited by the extent that they can be linked to a clinically identifiable diagnostic group.

The prototype of the third, or nosological approach is Kraepelin's (1896) three-dimensional model of classification, which was presented for

the first time in the 5th edition of his textbook of psychiatry. Kraepelin's classification is based on three successive stages (dimensions) of psychiatric disease. In the first four editions of his monumental work, Kraepelin used a syndrome-oriented approach to the classification of mental illness. Beginning with the 5th edition he adopted the medical concept of psychiatric disease and shifted emphasis from the "pathological picture" to the "criterion of progress" (Pichot, 1983). According to Kraepelin "the necessity" for the shift in emphasis was brought about "by practical needs," by the "limitations of grouping on the basis of pathological pictures (Krankheitsbilder)," and by the recognition of the importance of criteria "which derive from the developmental stages, the course and the outcome of individual disorders." Kraepelin's shift of emphasis from the cross-sectional picture to the course of illness had its origin in Kahlbaum's (1874) formulation of the notion of nosological entity. This was based essentially on Falret's (1864) contention that for a better understanding one has to learn about "the progression and the various stages of the natural form of mental disorders." For Falret a "natural form" of a disease "implies a well defined (natural) predictable course," which in turn "presupposes the existence of a natural form of disease with a specific pattern of development."

An alternative to the three-dimensional model is the four-dimensional model of nosological classification. This is based on all successive stages of psychiatric disease. Leonhard's (1957, 1979) classification of "endogenous psychoses" is based essentially on a four-dimensional nosological approach.

#### From One Dimensional to Four Dimensional Classifications

In the psychiatric literature the terms "axes" and "dimensions" are used interchangeably in an unconventional manner referring to different



aspects or components of the disease in an arbitrary manner (Mombour, 1975). With the term axes, emphasis is on the independence of the components; while with the term dimension, the emphasis is on relationships among the components in a time sequence. Hence, the four dimensions, or rather developmental stages include cross-sectional psychopathology (1st dimension or 2nd developmental stage), onset-etiology (2nd dimension or 1st developmental stage), course of illness (3rd dimension or 3rd developmental stage) and outcome (or end-state) features (4th dimension or 4th developmental stage). Inclusion of the entire disease from beginning to end is a prerequisite for a comprehensive picture which should provide for a better understanding of the nature of psychiatric illness. In keeping with this is Kahlbaum's (1874) notion that "only an inclusive and general use of the clinical method can advance psychiatry and increase understanding about the pathological process involved in mental illness." Corresponding with this notion are the findings that by encompassing an increasing number of developmental stages of the disease, the heterogeneous population of psychiatric patients can be separated into increasingly more homogenous and differentiated diagnostic groups. Thus, by employing a two-dimensional approach, the one-dimensional concept of unitary psychosis-vesania (Neumann, 1859; Griesinger, 1845, 1867, 1876), could be separated into two psychoses, i.e., exogenous and endogenous.

Introduction of the third dimension opened the possibility of separating patients within the population of exogenous psychosis into organic (including "symptomatic psychosis" and "psychosis associated with coarse brain disease") and psychogenic (also referred to as reactive) psychoses; and to separate patients within the population of endogenous psychosis into schizophrenic (dementia praecox) and affective (manic depressive) psychoses. Since psychogenic and endogenous psychoses are considered to be

sui generis, primary psychiatric illnesses, they are commonly referred to as "functional psychoses" to separate them from the nonspecific psychiatric disorders associated with neurological and/or other systemic diseases and from developmental inborn and/or learned anomalies such as "mental retardations" and "psychopathic personalities" (Schneider, 1925).

Finally, introduction of a fourth dimension, and with it a structural approach, has made it possible to separate patients within both the schizophrenic and the affective psychoses into two major diagnostic groups, i.e., nonsystematic and systematic. In addition, the four dimensional model of psychiatric diagnosis has focused attention on acute and chronic delusional psychoses, a population between the reactive and endogenous psychoses; and on cycloid psychosis, a population between the affective and schizophrenic psychoses (Table I). It has also brought to attention numerous subtypes within each group of the major diagnoses (Figure 1).

#### Proposed Classification: Supporting Data

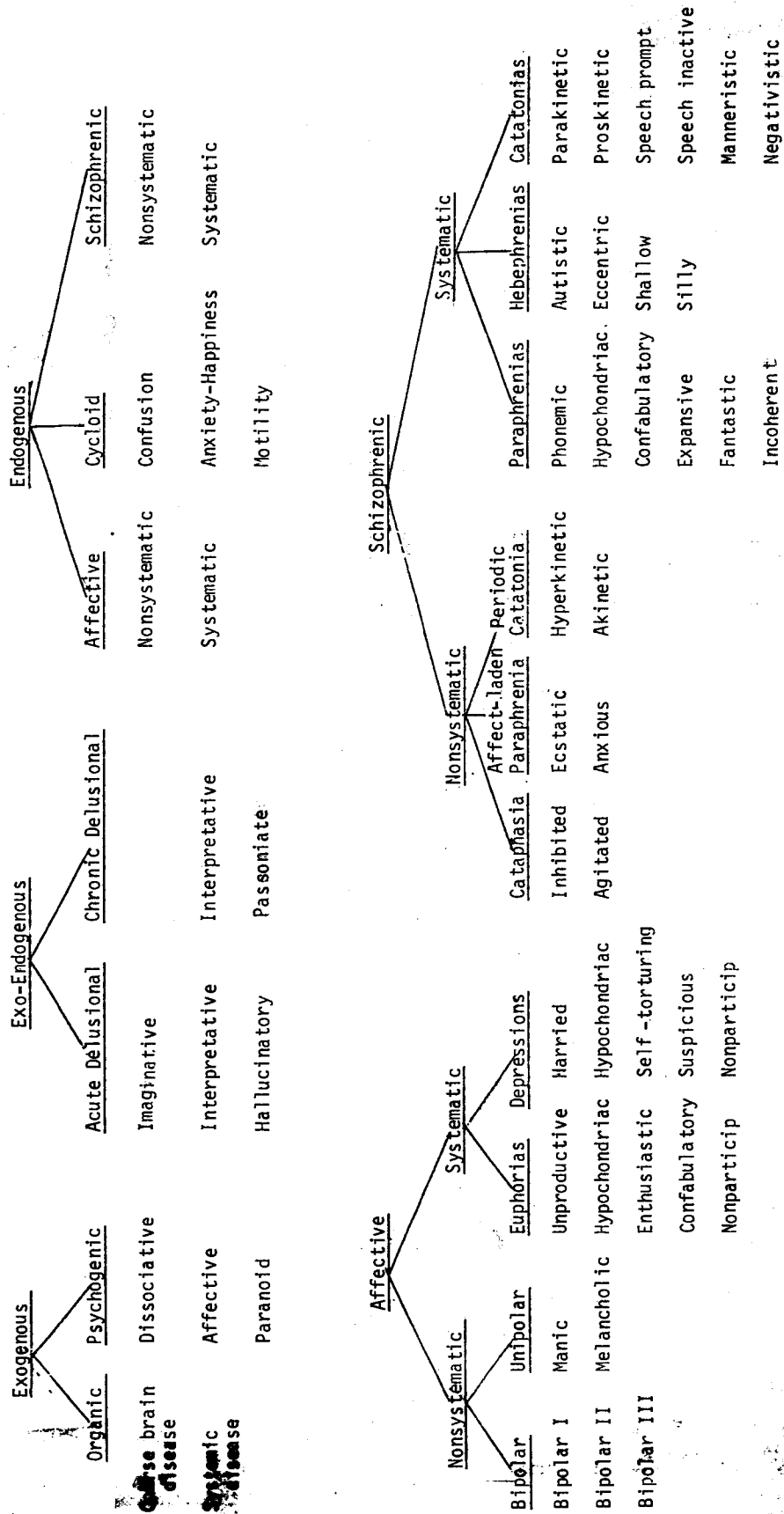
The proposed four-dimensional classification is firmly rooted, although not exclusively based, in cross-sectional psychopathology, extending its boundaries beyond experiential phenomenology into behavior, performance and holistic (Gestalt) characteristics of the disease (Ban, 1982; Conrad, 1958; Petho, Tolna and Tusnady, 1979; Petrilowitsch, 1969). It employs a decision tree model. Accordingly, alternative decisions are based not merely on a given set of knowledge (cross-sectional psychopathology) and a logical process moving within one set of data. It also follows the evolution of the subject (illness) under study in time (Petho, 1984b). In the course of this process first, endogenous and exogenous (reactive) psychoses are separated on the basis of the relative importance of a precipitating event in activating the disease. Subsequently, psychopathological syndromes are identified on the

Table I

Dimension	Cross-Sectional Psychopathology	Etiology-Onset	Course of Illness	Outcome or End-State
	2nd Stage	1st Stage	3rd Stage	4th Stage
1st	Psychosis	////////////////////	////////////////////	////////////////////
2nd	Psychosis	Exogenous VS Endogenous	////////////////////	////////////////////
3rd	Psychosis	Exogenous VS Endogenous	Organic VS Psychogenic and Affective VS Schizophrenic	//////////////////// //////////////////// //////////////////// ////////////////////
4th	Psychosis	Exogenous VS Endogenous	Organic VS Psychogenic and Affective VS Schizophrenic	DeLusional VS Affective-----Nonsystematic VS Cycloid Systematic VS Schizophrenic---Nonsystematic VS Systematic

Schematic presentation of psychiatric diagnoses within a one-dimensional, two-dimensional, three-dimensional and four-dimensional model of classification.

Figure 1



Proposed classification of functional psychoses.

basis of an analysis of psychopathological forms with consideration of their content. The formal characteristics of the course of the disease, such as rhythmicity, periodicity, polarity, etc. are distinguished from the contents of the course, such as time spent in hospital, intensity and duration of pharmacotherapy etc. (Petho, 1984a). Finally, the outcome characteristics are utilized in the validation of diagnoses (Petho, 1977, 1984b).

The diagnostic system proposed is undoubtedly more detailed and subtle than other diagnostic systems used in psychiatry today. It still must be shown, however, that its diagnostic subtypes are biologically more meaningful categories than the diagnostic types described in ICD-9, operationally defined by DSM-III, and/or identified by the various diagnostic systems employed in psychiatric research.

In favor of the contention that diagnoses within the four dimensional model represent biologically more homogenous populations (than diagnoses within the three dimensional model) are clinical psychopharmacologic findings (Astrup, 1959; Astrup and Fish, 1964). These findings suggest that in schizophrenic patients classified on the basis of Leonhard's (1957, 1979) system, therapeutic responsiveness to neuroleptics is considerably more predictable than in schizophrenic patients classified on the basis of other diagnostic classifications. By employing Leonhard's classification, Fish, as early as 1964, found that 117 out of 123 nonsystematic schizophrenic patients (95%) showed a favorable therapeutic response to neuroleptics, while only 289 out of 351 systematic schizophrenic patients (69%) showed a similar response (Fish, 1964a). The most important findings, from both a practical and a theoretical point of view, however, was that among nonsystematic schizophrenic patients, the favorable therapeutic response was rated marked to moderate in 79 percent of treatment responsive patients, while among

systematic schizophrenic patients it was rated marked to moderate in only 23 percent. It was also noted that, among the nonsystematic patients, those suffering from periodic catatonia responded less favorably than patients with affect-laden paraphrenia and especially cataphasia. Among the systematic patients, therapeutic responsiveness, was not evenly distributed among the three major classes of psychoses. Thus, while a moderate or marked therapeutic response was seen in as high as 40 percent of the patients belonging to one or another subtype of the systematic paraphrenias, a similarly favorable response was seen only in 23 percent of the patients belonging to one or another subtype of the systematic hebephrenias and 0.9 percent of the patients belonging to one or another subtype of the systematic catatonias.

That Leonhard's system of classification might identify biologically meaningful categories is also supported by preliminary findings regarding tardive dyskinesia in a multinational survey of 768 chronic hospitalized schizophrenic patients (Ban, Guy and Wilson, 1984a). In this survey the overall prevalence rate of tardive dyskinesia for the population was 11 percent when determined by clinical judgment and 13 percent when determined by the Research Diagnostic Criteria for Tardive Dyskinesia (Schooler and Kane, 1982). However, by employing Leonhard's diagnostic system, prevalence rates were found to be significantly lower in the therapeutically more responsive non-systematic group (4.3%), than in the therapeutically less responsive systematic group (13.3%). The manneristic subtype of the systematic catatonias attained a prevalence rate of 28 percent and the silly subtype of the systematic hebephrenias attained a prevalence rate of 53 percent. In the expansive and confabulatory subtypes of the systematic paraphrenias, tardive dyskinesia was not encountered at all (Guy, Ban and Wilson, 1985). Because there is no indication that the action mechanism of neuroleptics would be different in patients

belonging to different diagnostic groups, it seems likely that in the development of tardive dyskinesia, the biology of the host also plays an important role. Furthermore, because there is no indication that patients with different types of schizophrenias as classified by the ICD-9 or DSM-III develop tardive dyskinesia differentially to neuroleptics, the preliminary findings, of differential occurrence within Leonhard's classification favor the contention that diagnoses based on Leonhard's system, provide for biologically more homogenous populations than diagnoses based on other systems of classification.

Use of Terms: Psychosis, Endogenous, Psychogenic

The four-dimensional model of psychiatric diagnosis has evolved in the course of systematic research on "psychotic" patients. While the only purpose of these studies was to differentiate clinically meaningful groups within the psychotic population, the findings also indicated that the concept of psychosis should not be based on the intensity of psychopathological symptoms. If severity of illness is the basis of the distinction, one and the same disorder may appear in psychotic and non-psychotic forms. Because of this in the proposed classification Schneider's (1950, 1959) definition of psychosis is adapted. Thus, the term psychosis designates psychopathological syndromes resulting from disease and regardless of the intensity of the pathology. In this respect the proposed classification is in keeping with ICD-9 and is at variance with DSM-III in which according to Pichot (1983) intensity is of primary importance in the definition.

In the proposed classification the term psychosis is retained to separate disease-related psychopathological syndromes from disorders of personality which, according to Schneider represent psychic abnormalities, i.e., statistical deviations from the social norm (normal) with which, they are "united

by a series of imperceptible transitions" (Pichot, 1983). Thus, for Schneider, psychoses, in contradistinction to personality disorders, are always of somatic origin, regardless of whether a somatic etiology has been identified. It is within this frame of reference that the term "functional psychosis" is used in this monograph.

Within the conceptual framework of this monograph, endogenous psychoses are perceived as being the result of a seemingly spontaneous interaction between endogenous, assumedly genetic factors, and brain structures; while reactive (psychogenic) psychoses are perceived as the result of a precipitated interaction between endogenous, assumedly genetic factors, and brain structures. Considering that the essential difference between the two psychoses is the presence or absence of a need for an exogenous "psychological" factor to precipitate the psychosis, one may entertain the possibility of replacing the terms endogenous and psychogenic psychoses by the terms endogenomorphic and exogenomorphic psychoses respectively. Moreover, if subjects with deviant (abnormal) personalities would be referred to as "psychopathic personalities" as done by Schneider (1923, 1958), the term "psychosis" could be replaced by the term "disorder," as used in the DSM-III. However, if the term "endogenomorphic," is used, one must remember that the same term has been used by Klein (1973) in relation to depressive illness that mimics the characteristics of endogenous depression and which is usually responsive to a wide range of somatic interventions; and also by Berner (1982, 1983), in relation to axial syndromes which might indicate schizophrenic, manic or depressive developments. Although the terms exogenomorphic and endogenomorphic might be more appropriate than the terms presently in use, they will not be employed in this monograph. On the other hand, the term psychosis will be retained in recognition of the distinction



between psychiatric illnesses and developmental anomalies and within psychiatric illnesses between anxiety disorders (neuroses) in which patients have good insight and psychoses in which patients have no insight, even if they recognize to some extent, the nature of their pathological experiences. It is this latter group (psychoses) which will be the subject matter of this volume.

CLASSIFICATION AND CLINICAL PSYCHOPHARMACOLOGY

The practical need for developing a new system of classifying functional psychoses is closely linked to psychopharmacologic progress. It was in response to this need that the two most extensively employed diagnostic systems, the ICD-9 and the DSM-III, were introduced for general use. In addition, several research diagnostic criteria were developed. One of them, the Diagnostic Criteria of Research (DCR) served as the starting point for the development of the proposed classification of functional psychoses.

### Psychopharmacology

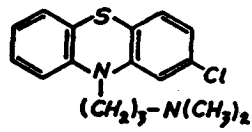
The psychopharmacological era began on January 19, 1952 when chlorpromazine was given for the first time to a psychiatric patient by Hamon, Paraire and Velluz (1952) at Val-de-Grace, the famed military hospital in Paris (Ban, 1972). From Val-de-Grace, chlorpromazine raced through the mental hospitals of France within the single year of 1952 (Delay and Deniker, 1952), transforming disturbed wards, reforming therapy and remodeling research (Caldwell, 1970). Swiss psychiatrists began to use chlorpromazine in January, 1953 (Staehelin and Kielholz, 1953), and by the Spring of 1953, the psychopharmacological "revolution" was well underway throughout continental Europe. Lehmann and Hanrahan's (1954) paper, the first American publication on chlorpromazine, appeared in February 1954 in the American Medical Association's Archives of Neurology and Psychiatry; and one year later, the first Australian (Webb, 1955) and Russian (Tarasov, 1955) publications were also in print.

Because chlorpromazine was introduced at a time when interest in psychiatric diagnosis was dormant the first publications reported on therapeutic effects with the drug on psychic disturbances (psychischen Storungen) in general and in psychotic patients (cas de psychoses) in particular

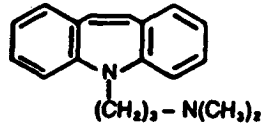
(Delay and Deniker, 1952; Staehelin and Kielholz, 1953). In the first American publication (Lehmann and Hanrahan, 1954), chlorpromazine was labelled as a "new inhibiting agent for psychomotor excitement and manic states" and subsequent articles suggested that chlorpromazine is an antipsychotic agent which can control psychoses whether organic or functional. In fact, it was not until the 1960's, that it was recognized that antipsychotics are particularly useful therapeutic agents in the treatment of "functional psychoses" and have an especially favorable action in the schizophrenias (Casey et al., 1960; NIMH Collaborative Studies, 1964).

The phenothiazine nucleus, the basic constituent of chlorpromazine, was first synthesized in 1883 by Bernthsen. It consists of two benzol rings attached to each other by a sulfur atom and a nitrogen atom. A structurally similar nucleus, the iminodibenzyl nucleus, the basic constituent of imipramine, was described 16 years later by Thiele and Holzinger (1899) (Figure 2). In the course of a search to find "chlorpromazine-like" compounds to treat "psychosis" and especially "schizophrenia," imipramine was chosen to be studied. It failed to show antipsychotic properties but Kuhn (1957) recognized its therapeutic potential in depression. The antidepressant effects of imipramine received additional substantiation within a year from Kielholz and Battegay (1958) in Europe and from Lehmann, Cahn and deVerteuil (1958) in North America. However, it was not until the mid-1960s, i.e., approximately eight years later, that the antidepressant effects of imipramine were established with reasonable certainty (Ban, 1974, 1981). By pooling data from 23 published reports which included 550 patients treated with imipramine and 459 with placebo, Klerman and Cole (1965) showed that the overall improvement rate was significantly higher with imipramine (65%) than with an inactive substance (35%). Similar findings were obtained by Angst (1970).

Figure 2



Chlorpromazine



Imipramine

Chemical structure of chlorpromazine and imipramine.

Lack of interest in psychiatric diagnosis made it even more difficult to recognize the mood stabilizing effect of lithium salts. As early as 1949 Cade reported on the successful treatment of ten manic patients with lithium and noted that the first patient relapsed when lithium treatment was stopped. However, it was not before the 1970s, i.e., more than 20 years later, that the therapeutic effects of lithium salts were proven beyond reasonable doubt in manic depressive patients during the acute, maintenance and prophylactic phases of treatment (Jefferson and Greist, 1977).

Chlorpromazine, imipramine and lithium have brought about fundamental changes in the treatment of "functional psychoses." In view of this, and in spite of all the acknowledged limitations of these psychotropic agents, the treatment of choice for functional psychoses today is pharmacotherapy with antipsychotics, antidepressants and/or mood stabilizing lithium salts. There is substantial evidence that no other single therapeutic procedure can compete with these treatments in terms of rapidity of effectiveness, sustained action, general availability and ease of application. These practical advantages have provided sufficient incentive to develop a large number of antipsychotic and antidepressant drugs (and also a number of different brands of lithium salts).

The large number of available antipsychotics (neuroleptics) were listed in a report, based on a multi-national survey, carried out in 768 chronic hospitalized schizophrenic patients in eight countries during the early 1980s. Findings revealed that 739 or 96.2 percent of the 768 patients were treated with one or more of 31 different neuroleptics (Ban, Guy and Wilson, 1984b) (see Appendix II, Table II). No similar figures are available for antidepressants. By 1981, however, at least ten structurally different groups of tricyclic and

ten other structurally different groups of non-tricyclic antidepressants were in clinical use and/or employed in clinical investigations. The ten groups of tricyclic antidepressants include the dibenzazepines, dibenzodiazepines, dibenzocycloheptadiens, dibenzocycloheptatriens, dibenzothiepinines, dibenzoxepines, dibenzoxazepines, anthracenes, anthridines, and acridans; and the ten groups of non-tricyclics include the dibenzobicyclo-octadienes, carboxylic acid esters, amides and amidoximes, arylalkyl and arylcycloalkylamines, phenoxyalkylamines, diaryl and diaryloxy-derivatives, arylbicyclic compounds, oxazoles, imidazoles and triazoles, benzpyrazoles and benzimidazoles, condensed indoles and quinolines and tetrahydroisoquinolines (Ban, 1981) (see Appendix II, Tables III and IV). Demonstration of therapeutic efficacy or possible differential activity of these drugs requires sensitive instruments for the assessment of change. Identification of therapeutically responsive patients and differentiation of these patients from the treatment refractory ones require valid diagnostic groups within the functional psychoses.

Another important factor in the renewed interest in the diagnosis and classification of psychiatric disorders in general and functional psychoses in particular is related to the recognition of the biological nature of these conditions. Because psychopharmacological agents may promptly reverse psychopathological symptoms and their continued administration may maintain patients in remission or even have a prophylactic effect, it is increasingly recognized that "psychodynamic theories," cannot offer a meaningful understanding about the nature of these conditions. On the other hand, description of the form of psychopathological symptoms may bring to attention distinct psychopathological structures which are affected by the disease. Similarly, understanding the action mechanism of drugs with specific therapeutic effectiveness in a distinct disorder, and with equal therapeutic effectiveness

during the different developmental stages of the disorder, may lead to the identification of functional alterations of the morphological substrate(s) responsible for the clinical manifestations. One of the essential prerequisites of such research is the delineation of valid diagnostic groups.

#### ICD-9

Well before the changes brought about by psychopharmacologic progress had crystallized, experts from 35 countries participated in a World Health Organization program on the standardization of psychiatric diagnosis, classification and statistics. Their review of the state of affairs resulted in the glossary of mental disorders, which was distributed as a companion to the 8th edition of the International Classification of Diseases (ICD-8). The same glossary, with some modification was incorporated in Chapter V of the 9th edition of the ICD (ICD-9) completed in 1975 and published in 1977 (Jablensky et al., 1983).

The mental disorders section of ICD-9 is primarily directed to fulfill the needs of epidemiological research and is firmly rooted in a traditional framework of psychiatric classification. It is based on the separation of "psychoses" from "neuroses" (personality disorders and other non-psychotic mental disorders) and on the dichotomy between organic psychotic conditions and other psychoses. Disorders subsumed under "other psychoses" in the ICD-9 are commonly referred to as functional psychoses, implying the absence of organicity.

Functional psychoses in the ICD-9 are divided into three endogenous and one reactive group of disorders. (It should be noted, however, that the terms "functional," "endogenous" and "reactive" are not used in the ICD-9.) The three endogenous groups of disorders are schizophrenic psychoses (including acute schizophrenic episode; latent and residual



schizophrenia; and simple, hebephrenic, catatonic, paranoid and schizo-affective types of schizophrenia); affective psychoses (including manic-depressive psychosis manic, depressed and circular types); and paranoid states (including paranoia, paraphrenia, induced psychosis and paranoid state simple type). The reactive group, referred to as other nonorganic psychoses, includes reactive confusion, acute paranoid reaction, psychogenic paranoid psychosis and other nonorganic psychosis depressive and excitative types (see Appendix III, Table I).

To update the ICD-9, a major International Conference on Diagnosis and Classification was convened in Copenhagen in 1982. Participants in this conference agreed that among the factors contributing to the revival of interest in psychiatric diagnosis were the advances in pharmacological treatment which require more refined diagnostic assessment; and the advances of biological research towards an understanding of the causal mechanisms underlying some of the major mental disorders. Other contributing factors considered were the attractions of new tools such as standardized instruments for diagnostic interviewing, operationalized diagnostic criteria and experiments with multi-axial recording systems.

No consensus was reached at the Copenhagen conference regarding a theory underlying the classification of mental disorders. Some participants expressed the view that disease entities in psychiatry are not intrinsically different from disease entities in general medicine with specific causes, symptoms, course, outcome (corresponding with the original contention of nosological theory) and response to treatment. At the same time, other participants maintained that the phenomenology of mental disorders seems to reflect etiologically non-specific responses of the personality to neuro-chemical events or altered cerebral structures. However, there was a widely

shared contention that distinctions like those between "organic" and "functional," or "endogenous" and "exogenous," or "psychosis" and "neurosis" were at least questionable and needed revision or at least qualification (Jablensky et al., 1983).

Regarding "functional psychoses" it was agreed that the designation of these disorders as such is misleading because "organic" features might be present in presumably "functional conditions," and because many of the syndromes within this category do not exhibit the features corresponding to the traditional notion of "psychosis." The participants agreed that the extensive clinical and genetic evidence for schizophrenia made it a valid and useful concept. It is a disorder, or a group of disorders, for which a predisposition is genetically transmitted and which is of worldwide occurrence. The same applies to manic and depressive illnesses. There is both clinical and genetic evidence for a distinction between unipolar and bipolar affective disorders. It was also agreed that there are good reasons to classify patients with "schizoaffective" symptoms separately from both the schizophrenic and the affective categories. There are acute psychoses of brief duration which obviously do not belong to either the schizophrenic or the affective diagnostic groups; and there is a variety of paranoid and other delusional states which tend to occur with a peak frequency in middle age or late middle age (Jablensky et al., 1983).

As a follow up of the Copenhagen Conference the Division of Mental Health of WHO held an informal consultation at which proposals for the classification of mental disorders and psychosocial factors in the ICD-10 were discussed. The ICD-10 is planned to be completed by 1990 and implemented in 1992 or 1993. If the present outline is accepted, the conditions traditionally subsumed under "functional psychoses," will be included under

the headings of schizophrenic and related disorders and mood (affective) disorders. Subsumed under the heading of schizophrenic and related disorders will be schizophrenia (paranoid, hebephrenic, catatonic, undifferentiated, and residual and postschizophrenic depression); schizophrenic spectrum disorders (schizotypal personality disorder and simple schizophrenia); persistent delusional disorders (paranoia and monosymptomatic, induced and other persistent delusional disorders); acute and transient psychotic disorders (acute delusional episode, cycloid psychosis, psychogenic delusional disorder, acute dissociative-confusional episode, acute schizophreniform episode and other acute psychotic disorder); and other non-organic psychotic disorders. Subsumed under the heading of mood (affective) disorders will be bipolar affective disorder (currently manic, depressive, mixed or in remission); recurrent depressive disorder (severe and mild); depressive episode (severe and mild); other affective disorder; schizoaffective disorder (schizomanic and schizodepressive); and chronic affective states (cyclothymia and dysthymia) (Report on Informal Consultation, 1984).

### DSM-III

In contradistinction to the ICD-9, and more in keeping with the goals of ICD-10, the Third Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) of the American Psychiatric Association is oriented to fulfill the needs created by and necessary for psychopharmacologic progress. It is a multi-axial system of evaluation (Axis I - Clinical Syndromes, Axis II - Personality Disorders, Axis III - Physical Disorders, Axis IV - Psychosocial Stressors and Axis V - Highest Level of Adaptive Functioning) which is based on operationally defined criteria (see Appendix IV, Tables I, II, III and IV).

Preparation of the DSM-III by a Task Force on Nomenclature and Statistics of the American Psychiatric Association (APA) began in 1976. It was completed and approved at the 1979 Annual Meeting of the APA and was published in 1980.

In DSM-III each mental disorder is characterized by a clinically significant behavioral or psychological syndrome which is associated with either a painful symptom or impairment in one or more important areas of functioning. DSM-III diagnoses imply behavioral, psychological, and/or biological dysfunction. DSM-III is not a classification of patients but a classification of disorders. It deals with illnesses and not with disturbances in the relationship between the person and society.

The origin of the DSM-III can be traced to DSM-I, published in 1952. DSM-I, the first edition of the Manual, was firmly rooted in Adolf Meyer's (1915, 1934) psychobiological view that mental disorders represent reactions of the personality to psychological, social, and biological factors. By the time the second edition, DSM-II, went into effect in 1968, the classification was brought in line with the 8th edition of the International Classification of Diseases of the WHO. The term "reaction," was not used any longer and the terms used by and large did not imply a particular theoretical framework for understanding nonorganic mental disorders. Subsequently, however, there was a divergence between the ICD and the DSM. Thus, for example, the traditional separation between psychosis and neurosis present in ICD-9 was eliminated, and both terms were replaced by the single term "disorder" in the DSM-III.

In the DSM-III disorders traditionally subsumed under functional psychoses are grouped under four major headings: schizophrenic disorders, paranoid disorders, psychotic disorders not elsewhere classified and affective disorders. Five types of schizophrenic disorders are differentiated, i.e., disorganized, catatonic, paranoid, undifferentiated and residual; within paranoid disorders, four diagnoses, i.e., paranoia, shared paranoid disorder, acute paranoid disorder and atypical paranoid disorder; within psychotic disorders not elsewhere classified, brief reactive psychosis,

schizoaffective disorder and atypical psychosis; and within affective disorders, bipolar disorders, major depression, cyclothymic disorder and atypical depression. Furthermore, in the DSM-III, consideration is given to the course of schizophrenic disorder, and each of the different types are identified as subchronic, chronic, subchronic with acute exacerbation, chronic with acute exacerbation and in remission; and to the "subclassification" of major depressive episode, in terms of "in remission," "with psychotic (mood-congruent or mood-incongruent) features," "with melancholia" and "without melancholia", (see Appendix IV, Table I).

There is little doubt that the DSM-III represents a major step toward reintegrating psychiatry with other medical disciplines. Canadian critics of this conceptual approach to diagnosis, however, contend that the quest for reliability, operational rigor, and completeness has overshadowed concern for validity, clinical flavor, and psychodynamic understanding. The same critics argue that dismissal of psychodynamic formulations, and neglect of humanistic approaches to complex and ambiguous realities reflect an arid view of psychiatric diagnosis. According to one of these critics "DSM-III is like a bikini--it shows you everything but the essentials." According to another, "DSM-III is "a gigantic defense against diagnostic problems in psychiatry." The same Canadian critics disagree with the elimination of terms, such as "psychotic," "neurotic" and "psychopathic" and the abandonment of the exogenous/endogenous and neurotic/psychotic polarities. They argue that despite the problematic nature of these dichotomies, the distinctions are important and are not adequately represented in DSM-III.

The diagnoses of paranoid disorders and schizophreniform disorders of DSM-III were faulted for their almost total neglect of the European

literature and consequently for relying heavily on the duration criterion in differential diagnosis (Engels, Ghadirian and Dongier, 1985). In spite of the critical comments, however, the Canadian survey revealed that over 90 percent of the 99 respondents (university based psychiatrists) used Axis I diagnosis in their undergraduate (94%) and postgraduate (99%) teaching and research (98%). Thus, the results of the survey corroborate the main findings of a former Canadian survey (with members of the Canadian Psychiatric Association), carried out by Junek (1983) who reported that the majority of his respondents ranked DSM-III as the future diagnostic system of choice.

#### Research Criteria

In addition to the diagnostic criteria of ICD-9 and DSM-III, introduced primarily for clinical use, several other diagnostic criteria relevant to the population of functional psychoses, were developed primarily for research purposes. Among them the most frequently employed are the St. Louis Criteria (Feighner et al., 1972), the Research Diagnostic Criteria (Spitzer, Endicott and Robins, 1978a and b), Taylor and Abrams Criteria (Taylor and Abrams, 1978; Taylor, Redfield and Abrams, 1981) and the Vienna Research Criteria (Berner and Katschnig, 1983).

The St. Louis criteria for the diagnosis of schizophrenia are based on methodological considerations relevant to improvement of diagnostic validity put forward by Robins and Guze (1970); and the St. Louis criteria for the diagnosis of affective disorder are based on the concepts of "primary" and "secondary" affective disorders developed by Robins et al. (1972). They are frequently referred to as Feighner's criteria because they were first presented in an operationalized format in a paper published by Feighner et al. (1972). The criteria for schizophrenia consist of psychopathological

symptoms and other manifestations. Because the St. Louis criteria for schizophrenia were designed to diagnose "poor-prognosis" patients and to separate them from "good-prognosis" patients, they represent a restricted view of schizophrenia that excludes many patients. The same applies to the St. Louis criteria for affective disorders, i.e., primary depression, secondary depression and mania. In spite of this, until the introduction of the DSM-III the St. Louis criteria were probably one of the most extensively employed research diagnostic criteria in the testing of therapeutic efficacy of antipsychotic and antidepressant drugs (Appendix V, Table I).

The Research Diagnostic Criteria (RDC) is an elaboration, expansion and modification of the St. Louis criteria by Spitzer, Endicott and Robins (1978a and b). It was developed as part of a collaborative project on the psychobiology of depressive disorders sponsored by the Clinical Research Branch of the National Institute of Mental Health of the United States (Maas et al., 1980). As a result of the modifications the RDC is considerably more inclusive than the St. Louis criteria. Although it allows only for a narrow definition of different disorders it can accommodate most patients. Furthermore by subtyping schizophrenic psychoses on the basis of its course and manifest psychopathological symptoms (phenomenology) and by subdividing major affective disorders into a number of different types it allows for the testing of many hypotheses relevant to schizophrenic and affective illnesses (Appendix V, Table II).

Considerably different than the St. Louis criteria and the RDC are Taylor and Abrams' criteria for schizophrenia, mania and endogenous depression (Abrams, Taylor and Gaztanga, 1974; Taylor and Abrams, 1978; Taylor, Gaztanga and Abrams, 1974; Taylor, Redfield and Abrams, 1981). These criteria developed in the course

of a dialogue with the St. Louis group (Taylor and Abrams, 1975) and are more in keeping with the Kraepelinian and Bleulerian tradition than the St. Louis criteria. Taylor and Abrams' criteria of mania and endogenous depression are derived from Slater and Roth's (1969) classical descriptions. Although they are essentially pragmatic and empirical, Taylor and Abrams' criteria have been included in heuristic studies comparing different diagnostic systems (Appendix V, Table III).

The Vienna Research Criteria (VRC) for schizophrenic psychoses, referred to as the endogenomorphic-schizophrenic axial syndrome, and affective disorders, referred to as endogenomorphic-affective axial syndromes superficially resemble Taylor and Abrams' criteria. Its development can be traced to Berner's (1965, 1969) follow up study on paranoiac patients; and the recognition that a proportion of these patients suffer from a schizophrenic or an affective (referred to as cyclothymic) disorder. With the syndromes derived from the initial psychopathological symptom profiles a catamnestic study was designed. The purpose of this study was to test the hypothesis that paranoiac patients can be assigned to one of the two diagnoses on the basis of operationally defined criteria at the time of their first (index) admission (Müller, 1981). The operationally defined criteria were referred to as "axial syndromes," a term first used by Hoche (1912). The adjective "endogenomorphic" was added for distinguishing axial syndromes from definitive diagnoses. The VRC consists of six endogenomorphic axial syndromes, one schizophrenic and five affective.

In the formulation of the six axial syndromes, Janzarik's (1948, 1959) concept of "structural dynamic coherency" has played an important role. Within this frame of reference Schneider's (1950, 1959) first rank symptoms (Mellor, 1982) and some of Bleuler's (1911, 1950) fundamental symptoms, such as ambivalence,



depersonalization and derealization are not considered to be of diagnostic significance. Other fundamental symptoms such as formal thought disorder, affective blunting and cryptic neologisms, are considered to be nonspecific. However, they remain acceptable criteria because diagnostically there are either schizophrenic or organic (but definitely not affective) in origin. Taking all these into consideration it is not surprising that the endogenomorphic axial schizophrenic syndrome has the narrowest concept of schizophrenia among all research diagnostic criteria.

The five endogenomorphic axial affective syndromes are referred to as depressive, manic, dysphoric, unstable mixed and stable mixed. Common characteristics of these axial syndromes are the disturbance of biorhythm manifest in the diurnal variation of symptoms and sleep disturbance. Differential characteristics are based on the different types of dynamic derailments described by Janzarik (1948, 1959) and Berner (1969), e.g., dynamic expansion (seen in the manic axial syndrome), dynamic restriction (seen in the depressive axial syndrome), dynamic instability characterized by rapid fluctuation or swings between the first two (seen in the unstable mixed axial syndrome). It remains to be seen whether the diagnostic groups, which are based on this highly sophisticated theoretical approach are biologically more homogenous than the diagnostic groups based on other diagnostic criteria for research.

#### Diagnostic Criteria for Research

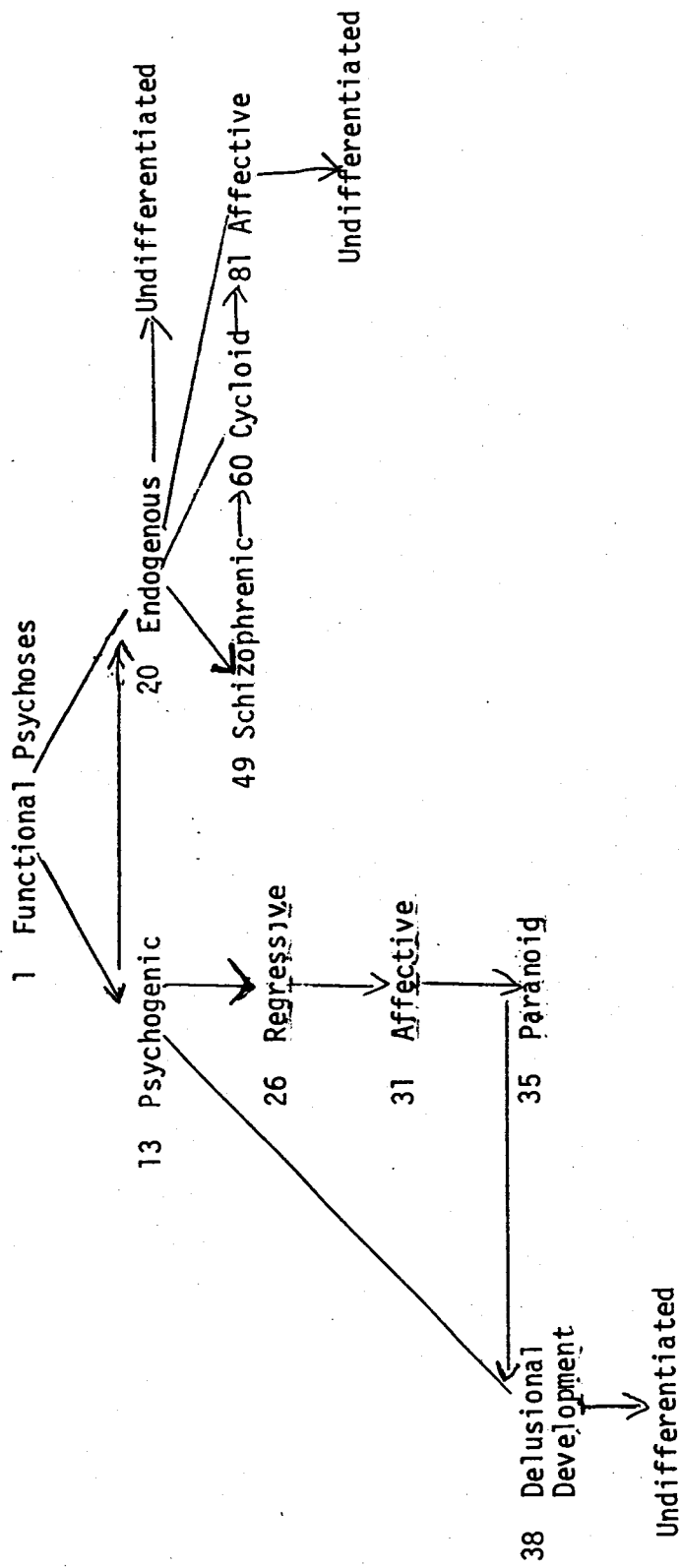
The Diagnostic Assessment Scale (DAS) of the Diagnostic Criteria for Research (DCR), developed primarily for research purposes, is one of the diagnostic assessment scales which includes all diagnoses within the functional psychoses. It is essentially based on the KDK Budapest which was published in Hungarian under the title Experimental Diagnostic Criteria for

the Diagnosis of Functional Psychoses by Petho, Ban, Kelemen, Ungvari, Karczag, Bitter and Tolna in 1984.

The DCR differs from the other research diagnostic criteria in that it is based on a four-dimensional model of diagnosis with consideration to all four developmental stages of psychiatric illness. In the course of the diagnostic process, functional psychoses are separated into psychogenic and endogenous; psychogenic psychoses into regressive, affective and paranoid psychoses and delusional development; and endogenous psychoses into schizophrenic, cycloid and affective (Figure 3a). Schizophrenic psychoses are subdivided into nonsystematic and systematic; nonsystematic schizophrenias into affect-laden paraphrenia (anxious, ecstatic and bipolar), cataphasia (agitated and inhibited), and periodic catatonia (hyperkinetic, akinetic and bipolar); and systematic schizophrenias into catatonias (parakinetic, prokinetic, speech prompt, speech inactive, manneristic and negativistic), hebephrenias (silly, eccentric, shallow and autistic), and paraphrenias (hypochondriacal, phonemic, incoherent, fantastic, confabulatory and expansive) (Figure 3b). Cycloid psychoses are subdivided into anxiety-elation (anxious and elated), confusion (inhibited and excited) and motility (akinetic and hyperkinetic) psychoses; and affective psychoses into melancholic and manic (both, pure and manic melancholic) psychoses. On the melancholic side there is an additional subdivision into depressions (harried, hypochondriacal, self-torturing, suspicious and nonparticipatory) and on the manic side there is an additional subdivision into euphorias (unproductive, hypochondriacal, enthusiastic, confabulatory and nonparticipatory) (Figure 3c).

The diagnostic instrument of the DCR is the DAS which consists of 396 items, presented in 12 tables, each table representing one step in the differential diagnostic process (Table II/1-12).

Figure 3a



Schematic presentation of the diagnostic process. (Functional Psychoses.) The numbers refer to reference points on the DAS.

Figure 3b

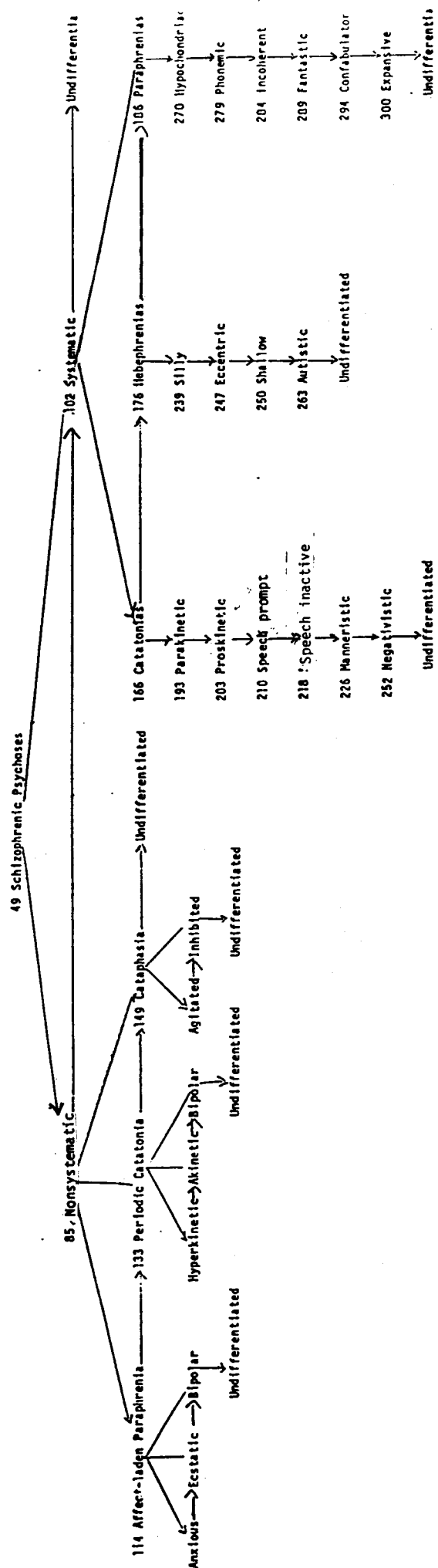
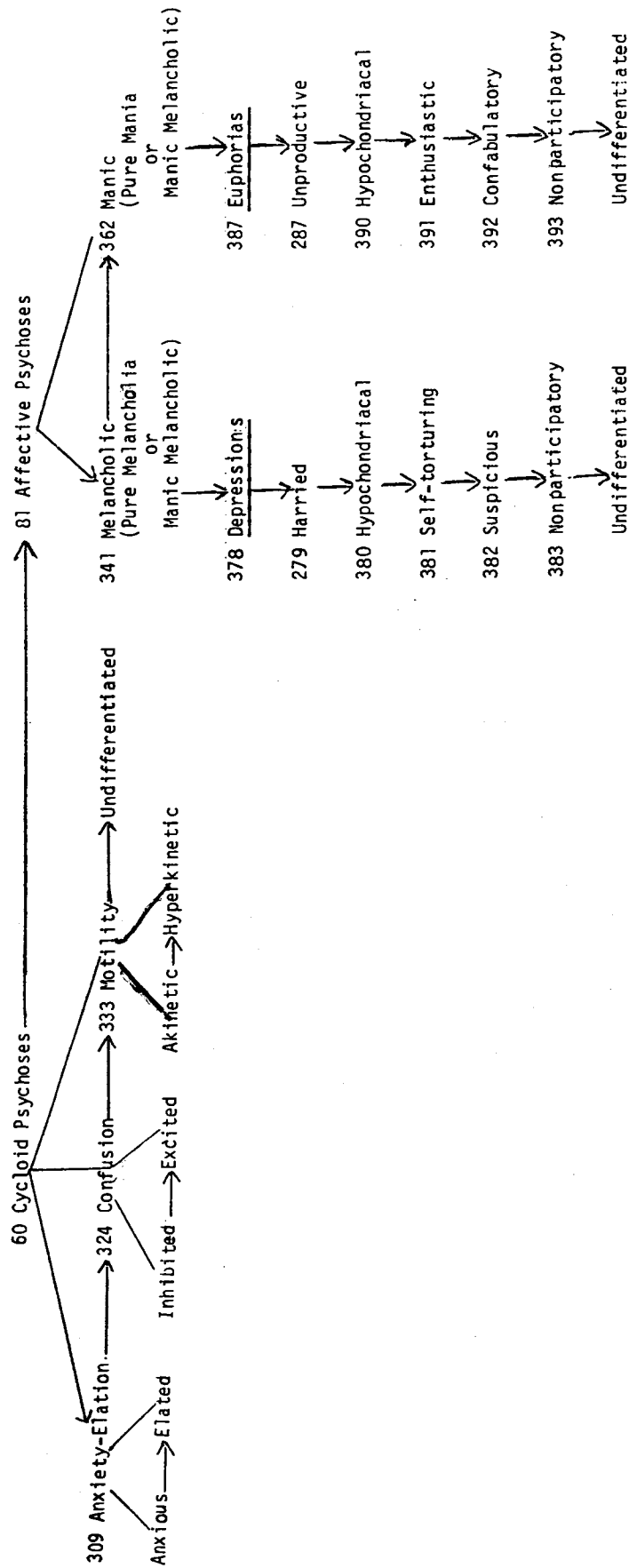


Figure 3c



Schematic presentation of the diagnostic process. (Cycloid and Affective Psychoses.)

Table 11/1

DAS Functional Psychoses

1. Psychopathology induced disruption of functioning (at present)
  2. Lack of insight (at present)
  3. Collapse of customary way of life (at present)
  4. Psychiatric hospitalization (at present)
    - Less than 3 go to 5
    - At least 3 go to 2
  5. Psychopathology induced disruption of functioning (in past)
  6. Lack of insight (in past)
  7. Collapse of customary way of life (in past)
  8. Psychiatric hospitalization (in past)
    - Less than 3 MINOR PSYCHIATRIC DISORDER
    - At least 3 go to 9
  9. Absence of somatic illness (at least 1 of 2)
    - a. at start of psychosis
    - b. immediately prior to start of psychosis
  10. Somatic illness not of sufficient severity to explain (at least 1 of 2)
    - a. disturbance of consciousness
    - b. mental deterioration
  11. Somatic illness and mental disturbance do not run parallel course
    - Less than 2 ORGANIC DISORDER
    - At least 2 go to 12
  12. IQ of 70 or above
    - Less than 1 MENTAL RETARDATION
    - go to 13
- Endogenous
- |   |  |
|---|--|
| <ol style="list-style-type: none"> <li>13. Psychosis is attributable to life event</li> <li>14. Psychotic content is understandable on the basis of (at least 1 of 3)           <ol style="list-style-type: none"> <li>a. life event</li> <li>b. life history</li> <li>c. patient's personality</li> </ol> </li> <li>15. Psychosis is an integral part of patient's life history           <ol style="list-style-type: none"> <li>Less than 2 go to 20</li> <li>At least 2 go to 16</li> </ol> </li> <li>16. Intensity of trauma explains emergence of psychosis</li> <li>17. Thematic continuity between trauma and content of psychosis</li> <li>18. There is a meaning to the psychosis           <ol style="list-style-type: none"> <li>Less than 2 go to 20</li> <li>At least 2 go to 19</li> </ol> </li> <li>19. Absence of endogenous psychopathological symptoms such as           <ol style="list-style-type: none"> <li>a. inhibited thinking</li> <li>b. tangential thinking</li> <li>c. flight of ideas</li> <li>d. perseveration</li> <li>e. neologisms</li> <li>f. blunted affect</li> <li>g. autistic behavior</li> </ol> <ol style="list-style-type: none"> <li>Less than 1 go to 20</li> <li>go to 26</li> </ol> </li> </ol> | <ol style="list-style-type: none"> <li>20. Psychosis is not attributable to life event</li> <li>21. Psychotic content is incomprehensible (at least 1 of 2)           <ol style="list-style-type: none"> <li>a. bizarre</li> <li>b. disorganized</li> </ol> </li> <li>22. Psychosis is not an integral part of patient's life history           <ol style="list-style-type: none"> <li>Less than 2 FUNCTIONAL PSYCHOSIS UNDIFFERENTIATED</li> <li>At least 2 go to 23</li> </ol> </li> <li>23. Lack of precipitating trauma</li> <li>24. No thematic continuity between trauma and content of psychosis</li> <li>25. There is no meaning to the psychosis           <ol style="list-style-type: none"> <li>Less than 2 FUNCTIONAL PSYCHOSIS UNDIFFERENTIATED</li> <li>At least 2 go to 49</li> </ol> </li> </ol> |
|---|--|

Table II/2

## DAS Psychogenic Psychoses

<u>Regressive Psychosis</u>	<u>Delusional Development</u>
26. Acute onset Less than 1 go to 38 1 go to <u>27</u>	
27. Clouding of consciousness	
28. Impaired orientation Less than 1 go to 31 At least 1 go to <u>29</u>	
29. Resolution of psychopathological symptoms within three months Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>30</u>	
30. Full remission Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 PSYCHOGENIC REGRESSIVE PSYCHOSIS	
	<u>Affective</u>
31. Exaltation	
32. Depression Less than 1 go to <u>35</u> 1 go to <u>33</u>	
33. Resolution of psychopathological symptoms within three months Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>34</u>	
34. Full remission Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 PSYCHOGENIC AFFECTIVE PSYCHOSIS	
	<u>Paranoid</u>
35. Delusions of reference Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>36</u>	
36. Resolution of psychopathological symptoms within three months Less than 1 go to 38 1 go to <u>37</u>	
37. Full remission Less than 1 go to 38 1 PSYCHOGENIC PARANOID PSYCHOSIS	
	38. Delusions (at least 2 of 4) a. logically derived systematized delusions b. delusions are spreading to a restricted area c. change of personality d. no disintegration of personality Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>39</u>
	39. Paranoid personality trait(s)
	40. Key experience Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>41</u>
	41. Passionate (1 of 3) a. idealists b. conjugal paranoia c. erotomania 1
	42. Litigious (1 of 2) a. querulous paranoia b. reformatory zealotry 1
	43. Monosymptomatic-hypochondriacal (1 of 2) a. delusions of parasitosis b. Shikano syndrome 1
	44. Shared (symbiotic) (1 of 2) a. folie a deux b. folie a trois Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>45</u>
	45. Subacute onset
	46. Tendency for chronicity Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED At least 1 PSYCHOGENIC DELUSIONAL DEVELOPMENT
	47. Transformation of personality
	48. Maladjustment Less than 1 PSYCHOGENIC PSYCHOSIS UNDIFFERENTIATED At least 1 PSYCHOGENIC DELUSIONAL DEVELOPMENT

Table II/3

DAS Endogenous Psychoses

<u>Schizophrenic</u>	<u>Cycloid</u>	<u>Affective</u>
49. Psychosis has no meaning and it is (at least 1 of 3) a. incomprehensible b. purposeless c. intruding event	60. Acute onset	81. Holothymic (mood-congruent) changes (at least 1 of 3) a. experience b. behavior c. performance
50. Dissociation (split)	61. Subacute onset Less than 1 go to 81 1 go to 62	82. Holothymic (mood congruent) delusions Less than 1 ENDOGENOUS PSYCHOSIS UNDIFFERENTIATED At least 1 go to 83
51. Catachymic involvement of content Less than 2 go to 60 At least 2 go to 52	62. Protoathic change of Gestalt (at least 1 of 3) a. tremat b. apophany c. apocalyptic	83. Monomorphous disease picture
52. Formal thought disorder that disturbs comprehensibility (at least 1 of 5) a. primary incoherence b. tangential thinking c. blocking d. derailment e. desultory thinking f. onomatopoesis	63. Polymorphous fluctuating	84. Polymorphous disease picture Less than 1 ENDOGENOUS PSYCHOSIS UNDIFFERENTIATED 1 go to 34
53. Delusions	64. Presence of contradictory influences	
54. Hallucinations	65. Change in the depth of emotions (1 of 4) a. apathy b. anxiety c. happiness d. ecstasy	
55. Affective change (at least 1 of 4) a. blunted b. inadequate c. inappropriate d. decreased depth	66. Holothymic (mood congruent) delusions	
56. Personality change (at least 1 of 4) a. abandonment of habits b. change in life style c. incomprehensibility of behavior d. autistic behavior Less than 1 go to 60 At least 1 go to 57	67. Emotional involvement in symptoms	
57. Clear consciousness	68. Harmony: experience, behavior and performance Less than 4 go to 81 At least 4 go to 69	
58. No holothymic evaluations Less than 2 go to 60 2 go to 59	69. Ideas of reference	
59. Consistent presence of psychopathological symptoms for two weeks Less than 1 go to 60 1 go to 85	70. Delusional perceptions	
	71. Misidentifications	
	72. Increase of expressive movements	
	73. Decrease of expressive movements	
	74. Increase of reactive movements	
	75. Decrease of reactive movements	
	76. Thematic incoherence Less than 1 go to 81 At least 1 go to 77	
	77. Rhythmic course	
	78. Bipolar course Less than 1 go to 81 At least 1 go to 79	
	79. Accentuated personality	
	80. Full remission Less than 1 go to 81 1 go to 309	



## DAS Schizophrenic Psychoses

## Systematic

85. Acute onset
86. Subacute onset  
Less than 1 go to 102  
1 go to 87
87. Polymorphous disease picture
88. Entire personality affected
89. Emotional availability
90. Affective participation in symptoms
91. Hyperthymic features
92. Dysthymic features  
Less than 3 go to 102  
At least 3 go to 93
93. Hallucinations
94. Emotionally loaded delusions
95. Catatonic symptoms (at least 1 of 2)  
a. excitement  
b. stupor
96. Schizophrenic type of formal thought disorder  
(at least 2 of 9)  
a. asyndetic thinking  
b. blocking  
c. derailment  
d. desultory thinking  
e. drivelling  
f. inhibited thinking  
g. neologisms  
h. primary incoherence  
i. tangential thinking  
Less than 1 go to 102  
At least 1 go to 97
97. Rhythmic course
98. Schub-type episodes
99. Bipolar course  
Less than 2 go to 102  
At least 2 go to 100
100. Transient remission(s)
101. Residual symptoms (at least 2 of 14)  
a. bizarre ideation  
b. blunted affect  
c. circumstantial speech  
d. ideas of reference  
e. inappropriate affect  
f. impairment in role functioning  
g. peculiar behavior  
Less than 1 go to 102  
At least 1 go to 114
102. Insidious onset of first episode
103. No full remission after first episode
104. Double-entry book-keeping
105. Monomorphous disease picture
106. Amorphous disease picture  
Less than 2 SCHIZOPHRENIC PSYCHOSIS UNDIFFERENTIATED  
At least 2 go to 107
107. Delusions
108. Hallucinatory excitement
109. Catatonic symptoms (at least 1 of 15)  
a. ambitendency  
b. automatic obedience  
c. cooperation in movements  
d. excitement  
e. mannerisms  
f. mutism  
g. negativism  
h. parakineses  
i. posturing  
j. proskineses  
k. rigidity  
l. stereotypies  
m. stupor  
n. waxy flexibility
110. Blunted affect  
Less than 1 SCHIZOPHRENIC PSYCHOSIS UNDIFFERENTIATED  
At least 1 go to 111
111. Chronic continuous course
112. Chronic episodic course
113. Defect syndrome (at least 1 of 2)  
a. clinical defect  
b. personality defect  
Less than 2 SCHIZOPHRENIC PSYCHOSIS UNDIFFERENTIATED  
At least 2 go to 166

Table II/5

DAS Nonsystematic Schizophrenias

Affect-laden Paraphrenia

- 114. Polymorphous stabilized
- 115. Polymorphous systematized
- 116. Primary affective change  
Less than 2 go to 133  
2 go to 117
- 117. Secondary delusions
- 118. Paralogically derived systematized delusional system
- 119. Paralogically derived non-systematized delusions
- 120. Logically derived non-systematized delusions
- 121. Strong delusional dynamics  
Less than 3 go to 133  
3 go to 122
- 122. Anxiety
- 123. Irritability
- 124. Ecstasy
- 125. Fluctuating affective state  
Less than 1 go to 133  
At least 1 go to 126
- 126. Delusions of reference
- 127. Delusions of grandeur
- 128. Fantastic delusions
- 129. Mixed delusions  
Less than 1 go to 133  
At least 1 go to 130
- 130. Anxious affect-laden paraphrenia (at least 2 of 4)  
a. anxiety  
b. irritability  
c. delusions of reference  
d. fantastic delusions
- 131. Ecstatic affect-laden paraphrenia (1 of 2)  
a. ecstatic mood  
b. grandiose delusions
- 132. Bipolar affect-laden paraphrenia (2 of 2)  
a. fluctuating affective state  
b. mixed delusions  
Less than 1 AFFECT-LADEN PARAPHRENIA UNDIFFERENTIATED  
1 (+ 130) ANXIOUS AFFECT-LADEN PARAPHRENIA  
1 (+ 131) ECSTATIC AFFECT-LADEN PARAPHRENIA  
1 (+ 132) BIPOLAR AFFECT-LADEN PARAPHRENIA

Periodic Catatonia

- 133. Polymorphous stabilized
- 134. Polymorphous fluctuating
- 135. Paralogically derived non-systematized delusions
- 136. Logically derived non-systematized delusions
- 137. Loss of natural harmony of movements
- 138. Decrease of expressive movements
- 139. Decrease of reactive movements  
Less than 2 go to 149  
At least 2 go to 140
- 140. Parakinesis
- 141. Motor stereotypy
- 142. Postural stereotypy
- 143. Impulsive acts
- 144. Negativism  
Less than 1 go to 149  
At least 1 go to 145
- 145. Hyperkinesia
- 146. Hypokinesia
- 147. Akinesia
- 148. Mixed kinesia  
Less than 1 PERIODIC CATATONIA UNDIFFERENTIATED  
1 (+ 145) HYPERKINETIC PERIODIC CATATONIA  
1 (+146 or 147) AKINETIC PERIODIC CATATONIA  
1 (+ 148) BIPOLAR PERIODIC CATATONIA

Cataphasia

- 149. Polymorphous stabilized
- 150. Monomorphous disease picture  
Less than 1 NONSYSTEMATIC SCHIZOPHRENIA UNDIFFERENTIATED  
1 go to 151
- 151. Agitation
- 152. Pressure of speech
- 153. Confusion
- 154. Asyntaxis
- 155. Paralogia
- 156. Paragrammatism
- 157. Behavior more coherent than speech
- 158. Responses to questions more coherent than spontaneous speech
- 159. Inhibition
- 160. Taciturn
- 161. Mute
- 162. Dull and empty facial expression
- 163. Neologisms  
Less than 4 NONSYSTEMATIC SCHIZOPHRENIA UNDIFFERENTIATED  
At least 4 go to 164
- 164. Agitated cataphasia (at least 4 of 8)  
a. agitation  
b. pressure of speech  
c. confusion  
d. asyntaxis  
e. paralogia  
f. paragrammatism  
g. behavior more coherent than speech  
h. responses to questions more coherent than spontaneous speech
- 165. Inhibited cataphasia (at least 3 of 4)  
a. inhibition  
b. taciturn  
c. mute  
d. dull and empty facial expression  
Less than 1 CATAPHASIA, UNDIFFERENTIATED  
1 (+ 164) AGITATED CATAPHASIA  
1 (+ 165) INHIBITED CATAPHASIA

Table II./6

PAS Systematic Schizophrenias

<u>Catatonias</u>	<u>Hebephrenias</u>	<u>Paraphrenias</u>
166. Loss of gracefulness	176. Amorphous clinical picture	184. Inhibited thinking
167. Loss of automatisms	177. Uninvolved	185. Desultory thinking
168. Sluggish-unresponsive	178. Blunted affect	186. Tangential thinking
169. Highstrung-hyperactive Less than 2 go to <u>176</u> At least 2 go to <u>170</u>	179. Emotional impoverishment Less than 1 go to <u>184</u> At least 1 go to <u>180</u>	187. Blocking
170. Parakineses	180. Silly	188. Primary incoherence
171. Mannerisms	181. Eccentric	189. Neologisms Less than 1 SYSTEMATIC SCHIZOPHRENIA UNDIFFERENTIATED
172. Proskineses	182. Shallow	At least 1 go to <u>190</u>
173. Negativism	183. Autistic Less than 1 go to <u>184</u> At least 1 go to <u>259</u>	190. Delusions
174. Speech prompt		191. Hallucinations
175. Speech inactive Less than 1 go to <u>176</u> At least 1 go to <u>193</u>		192. Disorders of ego (at least 1 of 6) a. derealization b. depersonalization c. thought broadcasting d. thought withdrawal e. thought insertion f. feelings of alien influences Less than 2 SYSTEMATIC SCHIZOPHRENIA UNDIFFERENTIATED At least 2 go to <u>270</u>

Table II/7

DAS Systematic Catatonias

<u>Parakinetic</u>	<u>Speech Prompt</u>	<u>Manneristic</u>
193. Continuous parakinesis	210. Speech readiness Less than 1 go to <u>218</u> 1 go to <u>211</u>	226. Hard mannerisms
194. Jerkiness	211. Echoialia	227. Decreased automatisms
195. Increase of pseudoexpressive movements	212. Perseveration	228. Affectation Less than 2 go to <u>232</u> At least 2 go to <u>229</u>
196. Increase of reactive movements	213. Agrammatism	229. Affectivity well retained
197. Choppy speech Less than 2 go to 200 At least 2 go to <u>198</u>	214. Contaminations	230. Perceptual psychopathology absent
198. Derailment	215. Empty autism Less than 1 go to <u>218</u> At least 1 go to <u>216</u>	231. Delusions absent Less than 2 go to 232 At least 2 MANNERISTIC CATATONIA
199. Contented mood Less than 1 go to 200 At least 1 PARAKINETIC CATATONIA	216. Stiffness	<u>Negativistic</u>
<u>Proskinetik</u>	217. Adversion Less than 1 go to <u>218</u> At least 1 SPEECH READY CATATONIA	232. Active negativism
200. Proskinesis Less than 1 go to 210 1 go to <u>201</u>	<u>Speech Inactive</u>	233. Passive negativism Less than 1 SYSTEMATIC CATATONIA UNDIFFERENTIATED At least 1 go to <u>234</u>
201. Perseveration	218. Sluggish Less than 1 go to <u>226</u> At least 1 go to <u>219</u>	234. Ambivalence
202. Verbigeration	219. Low initiative	235. Ambitendency
203. Mumbling	220. Low motivation Less than 1 go to <u>226</u> At least 1 go to <u>221</u>	236. Negativistic excitement's Less than 1 SYSTEMATIC CATATONIA UNDIFFERENTIATED At least 1 go to <u>237</u>
204. Fidgety	221. Persistent hallucinations	237. Blunted affect
205. Fumbling Less than 1 go to 210 At least 1 go to <u>206</u>	222. Hallucinatory distractions	238. Impulsive outbursts Less than 1 SYSTEMATIC CATATONIA UNDIFFERENTIATED At least 1 NEGATIVISTIC CATATONIA
206. Contented Mood	223. Hallucinatory excitements	
207. Blunted Affect	224. Primary incoherence	
208. Episodic ranting	225. Perplexed Less than 1 go to <u>226</u> At least 1 SLUGGISH CATATONIA	
209. Episodic excitement Less than 1 go to 210 At least 1 PROSKINETIC CATATONIA		

Table III/8

DAS Systematic Hebephrenias

<u>Silly</u>		<u>Shallow</u>
239. Immature behavior		256. Extreme emotional impoverishment
240. Inane giggling Less than 1 go to <u>247</u> At least 1 go to <u>241</u>		257. Formal participation relatively well preserved Less than 2 go to <u>263</u> 2 go to <u>258</u>
241. Empty euphoria		258. Carefree euphoria
242. Fluctuating mild depression		259. Episodes of markedly anxious mood Less than 1 go to <u>263</u> at least 1 go to <u>260</u>
243. Alogical thinking Less than 2 go to <u>247</u> At least 2 go to <u>244</u>		260. Hallucinatory episodes
244. Ethical blunting		261. Lack of initiative
245. Episodic irritability		262. Decreased activity Less than 1 go to <u>263</u> At least 1 <u>SHALLOW HEBEPHRENIA</u>
246. Episodic excitement Less than 1 go to <u>247</u> At least 1 <u>SILLY HEBEPHRENIA</u>		<u>Autistic</u>
<u>Eccentric</u>		263. Empty autism Less than 1 <u>SYSTEMATIC HEBEPHRENIA UNDIFFERENTIATED</u> 1 go to <u>264</u>
247. Soft mannerisms		264. Mood of discontent
248. Precocious chattering Less than 1 go to <u>256</u> At least 1 go to <u>249</u>		265. Feelings of rejection
249. Dysthymia		266. Off-putting verbal responses Less than 1 <u>SYSTEMATIC HEBEPHRENIA UNDIFFERENTIATED</u> At least 2 go to <u>267</u>
250. Querulous complaintiveness		267. Episodes of irritability
251. Hypochondriasis Less than 1 go to <u>256</u> At least 1 go to <u>252</u>		268. Episodes of (verbal or physical) aggression
252. Monotonous self-praise		269. Hallucinatory episodes Less than 1 <u>SYSTEMATIC HEBEPHRENIA UNDIFFERENTIATED</u> At least 1 <u>AUTISTIC HEBEPHRENIA</u>
253. Rituals		
254. Hoarding		
255. Senseless stealing Less than 1 go to <u>256</u> At least 1 <u>ECCENTRIC HEBEPHRENIA</u>		

## DAS Systematic Paraphrenias

<u>Hypochondriacal</u>	<u>Incoherent</u>	<u>Confabulatory</u>
270. Heteronom bodily hallucinations	284. Hallucinatory rich autism	294. Continuous confabulations
271. Phonemic hallucinations Less than 2 go to 279 2 go to <u>272</u>	285. Primary incoherence Less than 2 go to 289 2 go to <u>286</u>	295. Paramesias Less than 2 go to 300 2 go to <u>296</u>
272. Complaints of hearing voices	286. Delusions of persecution	296. Elated mood
273. Dysphoria Less than 1 go to 279 At least 1 go to <u>274</u>	287. Delusions of grandeur	297. Friendliness
274. Olfactory hallucinations	288. Hallucinatory excitements Less than 1 go to 289 At least 1 INCOHERENT PARAPHRENIA	298. Grandiose delusions
275. Gustatory hallucinations	<u>Fantastic</u>	299. Concrete ideation Less than 2 go to 300 At least 2 CONFABULATORY PARAPHRENIA
276. Visual hallucinations	289. Mixed (often scenic) hallucinations	<u>Expansive</u>
277. Explanatory delusions	290. Fantastic experiences Less than 2 go to 294 2 go to <u>291</u>	300. Grandiose delusions
278. Tangential thinking Less than 1 go to 279 At least 1 HYPOCHONDRIACAL PARAPHRENIA	291. Grandiose delusions	301. Grandiose mannerisms
<u>Phonemic</u>	292. Contented mood	302. Course paralogic thinking Less than 2 SYSTEMATIC PARAPHRENIA UNDIFFERENTIATED At least 2 go to <u>303</u>
279. Phonemic delusional hallucinations Less than 1 go to 284 1 go to <u>280</u>	293. Derailment Less than 1 go to 294 At least 1 FANTASTIC PARAPHRENIA	303. Grandiose aspirations
280. Audible thoughts		304. Restricted thinking
281. Explanatory delusions		305. Early hallucinations
282. Even mood		306. Early ideas of reference
283. Woolly thinking Less than 2 go to 284 At least 2 PHONEMIC PARAPHRENIA		307. Early states of excitement
		308. Late emotional blunting Less than 2 SYSTEMATIC PARAPHRENIA UNDIFFERENTIATED At least 2 EXPANSIVE PARAPHRENIA

Table II/10

## DAS Cycloid Psychoses

<u>Anxiety-Elation</u>	<u>Confusion</u>	<u>Motility</u>
309. Delusional perceptions	324. Decreased talkativeness	334. Confused stupor
310. Delusions of reference	325. Decreased activity	335. Akinesia Less than 1 go to 336 At least 1 AKINETIC MOTILITY PSYCHOSIS
311. Marked anxiety Less than 3 go to 321 3 go to <u>312</u>	326. Confusion Less than 3 go to 330 3 go to <u>327</u>	336. Agitation
312. Perplexed	327. Reactive stupor	337. Increase of expressive movements
313. Illusions	328. Misperceptions	338. Increase of reactive movements Less than 1 CYCLOID PSYCHOSIS At least 1 UNDIFFERENTIATED
314. Phonemic hallucinations	329. Phonemic hallucinations Less than 1 go to 330 At least 1 INHIBITED CONFUSION PSYCHOSIS	339. Hyperkinetic speech
315. Olfactory hallucinations	330. Excitement Less than 1 go to 334 At least 1 go to <u>331</u>	340. Thematic incoherence Less than 1 CYCLOID PSYCHOSIS At least 1 HYPERKINETIC MOTILITY - PSYCHOSIS
316. Bodily hallucinations Less than 2 go to 321 At least 2 go to <u>317</u>	331. Thematic incoherence	
317. Inhibition	332. Logorrhea	
318. Agitation	333. Fragmentary hallucinations Less than 1 go to 334 At least 1 EXCITED CONFUSION PSYCHOSIS	
319. Feelings of guilt		
320. Feelings of inferiority Less than 1 go to 321 At least 1 ANXIETY-ELATION PSYCHOSIS, ANXIOUS		
321. Elation		
322. Exaggerated self-esteem		
323. Misperceptions Less than 1 to go 324 At least 1 ANXIETY-ELATION PSYCHOSIS, ELATED		

Table II/11'

DAS Affective Psychoses 1

<u>Melancholia</u>		<u>Mania</u>	
341. Acute onset		362. Elation	
342. Subacute onset Less than 1 go to 378 go to <u>343</u>		363. Irritability Less than 1 At least 1	go to 387 go to <u>364</u>
343. Depressive mood Less than 1 go to 362 go to <u>344</u>		364. Hyperthymia	
344. Decreased appetite		365. Euphoria	
345. Increased appetite		366. Hyperactivity	
346. Insomnia		367. Logorrhea	
347. Hypersomnia		368. Flight of Ideas	
348. Decreased libido		369. Grandiosity	
349. Increased libido		370. Insomnia	
350. Decreased psychomotor activity		371. Distractibility	
351. Increased psychomotor activity		372. Tactless	
352. Anhedonia		373. Reckless Less than 6 At least 6	go to 387 go to <u>374</u>
353. Feelings of guilt		374. Unipolar course	
354. Self-incrimination		375. Bipolar course	
355. Concentration difficulties		376. Rhythmic course Less than 2	go to 387 go to <u>377</u>
356. Retarded thinking		377. Full remission Less than 1 1 (+ 374) 1 (+ 375)	go to 387 PURE MANIA MANIC MELANCHOLIC PSYCHOSIS MANIC
357. Suicidal behavior Less than 6 At least 6	go to 378 go to <u>358</u>		
358. Unipolar course			
359. Bipolar course			
360. Rhythmic course Less than 2 2	go to 378 go to <u>361</u>		
361. Full remission Less than 1 1 (+ 358) 1 (+ 359)	go to 378 PURE MELANCHOLIA MANIC MELANCHOLIC PSYCHOSIS MELANCHOLIC		



Table II/12

DAS Affective Psychoses 2

Depressions		Euphorias	
378.	Monomorphous Less than 1 go to 387 1 go to <u>379</u>	387.	Euphoria
379.	Harried depression (at least 3 of 4) a. motor restlessness b. marked anxiety c. driven complaintiveness d. poor thematization	388.	Monomorphous disease picture Less than 2 AFFECTIVE PSYCHOSIS UNDIFFERENTIATED
380.	Hypochondriacal depression (at least 3 of 4) a. hypochondriasis b. homonom bodily hallucinations c. hopeless complaintiveness d. corporization	389.	Unproductive euphoria (at least 2 of 3) a. radiant facial expression b. motiveless feeling of happiness c. contentless vital emotional tone
381.	Self-torturing depression (at least 3 of 4) a. self-accusations b. loss of self-esteem c. lamentativeness d. feelings of guilt	390.	Hypochondriacal euphoria (at least 2 of 3) a. homonom bodily hallucinations b. euphoric complaintiveness c. transient tearfulness
382.	Suspicious depression (at least 3 of 4) a. suspiciousness b. ideas of reference c. paranoid ideation d. lack of hostility	391.	Enthusiastic euphoria (at least 2 of 3) a. excessive happiness b. exaggerated self-esteem c. desire to make others happy
383.	Nonparticipatory depression (at least 3 of 4) a. lack of affective participation b. anhedonia c. feelings of alienation d. abulia Less than 1 DEPRESSIVE PSYCHOSIS UNDIFFERENTIATED More than 1 DEPRESSIVE PSYCHOSIS UNDIFFERENTIATED 1 go to <u>384</u>	392.	Confabulatory euphoria (at least 2 of 3) a. happy confabulations b. lively c. playful
384.	Unipolar course	393.	Nonparticipatory euphoria (at least 2 of 3) a. impoverishment of will b. impoverishment of emotions c. lack of feelings of sympathy Less than 1 EUPHORIC PSYCHOSIS UNDIFFERENTIATED More than 1 EUPHORIC PSYCHOSIS UNDIFFERENTIATED 1 go to <u>394</u>
385.	Tendency for chronicity	394.	Unipolar course
386.	Full remission Less than 2 DEPRESSIVE PSYCHOSIS UNDIFFERENTIATED 2 (+ 379) HARRIED DEPRESSION 2 (+ 380) HYPOCHONDIACAL DEPRESSION 2 (+ 381) SELF-TORTURING DEPRESSION 2 (+ 382) SUSPICIOUS DEPRESSION 2 (+ 383) NONPARTICIPATORY DEPRESSION	395.	Tendency for chronicity
		396.	Full recovery Less than 2 EUPHORIC PSYCHOSIS UNDIFFERENTIATED 2 (+ 385) UNPRODUCTIVE EUPHORIA 2 (+ 390) HYPOCHONDIACAL EUPHORIA 2 (+ 391) ENTHUSIASTIC EUPHORIA 2 (+ 392) CONFABULATORY EUPHORIA 2 (+ 393) NONPARTICIPATORY EUPHORIA

In completing DAS the following time frames are considered:

- a. Presence of psychosis (one-dimensional diagnosis) can usually be determined by a single examination. It should definitely be possible within eight days.
- b. At least two weeks of continuous observation and repeated--at least three--careful assessments are required to clarify the nature of the psychosis (two-dimensional diagnosis). This, however, does not imply that the psychosis must be present for at least two weeks and that treatment should be withheld for the same time period.
- c. Course of disease always refers to a specified period with a duration of at least five years (three-dimensional diagnosis). Formal characteristics of the course, such as rhythmicity-periodicity, polarity and deterioration are distinguished from the contentual characteristics, such as time spent in hospital, nature of therapies.
- d. The evaluation of outcome, e.g., after five years is always done in terms of the presence of psychopathological symptoms and impairment of social adjustment (fourth-dimension).

Thus, for a final diagnosis on the DAS cross-sectional findings (diagnostic impressions) have to be supplemented with information on the course of the disease (provisional diagnosis) and outcome data (final diagnosis). Or in other words, in the diagnostic hierarchy (impression, provisional and final) alternative decisions are based not merely on a given store of (cross-sectional) knowledge, but on the increasing store of knowledge in time.

In spite of all its complexities, inter-rater agreement was very high, 92 percent (12 of 13 patients) between two raters in a small pilot study on the DAS. For the most distal diagnostic endpoints of the decision tree (subtypes) agreement was only 77 percent but for the three major groups of

systematic schizophrenia (hebephrenia, catatonia and paraphrenia) the agreement was 100 percent (Daniel, Craig, Ban and Wilson, 1985).

In addition to reliability the pilot study also explored the relationship between DCR and DSM-III diagnoses. For this, 96 randomly selected patients from the acute and chronic services from a mental hospital were subtyped on the basis of DAS criteria and the resulting DCR diagnoses were cross-tabulated with DSM-III diagnoses. Although overall agreement for all diagnoses was only 45 percent (Cramer's statistics  $\Psi = 0.45$ ) of the patients with systematic schizophrenia on the DCR, 92 percent were diagnosed as schizophrenic by the DSM-III. Agreement was considerably lower (57%) between DCR diagnoses of nonsystematic schizophrenia and DSM-III diagnoses of schizophrenic disorders. However, the agreement for schizophrenic diagnoses between DCR and DSM-III would have been 100 percent if schizoaffective disorders would have been included among the schizophrenic disorders in the DSM-III (Daniel, Craig, Ban and Wilson, 1985).

Employing the DAS in the assessment of a large number of patients has brought to attention some of the shortcomings of the scale. Among them one of the most important is that within the current format, presentation of variables relevant to the form of onset, cross-sectional psychopathology, course of illness and outcome features, are not sufficiently distinct. Another important shortcoming of the scale is the lack of separation between the different forms of outcome and the different forms of end-states.

In addition to the shortcomings of the scale (DAS) there are also shortcomings of the system (DCR); and while shortcomings of the DAS may or may not be the result of shortcomings of the DCR, all problem areas

of the DCR are reflected in the shortcomings of the DAS. Among the identified problem areas one of the most important is related to the diagnosis of delusional development, a diagnostic concept which is not broad enough to accommodate all non-schizophrenic paranoid (delusional) patients who do not fit the diagnosis of psychogenic paranoid psychosis of the DCR. Studying this particular population, however, it has been revealed that all of these patients fulfill criteria of acute or chronic delusional psychoses, as defined in prevalent diagnostic schemes within the French language areas. Furthermore there has also been some indications that delusional psychoses provide a transition between the psychogenic (exogenous) and autochthonous (endogenous) psychoses. It was on the basis of these considerations that in the proposed classification (see pages 10 to 12) the concept of delusional psychosis was adopted and positioned between the exogenous and endogenous psychoses (exo-endogenous psychoses).

In contradistinction to empiricistic and experimental classifications, a nosological classification is based on a historical process in the course of which numerous clinical observations are integrated into distinct clinical pictures. Since both the DCR and the proposed classification are nosological, in the following the historical process of conceptual development of these classifications will be reviewed to provide the necessary background information for the construction of new diagnostic assessment instruments (or the correction of old ones) which are based on nosological principles. Special emphasis will be placed in this review to the development of a four-dimensional model of diagnosis, with consideration to the four developmental stages of psychiatric illness. It will also be examined whether a four-dimensional psychiatric diagnosis could offer advantages for psychiatric research and open new paths for psychopharmacologic progress.

**FOUR DIMENSIONAL CLASSIFICATION:  
CONCEPTUAL DEVELOPMENT**

Because the etiology is unknown, the diagnostic classification of functional psychoses is based on descriptive characteristics. Originally these characteristics were restricted to cross-sectional psychopathology; today they include characteristics of the course. There is also a tendency to include the final stage of the illness, referred to as outcome or end-state.

Extension of descriptive-psychopathological characteristics with biological measures opened unforeseen possibilities. Introduction of paper, liquid and gas chromatography, mass spectrometry and radioimmunoassay, including receptor binding techniques, rendered measurement of biochemical changes in the CNS accessible to laboratory investigations. Supplementation of traditional electroencephalographic (including evoked potential) and cerebral blood flow techniques with computerized tomographic mapping of electrophysiologic data, nuclear magnetic resonance measures, X-ray transmission tomography and positron emission tomography rendered the examination of specific brain sites possible (Buchsbaum, et al., 1982; DeMyer, et al., 1985; Dunlop and Shea, 1985; Gur, 1985; Hendrie, 1985; Mathew, 1985; Marihisa, 1985; Nasrallah and Coffman, 1985). The increasing use of this new technology is transforming psychiatry from a descriptive into an experimental discipline. Nevertheless, the meaningfulness of the findings generated by the new sophisticated technology depends upon whether they can be linked to a clinical diagnostic category. Such categories should be based on a comprehensive understanding of the disease with consideration of all of its developmental stages.

In the following the conceptual development of classification(s) relevant to functional psychoses will be outlined and the psychopharmacologic implications of the different developmental stages (dimensions) discussed.

### Concept of Psychosis

In spite of its extensive use, there is no generally accepted definition for the term "psychosis." In everyday psychiatric parlance it refers to mental illness of sufficient severity to produce conspicuously disordered behavior with lack of insight. This behavior cannot be understood as an extension or exaggeration of ordinary experiences (Leigh, Pare and Marks, 1972). While Jaspers (1913a, 1959, 1963) used the term in reference to disorders which "seize upon the individual as a whole," in the United States the term is employed primarily in referring to patients with hallucinatory experiences, delusional thinking and/or catatonic symptoms.

Probably the most important contribution to the conceptual development of the term was made by Schneider (1959). He contended that the term "psychosis" should be used only to designate psychopathological manifestations which are the consequence of a disease process. This corresponds with Jaspers' (1963) notion that psychoses are "disease processes, regardless whether they are hereditary disorders beginning at certain times of life or called into being by exogenous lesions."

The concept of psychosis put forward by Jaspers and Schneider was operationalized by Fish (1974). In Fish's definition the characteristic features of psychosis include lack of insight, distortion of the whole personality (by the illness), construction of a false environment (out of subjective experiences), gross disorder of basic drives (including that of self preservation) and inability to make a reasonable social adjustment (Hamilton, 1974). In an alternative definition, put forward by Petho, Ban, Kelemen et al. (1984), psychosis is a nonspecific syndrome characterized by lack of "insight" and psychopathological symptoms of sufficient severity to disrupt everyday functioning. The collapse of customary ways of social life may call for psychiatric hospitalization.

By definition, excluded from psychotic disorders are "psychic deviations which do not wholly involve the individual" (Jaspers, 1963). Thus, excluded are patients whose personality is only in part affected, who can distinguish between their subjective experiences and reality, and who do not construct a false environment (Hamilton, 1974). Excluded also are personality disorders (i.e., variations of human existence which differ from the norm quantitatively rather than qualitatively) and neuroses (i.e., reactions of abnormal personalities to moderate or mild stress and reactions of normal personalities to severe stress) (Schneider, 1959).

Psychosis is a diagnosis only within a one-dimensional model of classification, i.e., a classification which is based exclusively on cross-sectional (2nd developmental stage) assessment of psychopathology. Accepting psychosis as the end-point yields a one-dimensional treatment modality with an antipsychotic-neuroleptic drug. The underlying assumption is that the different forms of illness are only different stages of one and the same disease (psychosis) process and consequently can be controlled by one and the same (or pharmacologically similar) medication. This concept of "unitary psychosis" was first formulated by Neumann (1859).

~~If the unitary hypothesis is valid, the psychopharmacological agents~~ which come closest to fulfill ~~therapeutic~~ expectations are the chlorpromazine type of antipsychotic-neuroleptic drugs. Today there are at least 19 such antipsychotics, distributed among six different chemical classes available for clinical use in the United States and at least 12 more in other countries (See Appendix II, Table I). Most of these drugs are secondary or tertiary amines containing at least one aromatic ring linked to the amine position by an intermediate chain; and most of these drugs are active inhibitors of apomorphine-induced vomiting in dogs, apomorphine or amphetamine-induced



stereotypic chewing and non-stereotypic agitation, and norephrine or epinephrine-induced mortality in rats. They also inhibit intracranial self-stimulation and conditioned operant behavior in all laboratory animals. At somewhat higher doses, traditional neuroleptics induce cataleptic immobility with a reduction of spontaneous motility and indifference towards the environment, and, at considerably higher doses, they induce ptosis, ataxia, prostration and other signs of CNS depression (Janssen, 1973).

Antipsychotics share numerous common biochemical actions. They have a stabilizing effect on cell membrane, an inhibiting effect on the N-methyltransferase enzyme system and a decreasing effect on adenosine-triphosphate utilization. Since the early 1960s, however, most of the attention has been paid to the dopamine (DA) receptor blockade produced by these drugs. The original observation that antipsychotics increase the nialamide-induced accumulation of 3-O-methylated metabolites of DA and norepinephrine, i.e., 3-methoxytyramine and normetanephrine, was made by Carlsson and Lindquist as early as 1963. However, it was more than a decade later, employing X-ray crystallography (Creese, Burt and Snyder, 1975), before it was possible to demonstrate that DA receptor blockade actually takes place. Furthermore, by employing radioligand-binding techniques, it was revealed that clinical potencies, based on a mg/kg basis of neuroleptics correlate well with the binding affinities at D<sub>2</sub> receptors, i.e., receptors which can be selectively labelled with 3H-haloperidol and 3H-spiroperidol (Kebabian and Calne, 1979). In addition, there is some evidence that neuroleptics also have opiate receptor binding properties (Jacquet and Marks, 1976).

The most consistent finding following chronic (1 to 3 weeks) antipsychotic administration is D<sub>2</sub> receptor blockade and a consequent increase in the number, with a decrease in the affinity, of these receptors in the striatum and

mesolimbic areas (Burt, Creese and Snyder, 1977; Muller and Seeman, 1977, 1978; Theodorou et al., 1981). Therefore, one may hypothesize that the biochemical substrate of psychosis is in the DA structures of the limbic lobe. At variance with this contention, however, are findings in clinical psychopharmacological studies which suggest that there is a differential therapeutic response in psychotic patients to antipsychotic drugs. Although antipsychotics undoubtedly are the most effective treatment for psychoses, some psychotic patients remain refractory to antipsychotics and require other treatment modalities for control. Since a differential therapeutic response indicates biological heterogeneity, the findings of a differential therapeutic response is in line with the contention that psychosis consists of more than one diagnostic groups.

### Psychosis: Organic vs Functional

#### General Outline of Development

Conceptual separation of "organic" from "functional" psychoses represents the first meaningful dichotomy within psychiatry. The adjective "organic" implies that the psychosis is intrinsically linked, if not exclusively the result of, systemic, including neurological disease. On the other hand, the adjective "functional" implies that the psychosis is a result of a sui generis psychiatric illness in which there is a primary dysfunction in the operation and performance of the brain. This is in accordance with other branches of medicine in which a "functional disorder" refers also to a primary dysfunction with an unidentified structural change. Because the psychiatric concept of "functional disorder" assumes a structural change, Schneider's (1959) "somatogenic postulate" is based on the belief that functional psychoses "are always of somatic origin" even if cause is not known and/or the morphological substrate has not been identified (Pichot, 1983).

Conceptual separation of organic from functional psychoses was a significant step in the development of modern psychiatry. It has opened the possibility to identify cross-sectional psychopathological syndromes which indicate organicity with a high level of probability. This in turn has yielded etiologically based diagnoses and causal treatment in the majority of organically determined psychoses. With the decrease in the prevalence of "organic psychoses" in the nongeriatric adult psychiatric population, e.g., virtual elimination of general paralysis which once constituted 10 percent of all hospitalized psychiatric patients, there has been a transient shift in emphasis in adult psychiatry from the organic to the functional psychoses during the 1960s and 1970s.

The shift of emphasis from "organic" to "functional" has focused attention on "anxiety disorders," traditionally referred to as "neuroses." Introduction of propanediols (meprobamate) first, and subsequently of the benzodiazepines (chlordiazepoxide) have rendered anxiety disorders accessible to biological research (Berger, 1954, 1957, 1964; Sternbach, 1972; Tobin and Lewis, 1960). By now there is substantial evidence to believe that similar to functional psychoses, anxiety disorders are sui generis psychiatric illnesses and as such outside the realm of metapsychology. Classifying anxiety disorders among psychiatric disorders provides for a clear separation of genetic and/or learned abnormal personality development (mental retardation and psychopathic personality) from functional mental illness, i.e., psychoses and neuroses.

#### Acute Exogenous Predilectional Types

Conceptual separation of organic from functional psychoses provided the necessary end-point for Bonhoeffer (1909) to develop his concept of "acute exogenous psychoses," i.e., psychoses associated with and/or the result of systemic disease. Within Bonhoeffer's frame of reference "exogenous

psychoses" are non-specific secondary manifestations of systemic disease and as such distinct from sui generis psychiatric disorders.

Bonhoeffer's concept of "exogenous predilectional types" is based on the recognition that psychotic reactions associated with systemic disease appear in one of four forms, i.e., delirium (which may occasionally be disguised with hallucinosis as the dominant clinical feature), epileptiform reactions (which may present as states of anxious or frenzied motor excitement, or alternatively as quiet, affectless twilight states), stupor, and confusional states (which may show hallucinatory, catatonic, or dissociative features). Since similar reactions may occur in association with different illnesses, and the course of illness is not determined by the presenting clinical picture, but by the patient's general constitution and the severity and duration of the underlying physical disease, Bonhoeffer maintained that the prevailing psychopathological syndrome reflects a specific predisposition which does not provide interpretable clues for an etiological understanding of the disease.

Bonhoeffer's concept of "acute exogenous psychoses" is subsumed under the heading of "symptomatic psychoses" in the British literature. The typical obligatory feature of these psychoses is disturbance of consciousness. The altered state of consciousness varies in degree from the swimming head of the common cold to the loss of consciousness in the coma of enteric fever or septicemia. It may be seen in a severe form in the delirium accompanying acute disease. In the psychoses caused by subacute and chronic illness, consciousness is less clouded or may even be clear. This disorder has been differentiated from delirium and termed confusional state. It is also referred to as amentia in German psychiatry and as subacute delirious state in British psychiatry (Mayer-Gross, Slater and Roth, 1960). Other, atypical-facultative manifestations of exogenous psychoses are dependent

on a general or a specific predisposition. The development of a transient catatonic, hyperthymic, dysthymic or amnestic syndrome is attributed to a general predisposition, while the development of a transient schizophreniform, paranoid, or hallucinatory reaction is attributed to a special predisposition. The resultant "atypical forms" with full recovery (reversibility) were referred to as "transient organic syndromes" ("Durchgangsyndrome") by Wieck (1956, 1957). All these different typical and atypical forms of disease may terminate in full recovery, or yield to organic neurasthenia (also referred to as irritable debility or emotional hyperesthesia), Korsakoff's amnestic syndrome or generalized dementia (Nyiro, 1962). These latter manifestations provide for the link between the acute exogenous (symptomatic) psychoses with prevailing delirium and the subacute and the chronic exogenous (organic) psychoses with prevailing dysmnesia and dementia respectively (Table III).

#### Chronic (Generalized) Dementias

The recognition that the continuous presence of traumatic biological factors may result in dementia threw light on Bayle's (1822, 1825, 1826) thesis that persistence of arachnitis (during the third and final stage of its development) yields to dementia in patients. It also brought to attention some of the early contributions of Pinel (1801). In his classification of psychiatric disorders, he was the first to employ the term "dementia" to describe illnesses which lead to intellectual deterioration. It should be noted, however, that the crucial distinction between "inborn idiocy" and "acquired dementia" was made by Esquirol (1839) almost 40 years later.

It was the early 19th century French school of psychiatry which had delineated the essential psychopathological features that result from persistent (chronic) brain damage. However, the findings of the French school became meaningfully interpretable only after the delineation of the essential psychopathological

Table III

Area of Psychopathology	Acute	Subacute	Chronic
1. Disorders of Consciousness	+		
Lowered vigilance			
Decreased clarity			
Sopor			
Coma			
Clouded consciousness			
Oneroid			
Delirium			
Narrowed consciousness			
Twilight			
Fugue			
2. Disturbances of Orientation	+	+	+
Time			
Place			
Situation			
Self			
3. Disorders of Memory		+	
Memorization			
Retention			
Recall			
Amnesia			
Localized			
Systematized			
Congrade			
Retrograde			
Anterograde			
4. Amentia		+	
5. Dementia			+
Apperceptive			
Chrestic			
Amnestic			
Hyletic			
Structural			

The area of psychopathology (+) prevailingly affected in acute, subacute and chronic organic psychoses.

features of acute biological trauma by the early 20th century German school. Integration of the contributions of the two schools yields the still prevalent position that delirium, dysmnnesia and dementia indicate the presence of somatic factors in the etiology of psychotic disease with a high level of probability. The three "D's" provide the necessary clues for the separation of organic psychoses with psychopathological manifestations prevailing in the connecting functions (such as consciousness, memory and personality) from the functional psychoses with psychopathological manifestations prevailing in the perceptual-cognitive, relational-affective and motor-adaptive functions (such as perception, thoughts, emotions, mood and motor behavior). Identification of the differential psychopathological structures involved in organic and functional psychopathologies and recognition of the relationship between specific brain structures and the sites of psychopathology has raised the possibility that in case of non-specific organic psychopathology the primary impairment responsible for the psychopathological changes is in the reticular formation and temporal lobe structures intrinsically linked with connecting functions. On the other hand, in case of specific functional psychopathology the primary impairment responsible for the psychopathological changes might be in limbic lobe structures in general and in frontal, parietal, temporal and/or occipital structures in particular, intrinsically linked with relational-affective, motor-adaptive and perceptual-cognitive functioning (Table IV).

#### Two-Dimensional Diagnosis

The diagnosis of functional and organic (exogenous) psychosis cannot be made within a one-dimensional model of classification. It can be made only within a two-dimensional model, because cross-sectional psychopathological symptom profiles do not suffice. They need to be supplemented with information on the form of onset and antecedent etiological event(s), e.g., biologic factors such as somatic illness or brain disease, for the interpretation of findings. The

Table IV

Functions Affected	Organic	Functional
1. Connecting Functions	+	
Consciousness		
Memory		
Personality		
2. Perceptual-Cognitive		+
Perception		
Thinking		
3. Relational-Affective		+
Emotion		
Mood		
4. Motor-Adaptive		+
Behavior		
Speech		

The area of psychopathology (+) prevailingly affected in organic and functional psychoses.



presence of somatic illness (including brain disease) immediately prior to or at the onset of psychosis, however, does not exclude the possibility that the psychosis is functional in nature. The same applies when the somatic illness and the mental disturbance do not run a parallel course (Petho, Ban, Kelemen et al., 1984). Accepting functional and organic psychoses as endpoints divides the psychotic population into two major groups and only in one of these two populations, i.e., functional psychosis, do antipsychotic drugs remain the treatment of choice. In the organic psychoses the treatment should be directed against the etiology of the disease, e.g., nicotinic acid in case of pellagra, neurosurgery in case of brain tumor.

In the case of organic psychosis causal treatment may need to be supplemented transiently by the administration of an antipsychotic drug. The use of antipsychotics as primary treatment, within a two-dimensional model of psychiatric classification, becomes restricted to patients with the diagnosis of functional psychosis. Probably even more important is the fact that even within the functional psychoses, patients respond differentially to treatment with antipsychotic drugs. Because a differential therapeutic response is an indicator of diagnostic heterogeneity, the finding of differential therapeutic responsiveness among patients is in support of the contention that functional psychosis consists of more than one diagnostic group.

#### Functional Psychosis: Reactive vs Endogenous

There are at least two distinct populations in functional psychoses. One population is conventionally referred to as autochthonous or endogenous psychosis, and the other as reactive or psychogenic psychosis.

In spite of the controversy regarding both terms, i.e., endogenous and psychogenic, there is a general agreement that psychic reactions arising

from conflictual experiences and external events are exogenous (although the term is usually retained for the psychosis resulting from an exogenous biological reaction and the psychosis associated with "coarse brain disease"). Phases and processes arising from inner causes without an external event are endogenous (Jaspers, 1963). Within this frame of reference the concept of endogenous psychosis--which, according to Pichot (1983), has its origin in Morel's (1857, 1860) teachings--implies an innate genetic biological defect, while the concept of psychogenic or reactive psychosis implies the presence of a psychic trauma, regardless of whether it is the result of a conflictual situation or a life event. Accordingly, in case of endogenous psychosis the psychosis cannot primarily be attributed to an exogenous factor (life event) even if exogenous factors play a precipitating role, while in case of psychogenic (reactive) psychosis the psychosis cannot exclusively be attributed to an endogenous factor, even if endogenous factors play a predisposing role.

The concept of psychogenic psychosis has evolved through the work of the Danish psychiatrists Wimmer (1916), Faergeman (1945, 1963), Strömngren (1968, 1974) and Retterstal (1978). In the development of the concept, Jaspers (1913a and b) definition of "pathological reaction" played an important role. According to Jaspers, to fulfill the criteria of "pathological reaction" there must be an adequate precipitating factor, standing in a close time relationship with the reactive state. There must also be a meaningful connection between the content of the experience and those of the abnormal reaction; and reversibility, i.e., disappearance of the abnormality when the primary cause for the reaction is removed. In this respect pathological reactions contrast with morbid processes which appear spontaneously. Furthermore, Jaspers suggests that reactive states can be classified in at least three different ways, i.e., according to what precipitates the reaction, according to the particular psychic structure of the reactive

state and according to the type of psychic constitution that determines the type of reactivity. Hoenig (1985) maintained, however, that Jaspers was interested in "pathological reactions" only from a methodological point of view and did not consider "psychogenic psychosis" a nosological entity in spite of his contributions to its conceptual development.

In his classic monograph Wimmer (1916) defined psychogenic psychoses as "clinically independent psychoses" caused by "mental trauma" acting on a "predisposed foundation." Furthermore, he suggested that its two essential components, i.e., predisposition and mental trauma, determine the "moment for the start of the psychosis, the fluctuations of the disease, and very often also its cessation." On the other hand, he contended that "the form and the content of these psychoses were more or less directly and completely (comprehensibly) determined by the precipitating mental factors." Psychogenic psychoses almost always end in full recovery. If this is not the case, the diagnosis may need to be changed.

Important contributions to the understanding of "psychogenic psychosis" was made by Strömngren (1968, 1974). For Strömngren, these psychoses are psychogenic in the sense that "the mental trauma must be of such a nature that the psychosis would not have arisen in its absence." There must be a close temporal relationship between the onset and the traumatic experience. There is a relationship also between the traumatic situation and the course of the psychosis. This is to the extent that "if the situation ceases to exist the psychosis will usually stop immediately." But even if the situation persists, according to Strömngren "the psychosis will not go on forever." Furthermore, Strömngren asserts that "it is not the objective force of the trauma which determines

Insofar as the "etiology" of psychogenic psychosis is concerned, Strómgren divided the exogenous traumatic factors into five groups, i.e., experiences of an entirely impersonal character, social disasters, conflicts within the family, isolation and inner conflicts. He maintained, however, that "on the whole one cannot expect to find a clear correlation between the quality and the quantity of the trauma and the type or extent of the patient's reaction." This implies that much depends on the special sensitivity, i.e., "catathymic predisposition" of the patient, which in turn suggests that endogenous factors possibly play a predisposing role. In favor of this contention are the relatively uniform genetic findings that patients with psychogenic psychosis have a high incidence of "mentally abnormal subjects" in their families.

Taking all these factors into consideration Petho, Ban, Kelemen et al. (1984) suggest that in "psychogenic psychosis" the onset of psychopathology must be attributable beyond reasonable doubt to a precipitating life event. Psychotic content must be fully understandable with respect to the precipitating life event and/or on the basis of patient's life history and/or personality. The psychosis must appear as an integral part of patient's life history. In addition, in psychogenic psychoses the intensity of the traumatic experience should sufficiently explain the emergence of the psychosis. There should be thematic continuity between the traumatic experience and the psychotic content; and there should be a meaning to the psychosis appropriate to the situation with manifestations such as theatricality and protest directed towards the onlookers. To prevent overlap, the absence of certain endogenous psychopathological symptoms, such as inhibited thinking, tangential thinking, flight of ideas, perseveration, neologisms, blunted affect and/or autistic behavior is a prerequisite for the diagnosis of psychogenic psychosis.

Today psychogenic psychosis is recognized in many countries including Denmark, Norway (reactive psychosis: psychogenic and constitutional), France (psychoses reactionelles) and the USSR (reactive psychosis) (Giljarovski, 1960; Widlocher, 1958). There is probably also some overlap between psychogenic psychosis and Kasanin's (1933) schizoaffective psychosis, and Staehelin's (1946/47) schizophreniform affective psychosis (schizophrenieähnliche Emotionspsychosen) described in details by Labhardt (1963).

The diagnosis of endogenous and reactive (psychogenic) psychoses, similar to the distinction between functional and organic psychoses, can be made only within a two-dimensional model. Cross-sectional psychopathological symptom profiles should be supplemented with information on the form of onset and antecedent-etiologic event(s), e.g., psychological factors such as death of a beloved relative or retirement, for the interpretation of findings. Accepting endogenous and reactive psychoses as end-points divides the functional psychotic population into two major groups, and only in one of these two (i.e., endogenous psychosis) is treatment with antipsychotic drugs the primary choice. In reactive psychosis, treatment with antipsychotics usually does not suffice and should be combined with or substituted by other therapies.

In addition to the differential therapeutic response between the two populations, patients within both populations show a differential therapeutic response to antipsychotic drugs. Because a differential therapeutic response indicates biological heterogeneity, the findings of differential therapeutic responses within both populations is in line with the contention that both endogenous and psychogenic psychoses consist of more than one diagnostic group.

### Psychogenic Psychoses

Psychogenic (reactive) psychosis is a two-dimensional diagnosis. Accordingly, an essential prerequisite for this diagnosis is that the

emergence of the cross-sectional psychopathological picture of the psychosis can be satisfactorially explained by the "intensity of traumatic experience," i.e., antecedent etiology. Because the subject matter of the psychosis is organized around the traumatic experience, the content, but not the form of the psychosis, should be comprehensible. The third essential characteristic of psychogenic (reactive) psychosis is goal-directedness. It is through this goal-directedness that the psychosis becomes an integral part of patient's life history.

There is no general consensus about the incidence of psychogenic psychosis. Strömngren (1968) estimates a morbidity risk (lifetime expectancy) of about 1 percent. He found that 10 percent of all, and 15 to 20 percent of all newly admitted psychotic patients to the Aarhus Psychiatric Hospital in Risskov (Denmark), during the period from 1953 to 1968 belonged to the psychogenic group. On the other hand, Faergeman (1963) found that only about 2 percent of the patients admitted to the Psychiatric University Clinic at Copenhagen during the period from 1924 to 1926 were diagnosed as psychogenic psychosis.

On the basis of the clinical picture, Schneider (1927) separates psychogenic psychosis into three diagnostic groups, i.e., "emotional reactions" (approximately 65 percent), "disorders of consciousness" usually referred to as "dissociative-confusional states" (approximately 15 percent) and "paranoid states" (approximately 20 percent). Among the "emotional reactions," depression is the most frequent. In typical cases it is characterized by a passive attitude and lack of interest in the surroundings. However, atypical cases may occur. Included among the atypical cases are paradoxical reactions such as "funeral manias" (Hollender and Goldin, 1978) and "emotional paralyses," described by Baelz (1901).

Distinctly different from the emotional reactions are "dissociative-confusional" states with prevailing "disorders of consciousness" which in typical cases are manifested in the form of delirious reactions or clouded states. Included among the clouded states is the Ganser syndrome (Ganser, 1898, 1965) in which the flight from reality is goal directed.

The third group of psychogenic psychosis consists of "paranoid states." Among them the most frequently encountered is a "comprehensible paranoid reaction," the "sensitive delusions of reference" described by Kretschmer (1927, 1966, 1974).

While retaining the three forms of psychogenic psychosis, Petho, Ban, Kelemen et al. (1984) divided psychogenic psychosis into two major groups. One with an acute onset consists of three subtypes: psychogenic regressive psychosis, psychogenic affective psychosis and psychogenic paranoid psychosis. The other with a subacute onset, psychogenic delusional development, consists of four variants: passionate (idealists, conjugal paranoia, erotomania), litigious (queruleous, reformatory zealotry), hypochondriacal (delusions of parasitosis, Shikano syndrome) and symbiotic (folie a deux, folie a trois). The psychogenic psychoses (regressive, affective and paranoid) yield to full remission with resolution of psychopathological symptoms usually within three months, but psychogenic delusional development has a tendency for chronicity and may result in transformation without disintegration of the personality. Prevailing characteristics of psychogenic regressive psychosis are clouding of consciousness and impaired orientation; of psychogenic affective psychosis, exaltation or depression; and of psychogenic paranoid psychosis, delusions of reference. In contrast to the acute forms, psychogenic delusional development is characterized by a logically derived systematized delusional system, which spreads within a restricted area.

It is assumed that it develops to a "key experience" in patients with paranoid personality traits.

It is commonly held that the form of psychogenic psychosis depends on constitutional factors. "Syntonic" or "extrovert" patients respond with an "emotional reaction," "hysterics" display a "dissociative-confusional state" and "schizoids" react with a "paranoid response." However, Strömberg (1958, 1968, 1974) maintains that more important than constitution is the nature of the traumatic experience. He suggests that emotional reactions are the result of simple situational conflicts, dissociative-confusional states are the outcome of a sudden disruption of patient's image of his environment, and paranoid disorders are the consequence of a severe blow to one's "self-esteem" or to "one's self-image."

The question whether the three syndromes described are distinct diagnostic entities--whether they are meaningful in terms of prognosis and/or treatment--cannot be answered within a two-dimensional model of psychiatric classification. By employing a three-dimensional model, however, it was noted that the duration of illness was significantly different for the three acute psychogenic syndromes. Dissociative-confusional states last only from a few hours to a few days, emotional reactions (e.g., depression) from a few days to a few weeks, and paranoid reactions from a few weeks to a few months.

Corresponding with the diagnostic category of "psychogenic psychoses" is the diagnostic category of "other nonorganic psychoses" in the ICD-9. This category is restricted to a group of psychotic disorders largely or entirely attributable to a recent life experience. Included in this category are nonorganic psychoses depressive type (reactive depressive psychosis, psychogenic depressive psychosis), excitative type, reactive confusion (psychogenic confusion, psychogenic twilight state), psychogenic paranoid psychosis.



(protracted reactive paranoid psychosis), and other and unspecified reactive psychosis (hysterical psychosis, psychogenic psychosis, psychogenic stupor). Diagnoses corresponding to "psychogenic delusional development" is not limited to "psychogenic paranoid psychosis" in the ICD-9 but includes "induced psychosis" (folie a deux, induced paranoid disorder) and other paranoid states (paranoia querulans and "Sensitiver Beziehungswahn").

Closest to the category of "psychogenic psychoses" is the diagnosis of "brief reactive psychosis" in the DSM-III. However, the diagnosis of "brief reactive psychosis" does not correspond with any diagnosis within the "psychogenic psychoses." The only correspondence between the two diagnostic systems relevant to psychogenic psychoses is the one between "psychogenic paranoid psychosis" and "acute paranoid disorder" of the DSM-III. Patients with "psychogenic delusional development" may be diagnosed as "shared paranoid disorder" or "paranoia" in the DSM-III.

In the treatment of psychogenic psychoses, antipsychotics are extensively employed. In spite of this, the fact remains that there is no convincing evidence, on the basis of properly designed and conducted clinical experiments, that they are therapeutically effective and/or superior to the benzodiazepines. Especially disappointing is the limited therapeutic responsiveness to antipsychotics in paranoid reactions. Apart from decreasing delusional dynamics, i.e., the force or intensity of the affective drive which accompanies the delusion, they have little effect on the content-disorder of thinking (systematized delusions).

While psychogenic paranoid reactions seem to persist in spite of the administration of antipsychotics, psychogenic dissociative-confusional states promptly remit in the course of administration of the same drugs. In view of the usually short duration (natural course) and reported

therapeutic responsiveness of these conditions to barbiturate-induced abreactions (Sargant and Slater, 1963), it is difficult, in the absence of placebo-controlled experiments, to decide whether one is dealing with spontaneous remission or drug effects.

The situation is even more confounded in psychogenic emotional reactions. Because treatment with antidepressants does not seem to have satisfactory therapeutic effects (Bielski and Friedel, 1976), and antipsychotics may aggravate depression, as an ultimate resort not infrequently patients with psychogenic depressive (emotional) reactions are treated with electroconvulsive therapy.

### Delusional Psychoses

It has been recognized that psychogenic paranoid reactions are resistant to treatment and may persist in spite of the administration of antipsychotic drugs. Because by definition a psychogenic reaction has a time limited course, its persistence, especially if associated with further delusional elaborations, indicates that the diagnosis should be changed from psychogenic paranoid reaction to "delusional development" also referred to as "paranoiac development" (Meyer, 1917) or "paranoid psychosis" (Gaupp, 1914a and b, 1938, 1974a and b).

Paranoiac development, one of the six basic reactions described by Adolf Meyer, refers to an anomalous development which depends partly on the person's genetic-constitutional make-up and partly on environmental factors. At first, delusional psychotic development was regarded as a disorder providing for the transition between psychogenic and endogenous psychoses. More recently there has been increasing evidence that delusional psychotic development is a form of chronic delusional psychosis (Clerambault, 1921, 1942).

### Delusional Development

The concept of delusional development dates back to the Tübingen school of psychiatry and the work of Gaupp (1914a and b, 1938, 1974a and b) who in his articles on the mass murderer, Ernest Wagner, made the first attempt to demonstrate that paranoid psychoses are not always endogenous, i.e., the result of an intruding "process" of inner origin. According to Gaupp some delusional psychotic developments are "understandable psychologically" and can be viewed as developmental anomalies that are the "direct result of experiences in persons with an abnormal psychopathic personality." Gaupp's concept was further elaborated by Kretschmer (1927) who put forward the notion that paranoid psychoses, which he referred to as "the sensitive delusions of reference" (Die sensitive Beziehungswahn) are understandable developments of sensitive personalities. For Kretschmer the term "sensitive" implies sensitiveness about one's own shortcomings (regardless whether social, physical or psychological) to the extent that it interferes with one's success. A common characteristic of sensitive personalities is the coexistence, i.e., simultaneous presence of conflicting traits, such as gentleness, softness, sensitiveness and excessive vulnerability on the one hand and assertiveness, ambitiousness and stubbornness on the other. According to Kretschmer, it is in such a person that a full-blown paranoid psychosis may develop in reaction to a key experience (that exposes patient's weakness). Kretschmer placed special emphasis on the personality type, that he considered to be on a continuum from the normal through abnormal to psychotic, in the development of paranoid psychosis. Thus, in Kretschmer's conceptual framework there is a quantitative but not a qualitative difference between a normal subject and a psychotic patient.

Kretschmer's typology served as a reference point to the work of Sheldon and Tucker (1940) in the United States; and his concept of the

"sensitive delusions of reference" was adopted in France where according to Pichot (1983) "it was even more successful than in its country of origin." Nevertheless by the late 1960s the trend was reversed. With greater recognition of a qualitative difference (i.e., contiguity) between the thinking of non-psychotic subjects and the thinking of psychotic patients, it has been recognized that "understanding" the meaning of a delusional state is not possible. In Gruhle's (1915, 1936) words: "A delusional state does not arise from subliminal wishes or from certain suppressed movements of the mind," but it is the production of cerebral pathology "which cannot be derived from and grasped by intuition."

There is now substantial evidence that "delusional development" is distinct from psychogenic paranoid psychosis in terms of the role of the identifiable trauma, and/or the time relationship between the precipitating trauma (if present) and the manifest syndrome which is characterized by a logically derived systematized delusional system. In this respect the paranoid psychosis of prisoners and deaf people is closest to delusional development. Other delusional developments include the syndrome of Allers, monosymptomatic hypochondriacal delusions and induced psychosis, also referred to as symbiotic or shared paranoid psychosis (Strömberg, 1968). The essential feature of the latter is a delusional system, usually persecutory, that develops as a result of a close relationship with another person who already has a disorder with the same or similar delusions.

Other features, distinguishing delusional development from psychogenic paranoid psychoses, include the tendency for chronicity and for transformation of personality.

The diagnostic concept of delusional or paranoid development has received support from Berner (1965) who, on the basis of the results of his follow-up study with paranoid patients, was able to formulate criteria for the separation of patients with schizophrenic and affective psychoses from the core group. Berner's criteria have received further substantiation in the Lausanne survey of the same patients by Muller (1981). It, therefore, seems that the diagnostic concept of paranoid or delusional development is valid and the diagnosis of paranoid development is distinct from that of schizophrenic or affective psychoses.

#### Paranoia and Paraphrenia

It might be argued that delusional development shares some common characteristics with psychogenic paranoid reactions, but the same does not apply to "paranoia," a term adapted from the Greek by Heinroth in 1818. By describing delusional states as "disorders of intellect" (Verrucktheit) that virtually do not affect other faculties of the mind, Heinroth opened the path for Kahlbaum (1874) and Kraepelin (1919) to develop their concepts of paranoia and paraphrenia respectively.

Kahlbaum used the term "paranoia" for chronic fixed delusions of persecution and/or grandeur and distinguished the disorder from those "endogenous" disorders characterized by a deteriorating course (e.g., schizophrenias). Kahlbaum's formulation was further elaborated by Kraepelin's contribution. He characterized "paranoia" as a disorder with a "permanent and unshakable delusional system, which is accompanied by perfect preservation of clear and orderly thinking, will power and action"; and separated paraphrenia, another content-disorder of thinking with a logically derived systematized delusional system. While in paraphrenia perceptual psychopathology (hallucinations) is interwoven with the systematized delusional system, in contradistinction to paranoid schizophrenia

deterioration does not occur in the course of the illness. In the 8th edition of his textbook, Kraepelin (1913) separated paraphrenia from dementia praecox on the basis of the absence of emotional and volitional pathologies in the clinical picture (Ban, 1973). Late paraphrenia, first described by Roth (1955), is a special form of paraphrenia, which can only be distinguished from "paraphrenia" by its time of onset in the late middle age or even later (Hamilton, 1976).

Kraepelin's concepts of both paranoia and paraphrenia have been questioned by Koelle (1931) who followed 66 patients diagnosed paranoia, including the 19 on whom Kraepelin's definition was based. Because he found a higher incidence of schizophrenia among the relatives of these patients than in the general population but a lower incidence than among the relatives of schizophrenics, he contended "that paranoia must be regarded as a variety of schizophrenia" (Hamilton, 1976).

Similarly, Meyer (1921) followed the 78 patients on whom Kraepelin's definition of paraphrenia was based. Because he found that 40 percent of these patients showed obvious signs of "dementia praecox" within a few years, he concluded "that paraphrenia was not a disease entity, which could be sharply distinguished from schizophrenia."

The inference that neither paranoia nor paraphrenia are valid concepts and should be merged with the schizophrenias brings to attention the limitations of the empiricistic-statistical approach to psychopathological research. These studies actually show that both are valid diagnostic concepts. Within a two-dimensional model of psychiatric classification it is difficult to distinguish the 60 percent truly paraphrenic patients from the 40 percent schizophrenic patients, and impossible to identify the patients with the diagnosis of paranoia responsible for the lower

genetic loading for schizophrenia in the experimental cohort. The importance of Meyer's (1921) and Kollé's (1931) findings is in the recognition that delusional psychoses exist but their forms (paranoia and paraphrenia) are ill-defined within the frame of reference of Kraepelin. If Meyer and Kollé would have employed a different frame of reference in the interpretation of their findings they probably would have provided support for the diagnostic concepts of acute and chronic delusional psychoses.

#### Acute Delusional Psychosis

The origin of the diagnostic term "acute delusional psychosis" is in the work of Magnan (1886) who first described a syndrome he referred to as "bouffées delirantes" because of the sudden appearance of spontaneous delusions. Prior to him, Westphal (1878) had recognized "acute paranoia" as a distinct disorder characterized by acute delusional experiences. His work, however, remained isolated from the main stream. In contrast, Magnan's concept of "bouffées delirantes" received support from the work of Seglas (1895), Halberstadt (1922), Dublineau (1931) and Ey (1954).

In their Manual of Psychiatry, Ey, Bernard and Brisset (1960, 1974) characterized "bouffées delirantes" or "acute delusional psychoses" by the sudden onset of a transient delusional state. They emphasized the importance of "true delusional experiences" in the sense that the delusions are "lived out as part of an altered state of consciousness," as experiences which are "imposed on the subject." With consideration of the prevalent state of consciousness, they consider "acute delusional psychoses" similar to the "oneiroid states" described by Mayer-Gross in 1924.

The pivotal psychopathology in "acute delusional psychosis" is the acute delusional experience. In describing this experience Magnan used

the term "delire d' emblee" because from the first moment the delusions are fully formed and "are truly all of a piece." The sudden onset of delusional ideas corresponds with Jaspers' (1963) concept of "primary delusional experience" and Clerambault's (1942) "mental automatism." It also corresponds with the concept of "primary delusions" which arise "without prior condition or motive" as described independently by Gruhle (1936) and Schneider (1949).

Polymorphousness (multiformness) is another important characteristic of acute delusional states. This implies the presence of many and various themes which are blending into each other and changing like in "kaleidoscopic succession of oneiric images." There is a shift in the clinical picture virtually from day to day.

Corresponding with the sudden appearance of delusional activity and the constantly changing clinical picture are mood changes which are congruent with the pathological experience. The altered state of consciousness is characterized as a "dreamlike state," which is polarized between the "dominating delusions and reality." While the patient seems to be detached, his or her whole attention is diverted by the shifting delusions which are "like the unfolding of an experience of which he is at once the plaything, the spectator, and the author and from which he will emerge, when he recovers, as from a nightmare or some strange spell."

On the basis of the prevailing clinical features there are three types of "acute paranoid psychoses." These are "acute imaginative psychosis," described by Dupre and Logre (1917), characterized by the "sudden confabulatory flowering of rich and varied themes"; "acute interpretative psychosis", described by Valence (1927), characterized by "delusional attacks, entirely interpretative in nature"; and "acute hallucinatory psychosis" in which



"all types of hallucinations," superimposed on the delusions, "dominate" the clinical picture. However, because similar clinical forms have been described in "chronic delusional psychoses" there is the possibility that patients who present with these specific manifestations suffer from "chronic delusional psychoses."

In his original formulation Magnan (1886) suggests that "bouffees delirantes" are disorders seen in a single episode and "not followed by sequelae or mental complications." However, Legrain (1886) has shown that "recurrent delusional psychoses" may occur. He referred to these recurrent, intermittent delusions as "delires a eclipses." Regardless, whether single or recurrent, the diagnosis of "acute delusional psychosis" is of prognostic significance because, if the diagnosis is correct there is usually full remission within a few weeks.

In their publication Ey, Bernard and Brisset (1960) assert that "acute delusional psychosis" respond promptly to treatment with antipsychotic-neuroleptics such as "chlorpromazine" or "reserpine" and also to treatment with "electroshock." In this respect it is distinct from both "psychogenic paranoid reaction" and "chronic delusional psychosis" which respond considerably less favorably to similar therapeutic approaches. If the favorable treatment response can be substantiated in properly designed clinical studies, it will support the contention that "acute delusional psychosis" is a biologically distinct and clinically meaningful diagnostic group.

#### Chronic Delusional Psychosis

"Imaginative psychosis" (Dupre and Logre, 1911), "interpretative psychosis" (Serieux and Capgras, 1911) and "hallucinatory psychosis" (Ballet 1913a and b; Ballet and Mallet, 1913) have also been described as subtypes of Magnan's (1886) "chronic delusional psychosis" (delire chronique a evolution systematique).

In spite of this there are indications that acute and chronic delusional psychoses are distinct. This is best exemplified by the differential therapeutic response to antipsychotics in patients with acute (favorable response) and chronic (unfavorable response) delusional psychoses.

On phenomenological grounds, based on patients experience of their illness, Clerambault (1923) and Baruk (1959, 1974) differentiated two major groups of illnesses within the chronic delusional psychoses; one characterized by interpretative delusions and the other by delusions of passion. While Clerambault distinguished three subtypes of delusions of passion, i.e., erotomania, querulant delusions, and delusions of jealousy, some believe that all three subtypes (and even delusions of passion) are parts of a syndrome referred to as "idealistes passionne's" by Dide (1913a and b). However, Clerambault and Lamache (1923) maintain that "erotomanics" are not true "idealistes" because their feelings of idealism are mixed with pride and fantasy or even with straightforward eroticism. Patients with "erotomania" are less spiritual and more carnal in their interests than Dide's "idealistes passionne's."

There are distinct phenomenological differences between the two major groups of delusional psychoses with the essential difference being in that "interpretative delusions" constitute a passive-defensive experience with an insidious onset, while "delusions of passions" constitute an active-driving experience with an acute beginning. According to Baruk, patients with "interpretative delusions" live in a state of constant expectations. "His path seems to be beset by mystery, he is anxious, surprised and passive, questioning everything he sees, and seeking explanation which he only discovers gradually." Another important characteristic of patients with "interpretative delusions," is a feeling of suspiciousness. The

whole personality is affected by the gradually widening, logically derived, consistently changing and progressive delusional system.

In contrast, patients with "delusions of passion" are constantly striving. They advance toward their goal with conscious and clear-cut demands from the outset. They are deluded only about their own desires while their thoughts are polarized in relation to their will power. Delusions of passions are characterized by emotional excitement (hypersthenic state), the quality of which may extend to the point of hypomania. Other distinguishing features include the "initial act of the will, the sense of purpose, the one dominant concept, the accompanying vehemence, the fact that patient's ideas are fully formed from the start, and the claims made on other people" (Baruk, 1959).

Among the three subtypes of delusions of passion, "erotomania" is encountered in both acute and chronic forms. However, even if encountered as an acute syndrome, "erotomania" shares common characteristics with "chronic delusional psychoses" in a relatively unfavorable therapeutic response to antipsychotic drugs.

Although the term "erotomania" or "amorous delusions" was used by Esquirol (1838), it was Clerambault and Lamache (1923) who employed it first for the designation of a specific clinical syndrome which develops in two stages, i.e., a phase of hope, followed by a phase of resentment. At the core of erotomania is the belief that the person on whom the patient is fixed (referred to as the "desired object") is in love with the patient, and consequently it is not the patient but the "desired object" who has made the "initial advances." The patient believes that the "desired object" is single or not properly married, and even more important, cannot find happiness and be a complete person without the patient. From these

"fundamental postulates" a continuous vigilance and/or protection of the "desired object" follows with indirect conversations with the "object." The patient pursues the "desired object" by any and all means and none of the "paradoxical and contradictory behavior" of the "desired object" modifies the strength of the delusions.

Distinctly different from "erotomania" or "the fantasy lover" is "delusions of jealousy." One of the prototypes is the husband who becomes more and more convinced about his wife's infidelity and whose ideas at a certain point reach delusional intensity. The helpless spouse is interrogated unceasingly and may be kept awake for hours at night; has underclothes searched for stains of semen; and her vaginal moisture is "pieced together" in "evidence" of "frequent sexual intercourse with someone else" (Fish, 1974).

The third subtype of "passionate delusions" are "querulant delusions" first classified by Beer in 1869 and specially studied by Krafft-Ebing (1879). According to Baruk (1959) patients with this clinical syndrome "indulge in a host of claims, legal proceedings and complaints lodged with the authorities." Closely related to the "querulants" are the "litigious" patients and closely related to the "litigious" are the "hypochondriacal claimants." While the "litigious" patient undertakes a series of lawsuits, the first leading to others, the "hypochondriacal claimant" reproaches the doctor for not having cured him, or even for giving him some harmful treatment.

In some instances delusions of passion are centered either on religious or philosophical themes or on political ideas. Considering the common characteristic of these patients Dide (1913a and b) refers to them as "idealistes passionnes" and perceives them as a distinct diagnostic group. Regardless,

however, of the topic (content) of the delusions, patients with "delusions of passion" constitute a dangerously violent diagnostic group. The problem is compounded by limited success with different treatment approaches including antipsychotic drugs. In spite of the commonly held belief that diphenylbutylpiperidines, such as pimozide are superior in their therapeutic effect to other psychotropic drugs, because of their greater specificity for the DA<sub>2</sub> receptors, there is no evidence on the basis of properly designed clinical experiments that any one of the antipsychotic drugs is superior to another in this diagnostic group.

#### Psychopharmacologic Implications

Delusional psychoses, acute and chronic are syndromatologic diagnoses and their systematic exploration has set French psychiatry, based on syndromatologic diagnoses, on a different path from German psychiatry which is based on nosological diagnoses. From a heuristic point of view considerably more important than the separation of the two major schools of psychiatry is that the concept of delusional psychosis has provided the link between reactive (psychogenic) and endogenous (autochthonous) psychoses, and between endogenous and exogenous psychoses. Accordingly, psychogenic paranoid reactions may yield to chronic delusional psychoses bridging the psychogenic with the endogenous; and acute delusional psychoses may result from a variety of structurally different psychotropic drugs linking an assumedly specific-endogenous syndrome ("bouffees delirantes") with non-specific exogenous factors. The various drugs which may induce the syndrome include hashish which provided Moreau de Tours (1845) with the experience for his precise account of a "primary delusional state," opium (Dupouy, 1912), cocaine (Maier, 1926, 1928), alcohol, chloral (Clerambault, 1909), atabrine (Fabre, 1949), peyote, mescaline (Rouhier, 1927; Beringer, 1927;

Allaix, 1953), ergot alkaloids and lysergic acid diethylamide (Stoll, 1947; Delay and Benda, 1958a and b. Because the syndrome has also been countered in patients with epidemic encephalitis, acute delusional psychoses fulfill criteria of a non-specific exogenous psychosis in which a specific gene structure predisposing to delusional development is activated by a brain disease. The nature of such psychoses is unrelated to the specific action mechanism of drugs which can induce the syndrome. This implies that one should not expect to attain a better understanding of the nature of the syndrome by employing psychopharmacologic means. In this respect "acute delusional psychoses" resemble "exogenous psychoses" in which one-dimensional cross-sectional psychopathology (symptom analysis) does not suffice to provide the necessary clues for prognosis and/or treatment because of the lack of specificity of the response.

Although delusional psychoses can be induced by various structurally different psychotropic drugs, they are most frequently seen in the course of chronic consumption of amphetamines. In fact, they were encountered in 201 of 242 reported cases of chronic amphetamine toxicity reviewed by Kalant (1966).

It is a common clinical experience that the psychotic syndrome of chronic amphetamine toxicity, closely resembles paranoid schizophrenia. An examination of the psychopathologic symptom profile of Kalant's 201 reported cases, however, revealed that the syndrome fit more closely delusional psychoses and especially "bouffee delirantes" and the hallucinatory form of Magnan's (1886) "delire chronique."

The first report which brought to attention the possible link between chronic consumption of amphetamine and psychotic illness was published by Young and Scoville in 1938. As the title of this paper reveals it was

"paranoid psychosis" and not paranoid schizophrenia which they observed in the course of "benzedrine treatment" in patients with "narcolepsy." Three years later Staehelin (1941) in Switzerland and Greving (1941) in Germany independently described 1 and 2 cases of methamphetamine psychoses and noted the resemblance to cocaine and mescaline-induced psychoses. Both of these substances were listed by Ey, Bernard and Brissett (1960;1973) among the various agents which can induce "bouffee delirante." In keeping with this are the findings of Daube (1942) who presented 4 patients in whom prolonged methamphetamine abuse induced illusions and hallucinations of all sensory modalities. Because the perceptual psychopathology was associated with anxiety and ideas of reference (also ideas of influence) the possibility has been raised that the methamphetamine-induced psychosis might be a suitable model for the study of schizophrenia.

The most comprehensive report on amphetamine psychosis is that of Connell's (1958, 1964). His findings in 29 carefully analyzed cases were compared in terms of psychopathology and other features with the 87 cases of Kalant (1966). The comparison revealed considerable similarities between the two samples. In both samples the most frequently considered psychopathological symptoms were delusions of persecution and the second most frequently encountered symptoms were hallucinations. In Kalant's sample delusions of persecution were present in 83 percent of patients, visual hallucinations in 54 percent, auditory hallucinations in 40 percent, somatic and/or tactile hallucinations in 12 percent and olfactory hallucinations in 6 percent. Corresponding figures in Connell's sample were 81 percent, 50 percent, 69 percent, 19 percent and 9 percent respectively. While ideas of reference were present in only 19 percent of the patients in Kalant's series, they were present in 59 percent of the patients in

Connell's series. On the other hand, disorientation was present in 7 percent of the patients in both series (Table V). Because the other psychopathological symptoms encountered in Kalant's series were hyperactivity or excitation (41%), anxiety (26%), hostility or aggressiveness (22%), agitation (17%) and depression (15%), he concluded that the psychopathological manifestations during the psychotic episode in the majority of patients are essentially the same as those described by Connell and consist of (in Connell's words) "primarily a paranoid psychosis with ideas of reference, delusions of persecution, auditory and visual hallucinations, in a setting of clear consciousness" (Table VI). Thus, the psychoses associated with chronic amphetamine use may share some common features with paranoid schizophrenia. They resemble, however, much more closely acute and chronic delusional psychoses. Or in other words, if a model psychosis based on a one-dimensional, cross-sectional syndrome is acceptable at all to provide for the basis of further research, the amphetamine model of psychosis might be relevant for delusional psychoses but not for paranoid schizophrenias.

If the amphetamine hypothesis of paranoid schizophrenia is correct regardless of the psychopathological data, it would imply a more favorable therapeutic response in paranoid schizophrenia to antipsychotic-neuroleptics (i.e., drugs which counteract some of the amphetamine effects in animals) than in the other types of schizophrenia. This, however, does not seem to be the case. In fact, there are indications that during the second half of the 20th century the greatest reduction in patient populations occurred in the catatonic schizophrenias. Nevertheless, since the decrease in catatonic patients in the hospitalized population preceded the psychopharmacological era, some believe that it resulted from the introduction of social therapies and not from the introduction of new drugs.



Table V

Variables	Connell 29 Patients	Kalant 87 Patients
Ideas of reference	59%	19%
Delusions of persecution	81%	83%
Visual hallucinations	50%	54%
Auditory hallucinations	69%	40%
Somatic or tactile hallucinations	19%	12%
Olfactory hallucinations	9%	6%
Disorientation	7%	7%

Psychopathological symptoms (in percentages) occurring in Connell's (1958) and Kalant's (1966) series of patients.

Table VI

Symptoms	In % of Patients
Hyperactivity or excitation	41
Hostility or aggressiveness	22
Agitation	17
Depression	15

Psychopathological symptoms present in chronic amphetamine toxicity in percent of 87 patients reviewed by Kalant (1966). In a considerable proportion of these patients they were also delusions of persecution and various hallucinations present.

While clinical psychopharmacological findings do not support the amphetamine hypothesis of paranoid schizophrenia, they are in favor of the amphetamine hypothesis of acute delusional psychoses (bouffée délirante's) which is distinct from psychogenic paranoid reaction and chronic delusional psychoses and which respond favorably to antipsychotic-neuroleptic drugs.

### Endogenous Psychoses

The place of "delusional psychoses" is not clearly defined within the two major schemes of psychiatric classifications, i.e., ICD-9 and DSM-III, both of which have their focus on disorders traditionally subsumed under the category of endogenous psychoses. The same applies to the DCR (Petho, Ban and Kelemen et al., 1984).

Within a two-dimensional model of psychiatric classification "endogenous psychoses" are like mirror images of psychogenic-reactive psychoses. Although in some instances there might be a precipitating factor, the severity of the event is usually insufficient to explain the emergence of the psychosis and the subject matter of the psychosis is unrelated to the traumatizing experience. In this context, the content of the psychosis remains incomprehensible. Endogenous psychoses do not have an identifiable purpose. They appear as intruding events which undermine the livelihood of affected patients.

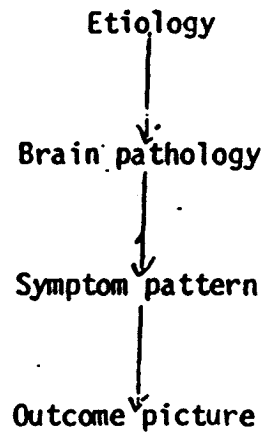
Attempts to classify endogenous psychoses range between two extremes. At one extreme, there is the "individual psychoses," unique, occurring once only in the particular form, the end-product exclusively of its own internal and external components, such as constitution, age, sex, character, milieu, situation and life experience; while at the other extreme there is the "unitary psychosis," completely amorphous and undefined, the general outcome of

an interaction between an endogenous predisposition to mental illness and some form of exogenous provoking factor, with idiosyncratic structural elements giving the illness its own peculiar stamp (Birnbaum, 1923, 1974). This concept of "unitary psychosis" is different from Neumann's (1859) who contends that different forms of illness are only different stages of one and the same disease process.

The greatest impetus for the conceptual development of endogenous psychoses was Kahlbaum's (1874) formulation of the notion of "nosological entity" which postulates a close correspondence between etiology, brain pathology, symptom pattern and outcome picture (Jablensky, 1981) (Figure 4). The origin of the notion dates back to Bayle's now classic work on the Diseases of the Brain and Its Membranes (*Traite des Maladies du Cerveau et de ses Membranes*) published in 1826. He put forward the thesis that general paralysis has one cause, i.e., "chronic arachnitis," which is clearly defined in terms of pathological anatomy; has a specific symptomatology which combines motor and mental signs; and most important, has a specific pattern of development comprising three phases, each marked by different symptoms. These phases are "delire monomaniaque" characterized by prevailing exaltation; "delire maniaque" characterized by prevailing delusions and overvalued ideas; and "etat de demence," the terminal phase, which is characterized by dementia.

Although virtually forgotten outside of France, Bayle's treatise provided fertile ground for the development of psychiatry as a medical discipline. By linking psychopathology to cerebral pathology (chronic arachnitis) he opened the path for German "somaticism." One of the most prominent exponents of this approach was Griesinger (1845, 1876) who in his famous "treatise" published in 1845 declared that "mental diseases are somatic diseases, that is, diseases of the brain." He also asserted that there are no differences

Figure 4



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Kahlbaum's (1874) notion of "nosological" entity postulates a close correspondence between etiology, brain pathology, symptom pattern and outcome picture. It serves as the underlying assumption for biologic research in psychiatry.

between organic and functional disorders, that psychiatry and neuropathology are not merely two closely related fields, but they are one field in which "one language should be spoken" and in which "the same laws prevail" even if "there are many physicians even whole schools of psychiatry, who demand proof." Griesinger's contentions were elaborated in the work of Westphal (1871a and b), who made a systematic attempt to establish the nature of cerebral lesions in psychoses and whose work, according to Pichot (1983) "formed a bridge between Griesinger, for whom organo-clinical correlations were a particular article of faith, and psychiatrists like Meynert and Wernicke, who made use of their anatomical discoveries to work out and formulate general conceptions in psychiatry."

It has not been recognized sufficiently that Bayle's treatise yielded our present conception of "dementia," i.e., a specific end-state which is the result of chronic organic-neurological changes in the brain regardless of their cause or etiological specificity. It is even less well known that it was Bayle's treatise that focused attention on the importance of the course of illness determined in his view by the brain pathology intrinsically linked to etiology. It is this three-dimensional model, i.e., etiology, cross-sectional psychopathology and course of illness that has served as the basis for Kahlbaum's (1874) concept of "nosological entity." It is this three-dimensional model that allowed for the assumption that seemingly disparate clinical states and syndromes may belong together in a "disease." It also opened the way for Kraepelin (1896) to group together several clinical syndromes into the nosological entities of manic-depressive insanity and dementia praecox. By employing a three-dimensional approach and separating phasic-remitting affective psychoses from processual-progressing schizophrenias, Kraepelin succeeded in laying down the foundation for the dichotomy of endogenous psychoses, which, according to Jablensky (1981) served as the basis for our classification of these disorders to date (Table VII).

Table VII

	Dementia Praecox	Manic Depressive Insanity
<u>First Dimension</u> Cross-Sectional	<p>Disturbances of attention and comprehension</p> <p>Hallucinations, prevailingly auditory (phonemic)</p> <p>Audible thoughts</p> <p>The feeling that one's thoughts are directed (influenced) by outside forces</p> <p>Disturbance in the continuity of thinking (flow of thought) with the predominance of loosening of associations</p> <p>Impairment of cognitive function and judgment</p> <p>Affective flattening</p> <p>Manifestations (appearance) of morbid behavior:            Reduced drive            Automatic obedience            Echolalia            Echopraxia            Acting out            Catatonic frenzy            Stereotypy            Negativism            Autism            Disturbance of verbal expression</p>	<p>Manic states: Flight of ideas Heightened mood</p> <p>Increased drive</p> <p>Depressive states:            Sad or anxious mood            Thought retardation            Decreased drive</p> <p>Mixed forms</p>
<u>Second Dimension</u> Etiology-Onset	Endogenous	Endogenous
<u>Third Dimension</u> Course of Illness	Deterioration (leading to invalidity)	Episodic Remitting Relapsing

Kraepelin's (1913,1919,1921) criteria for the diagnosis of manic depressive insanity and dementia praecox presented within the three dimensional model of psychiatric diagnosis, based on the 8th edition of his textbook.

The two diagnostic end-points provided by the dichotomy (i.e., schizophrenic and affective psychoses), received support at first from the differential responsiveness within the endogenous psychoses, to antipsychotic-neuroleptics and mood-stabilizer lithium salts. Later on it received support from the demonstration that antipsychotics are therapeutically more effective than other agents in the treatment of schizophrenias, whereas mood-stabilizer lithium salts and tricyclic antidepressants are therapeutically more effective than other agents in the treatment of manic-depressive psychoses and endogenous depressions respectively.

By following the pharmacological profile of chlorpromazine-type of antipsychotics (neuroleptics) and imipramine-type of antidepressants, a large number of psychoactive drugs, with similar action mechanisms have been synthesized and introduced into clinical practice for the treatment of schizophrenic and affective (primarily depressive) disorders. Although there is no agreement as to what extent these drugs fulfill therapeutic expectations, there has been an increasing consensus that they cannot be considered specific for a particular illness and do not have equal therapeutic effectiveness during the different developmental stages of the same illness. Because they do not fulfill these two prerequisites, neither the action mechanism of antipsychotics nor of antidepressants can provide sufficiently reliable and valid clues for the generation of hypotheses relevant to the understanding of schizophrenic and/or affective psychoses.

Regardless of their immediate contribution to psychiatric theory, systematic studies designed to reveal the action mechanism of antipsychotics and antidepressants contributed greatly to the development of the technology necessary for *in vivo* exploration of brain mechanisms and brain functions. It remains to be seen, however, whether the newly developed technology will



provide the necessary basis of meaningful research in the schizophrenias and affective psychoses within a four-dimensional model of psychiatric diagnosis.

Similarly, regardless of its relevance to psychopharmacology, Kraepelinian nosology proved to be a long step forward by introducing order in a chaotic field. In spite of its limitations it has provided the necessary diagnostic orientation for the initial development of drugs with therapeutic effects in the functional psychoses. It has not succeeded, however, in providing the necessary end-points for the identification of individual patients who are responsive to one or another drug.

By definition a three-dimensional model of diagnosis does not take into consideration the last developmental stage of psychiatric illness. Wernicke (1894, 1900), recognizing the limitations of Kraepelinian nosology, pointed out the low prognostic validity of the Kraepelinian diagnoses. He also developed a finely differentiated symptomatology of the endogenous psychoses. This symptomatology provided a description of the psychiatric syndromes that was considerably more adequate than Kraepelin's (Leonhard, 1961). Kleist (1921), a pupil of Wernicke was able to separate many of Wernicke's syndromes as distinct forms of psychiatric illness. He also revealed, that some of these highly differentiated forms of illness--subsumed under the heading degenerative psychoses--could only partially be allotted to one or the other of Kraepelin's two major diagnostic groups (Table VIII). Included among them are a number of "affective," "conative" and "intellectual" illnesses with a "shift-like" or a "phasic" course following a simple-monopolar or a multiform-bipolar pattern (Silveira, 1961).

Table VIII

PATHOGENESIS	PHASIC COURSE		SHIFT-LIKE COURSE
	Simple-Monopolar Pattern	Multiform-Bipolar Pattern	
Affective	Hypochondriacal agitation	Acute anxious-ecstatic hallucinosis	Episodic hypnotic states
	Hypochondriacal depression		
	Anxious reference psychosis		
	Perplexed strangeness psychosis		
Conative	Expansive confabulations	Akinetic-hyperkinetic motility psychosis	Periodic morbid impulses
Intellectual	Ecstatic inspiration psychosis	Stuporous-agitated confusion	Episodic twilight states
		Acute perplexed interpretation psychosis	

Kleist's (1924) classification of "degeneration psychoses," consisting of disorders which cannot be allotted to one or the other of Kraepelin's two major diagnostic categories. Based on Silveira's (1961) presentation at the Third World Congress of Psychiatry.

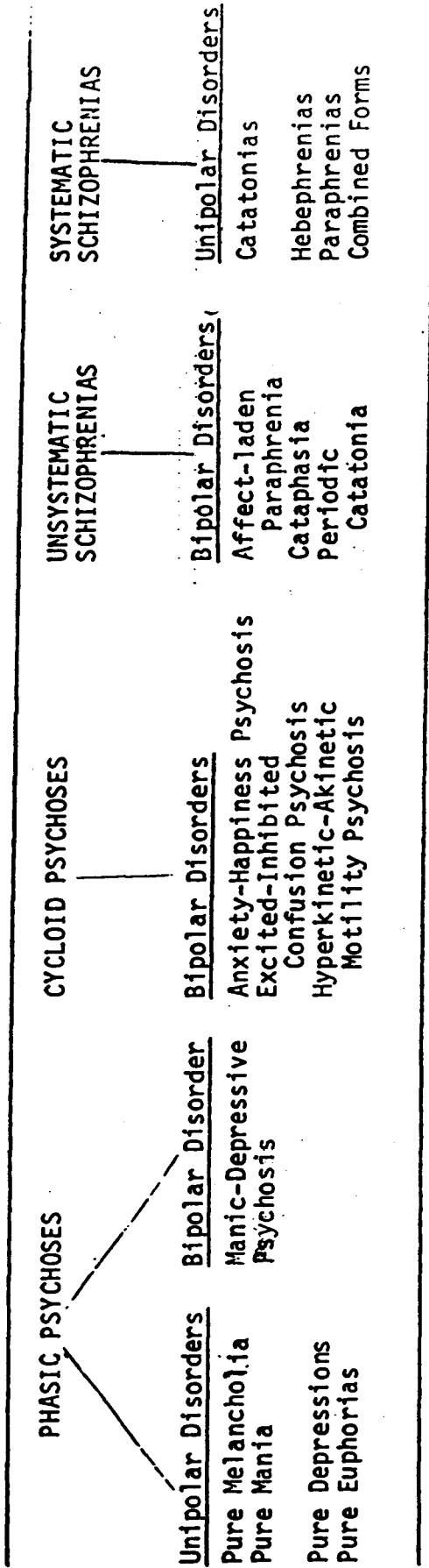
Recognition of the difficulties in separating schizophrenic (dementia praecox) and affective (manic depressive) psychoses on the basis of cross-sectional assessment of psychopathological symptoms created a diagnostic crack with a considerable percentage of patients not fitting either of the two diagnoses. Similarly, recognition of the low prognostic validity of the two diagnoses created a diagnostic gap in which patients suffering from a number of different illnesses are given the same diagnosis.

There are some indications that at least some of these problems might be overcome by adopting the principles of the Wernicke school--a four-dimensional classification with emphasis on the end-state (subtypes)--as developed through the work of Kleist by Leonhard and his collaborators. Leonhard's (1979) classification of endogenous psychoses recognizes within affective or phasic (unipolar and bipolar) and schizophrenic (systematic and unsystematic) psychoses a number of different illnesses and identifies a third group of psychoses, referred to as cycloid psychoses, resembling the group of phasic psychoses in their course and the group of unsystematic schizophrenias in their content (Figure 5).

At first sight Leonhard's classification appears to be bewilderingly complex. If its basic tenets are understood, however, the system becomes rational and simple. The classification is based on a four-dimensional model of psychiatric diagnosis with emphasis on the final stage of psychiatric illness which in the ultimate analysis ranges from full recovery (phasic psychoses) to moderate or marked defect states (systematic schizophrenias) with personality transformation (cycloid psychoses) and mild to moderate defect (nonsystematic schizophrenias) in between.

Regarding the course of illness, Leonhard contends that endogenous psychoses may follow an episodic (phasic psychoses, cycloid psychoses and

Figure 5

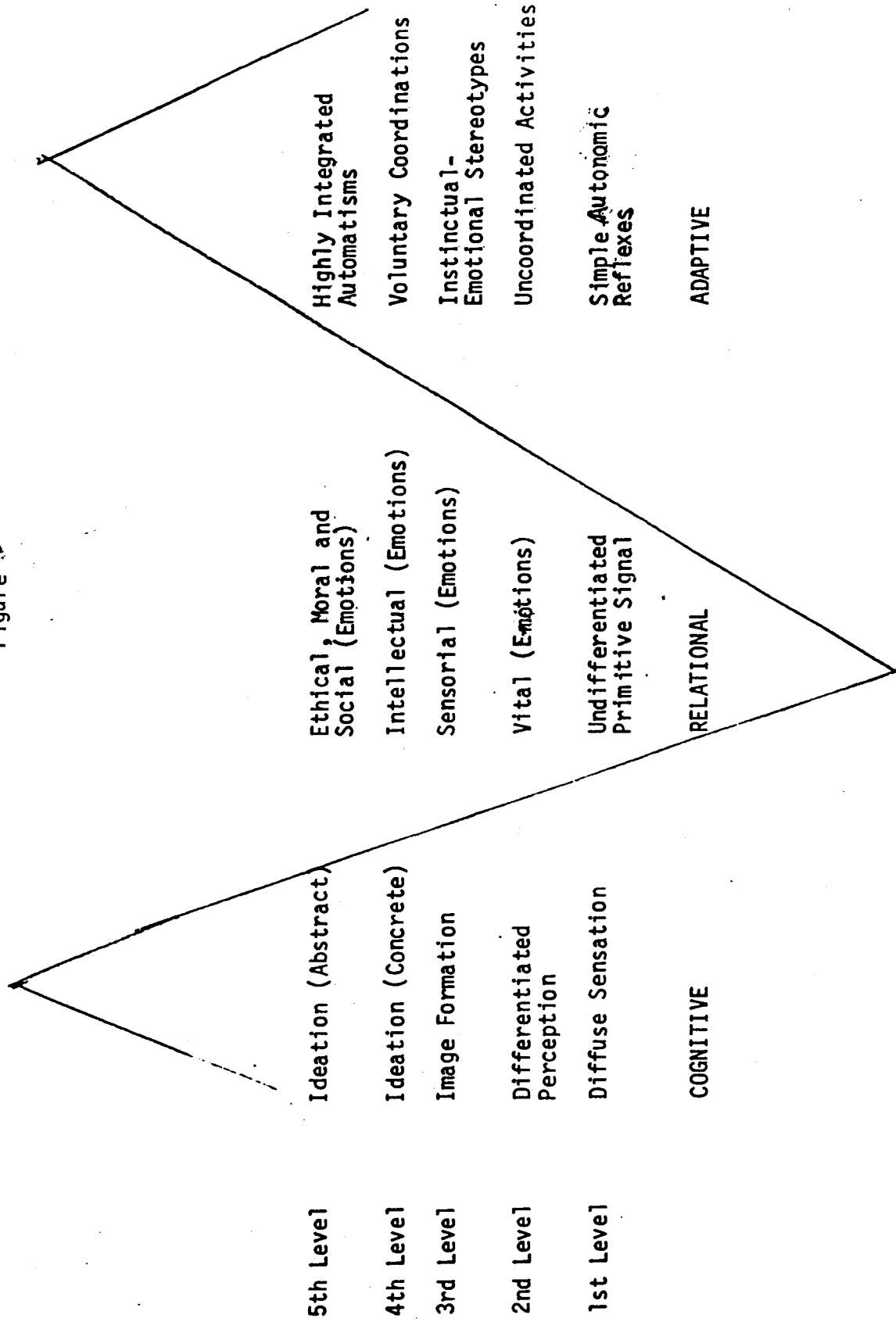


Leonhard's (1957) system of classification of endogenous psychoses.

unsystematic schizophrenias) or continuous (systematic schizophrenias) course; and phasic psychoses may appear as unipolar (mania or depression) or bipolar (manic-depressive psychosis) illnesses.

Insofar as cross-sectional psychopathology is concerned, Leonhard follows the principles of Wernicke's (1881, 1894, 1900, 1906) structure-analysis. Wernicke considered the reflex arc as his functional working unit and saw the cerebral cortex as the organ of "associations." In his "reflex pathology" he dealt with the three functional aspects of the reflex arc, i.e., sensory input, interneuronal associations, and motor output. He maintained that any of the three could be disturbed separately and also in various combinations. Within this model psychopathological syndromes are perceived as a decrease, increase, or a dysfunction in the activity of these structures which become manifest through the effect of the disturbance of "transcortical associations." A further elaboration of this model was put forward by Nyiro (1958, 1962) for whom the three aspects of the reflex arc represented three "pyramidal structures," i.e., perceptual-cognitive (sensory input), relational-affective (intrapsychic) and motor-adaptive (motor output) (Figure 6). Within this frame of reference Leonhard distinguished among psychopathological syndromes which affect primarily one of three structures, e.g., systematic schizophrenias, and psychopathological syndromes which affect primarily more than one structure, e.g., nonsystematic schizophrenias. He also distinguished between disease groups characterized by dissociation among the three "structures" (nonsystematic and systematic schizophrenias) and disease groups in which the functioning of the three "structures" is congruent or harmonious (phasic and cycloid psychoses). In addition to these general features he brought to attention that both groups of schizophrenias and

Figure 6



Nyiro's (1958) "structural view" of psychological functions. The three structures, cognitive, relational and adaptive, resemble three pyramids with the apex of the one in the middle turned downwards. (Adapted from Ban TA; Schizophrenia: A Psychopharmacological Approach. Charles C. Thomas, Springfield, 1972).

some of the cycloid psychoses are characterized by prevailing changes in perceptual-cognitive structures (systematic paraphrenias, cataphasia and confusion psychosis). Other disorders and groups of disorders are characterized by prevailing changes in relational affective structures (systematic hebephrenias, affect-laden paraphrenia and anxiety-elation psychosis) and others again by prevailing changes in motor-adaptive structures (systematic catatonias, periodic catatonia and motility psychosis). In phasic psychoses as a rule the primary disturbance is in the relational-affective structure (mood). In some of the subtypes (manic-melancholic psychosis, pure melancholia and pure mania), however, there are corresponding disturbances in the other two structures; and in some of the other subtypes (pure euphorias and pure depressions), there are disturbances in one additional structure, i.e., either perceptual-cognitive or motor-adaptive (Table IX).

Although Leonhard's system of classification is based on Wernicke's model of structure-analysis in psychopathology he also paid considerable attention to Kleist's (1929, 1939) contributions. His diagnoses provide for detailed analyses of psychopathological syndromes with emphasis on the identification of the prevailing structure in the holistic picture. They open a natural path for studies with advanced brain imaging techniques, e.g., PET, SPECT, and MIR.

The same applies to the DCR (Petho, Ban, Kelemen et al., 1984) which differs from Leonhard's classification in that it separates a group of systematic and non-systematic diseases within both affective and schizophrenic psychoses. It also distinguishes between the characteristics of experience and behavior and emphasizes the importance of the characteristic changes in form (Gestalt) and overall picture. Further, the DCR shifts the point of departure from the end-state to the first

Table IX

Variables	Phasic Psychoses	Cycloid Psychoses	Unsystematic Schizophrenias	Systematic Schizophrenias
Prevaillingly perceptual-cognitive pathology		Confusion	Cataphasia	Paraphrenias
Prevaillingly relational-affective pathology	+	Anxiety-Happiness	Affect-laden Paraphrenia	Hebephrenias
Prevaillingly motor-adaptive pathology		Motility	Periodic Catatonia	Catatonias
Pathology prevaillingly in one structure				+
Pathology prevaillingly in two structures	Pure Euphorias Pure Depressions	+	+	
Pathology in all three structures	Manic Melancholic Pure Mania Pure Melancholia			
Dissociated functioning among three structures			+	+
Harmonious functioning among three structures	+	+		
Episodic course	+	+	+	
Continuous course				+
Unipolar course	Pure Euphorias Pure Depressions Pure Melancholia Pure Mania			
Bipolar Course	Manic Melancholic	+		
Full remission	+	+		
Lack of full remission			+	+
Mild to moderate defect			+	
Moderate to marked defect				+

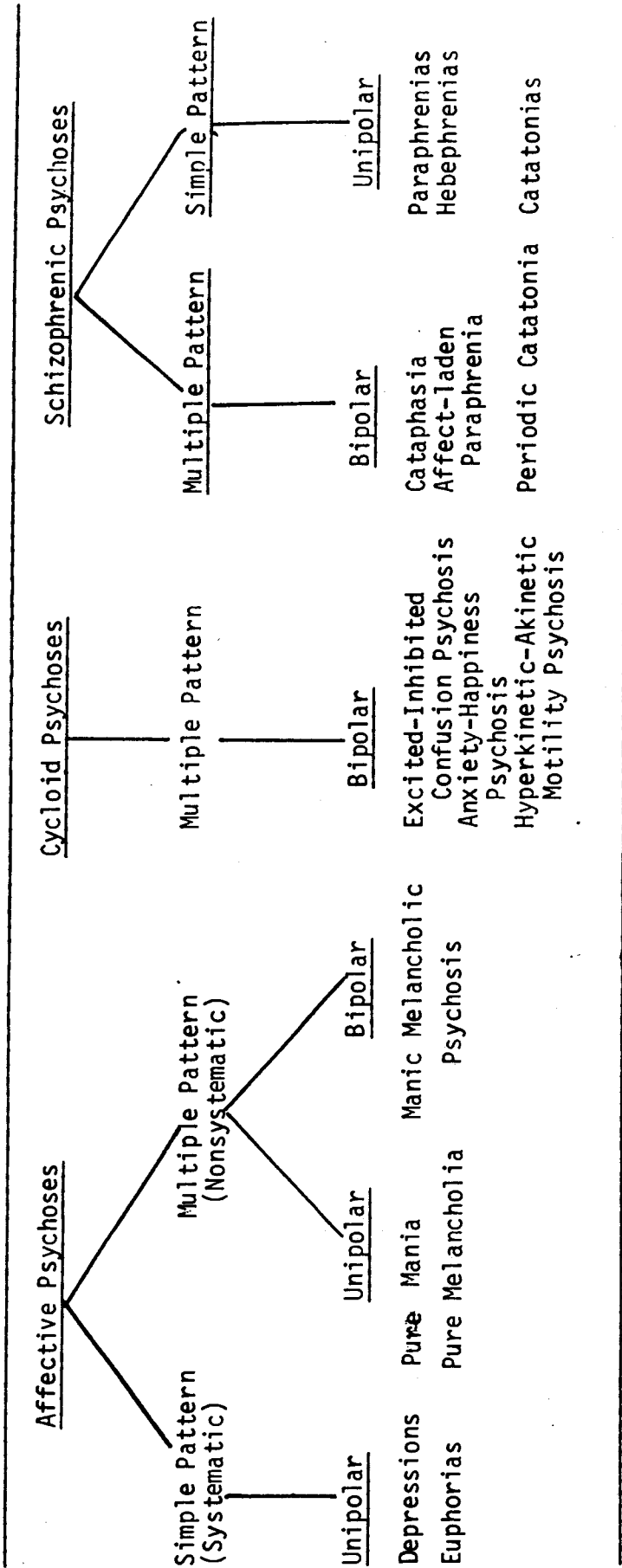
Prevailling structural characteristics of different diagnostic groups in Leonhard's (1957) system.



or index psychosis, and takes into consideration the course of illness and the characteristics of the outcome not only in terms of psychopathological symptoms, but also in terms of personality characteristics and social adjustment (Figure 7). Within the frame of reference of this classification an important prerequisite for the diagnosis of schizophrenic psychoses is the dissociation among the perceptual-cognitive, affective-relational and motor-adaptive structures that appears to be a "split" to an outside observer. It is difficult to understand the subject matter because it evolves in a catathymic manner or through other mechanisms. Contrary to common belief, hallucinations and/or delusions are not obligatory symptoms of schizophrenic psychoses. Considerably more specific are manifestations of formal thought disorder that disturbs comprehensibility (primary incoherence, tangential thinking, blocking, derailment, desultory thinking, onomatopoesis), affective changes (blunted, inadequate, inappropriate) and changes in personality (abandonment of habits, change in life style, incomprehensibility of behavior, autistic behavior).

Unlike the schizophrenic psychoses, which are characterized by an irreversible process, cycloid psychoses are characterized by complete recovery from each phase, although personality changes may occur. Patients with cycloid psychoses are diagnosed on the basis of a number of distinctive characteristics in the DCR. Among them probably the most important is that the whole field of patient's experience is transformed (protopathic change of Gestalt), with a change in the state of mind and depth of emotions. However, experience, behavior and performance remain in harmony (congruent). Onset is acute or subacute while the psychosis as a rule is multifold (polymorphous) and fluctuating with contradictory influences of healthy and pathological tendencies creating a feeling of uncertainty

Figure 47



Classification of endogenous psychoses in the DCR (Petho, Ban, Kelemen et al., 1984). It differs from Leonhard's classification that it separates patients with simple or systematic and multiple or nonsystematic pattern of illness.

and/or confusion. Nevertheless, there is a strong emotional involvement in symptoms. Other manifestations include ideas of reference, delusional perceptions, holothymic delusions, misidentifications, thematic incoherence and changes (increase or decrease) of reactive and expressive movements.

Similar to the cycloid psychoses which usually display complete recovery from each phase, affective-phasic psychoses are characterized by a remitting course with periodicity and/or rhythmicity. An essential prerequisite, although not necessarily exclusive criterion for this diagnosis is that experience, behavior and performance are in keeping with mood. The same applies to delusions. Nevertheless, the disease picture may be simple (monomorphous) or multiform (polymorphous).

Application of sophisticated technology is warranted only in biologically homogenous populations which meet optimal contemporary standards. There is sufficient evidence to believe that the diagnoses based on Leonhard's system fulfill these requirements. The "heredofamilial" distinctness of unipolar and bipolar illnesses within the phasic psychoses has been supported by Angst and Perris (1968, 1972); and the "genotypical" distinctness of cycloid psychoses and systematic schizophrenias by Ungvari (1984). This genetic distinctness was also substantiated by multiple threshold analysis which rejected the possibility of identical liability and confirmed the separateness of these two diagnostic categories. In the same study the nonsystematic schizophrenic category displayed a considerable genotypical overlap with the cycloid and the systematic schizophrenic categories ("as if it were a connecting link"). In favor of Leonhard's schizophrenic subtypes are the findings of a high correlation between the distribution of subtypes in the original sample of Leonhard from the late 1930s and early 1940s and in Astrup's sample 20 years later (Wilson and Ban, 1983). In

favor also are the statistically significant correlations in rank order of frequency of occurrence of the six paraphrenic, four hebephrenic and six catatonic subtypes in eight countries, in a study carried out in the late 1970s and early 1980s (Ban, Guy and Wilson, 1984a). The finding of differential therapeutic responsiveness between the systematic and the non-systematic schizophrenic populations and within both populations among the different types of patients by Fish (1964c) is also in support of Leonhard's system.

Leonhard's classification is important from a psychopharmacological point of view because it might provide the possibility of identifying patients therapeutically responsive to antipsychotics, antidepressants and mood stabilizer-lithium salts. It might also provide new end-points for research development. While a three-dimensional psychiatric classification is suitable to establish the therapeutic efficacy of drugs with an accepted level of statistical probability within a particular population, a four-dimensional model of psychiatric classification might be suitable to identify treatment responsive patients, i.e., diagnostic subtypes with a reasonable clinical accuracy. Similarly, while within a three-dimensional model of classification psychotropic drug development is restricted to the modification of speed on onset, efficacy and toxicity of drugs which share common pharmacological properties with conventional psychotropics, within a four-dimensional model of classification there are new end-points that open new paths for the development of new drugs with different pharmacodynamic properties. Thus, a four-dimensional model of classification could facilitate the development of a new class of drugs, e.g., "transition compounds" ("les produit de transition"). Drugs which belong to this category include carbamazepine, an anticonvulsant which is structurally related to tricyclic

antidepressants and which may have a place in the treatment of bipolar affective disorders and/or cycloid psychoses; and carpipramine and chlorcarpipramine, i.e., dibenzazepines (tricyclic antidepressant structure) with a butyrophenone (antipsychotic) side chain, which may have a place in the treatment of cycloid psychoses and/or affect-laden paraphrenia, one of the three diagnostic types of the nonsystematic schizophrenias. The same applies to the dibenzoxazepines, such as loxapine, an antipsychotic which demethylates in part to amoxapine, an antidepressant, which in turn hydroxylates in part into a dopamine receptor blocking antipsychotic drug. The dibenzoxazepines today are profiled as a traditional antipsychotic (loxapine) and a traditional antidepressant (amoxapine) because of their common pharmacological properties with prototype antipsychotics and antidepressants. By this, special emphasis is placed on some of their possible adverse effects without full appreciation of their unique therapeutic potential in certain diagnoses that require the combined administration of an antipsychotic with an antidepressant for optimal treatment.

### Affective Psychoses

The origin of the concept of affective psychosis dates to the 1850s when Falret stated that a predictable "natural course" of an illness "presupposes the existence of a natural species of disease with a pattern of development." It was the application of this notion to the description of a "natural species" ("endogenous") of disease, that presents with two specific cross-sectional psychopathological syndromes (i.e., manic and melancholic) and follows a predictable or "natural course" that led to the recognition of manic-depressive illness.

Falret (1864), in his lectures at Salpêtrière (Léçons à l'Hospice de la Salpêtrière) during 1850-1851, was first to describe "folie circulaire," the disorder later to become known as manic-depressive psychosis. In the

same year (1854) that Falret published his thesis on "De la folie circulaire," Baillarger (1854) presented the same concept, referring to it as "folie a double forme," to the French Academy of Medicine. There has been some controversy regarding priority.

#### Manic-Depressive Illness

In spite of the early recognition by Falret and Baillarger, "folie circulaire" (a three-dimensional diagnosis, which takes into consideration onset, cross-sectional psychopathology and course), was not recognized as a nosological entity until the publication of the fifth edition of Kraepelin's textbook of psychiatry in 1896. In this edition Kraepelin replaced cross-sectional syndromatologic diagnosis with longitudinal-nosological diagnosis for the first time. In the first edition of his textbook (1883) Kraepelin described six different forms of melancholia: simplex, gravis, stuporous, paranoid, fantastic and delirious, and four different forms of mixed states: depressed mania, agitated depression, depression with flight of ideas and depression with partial inhibition. In his 1896 presentation he contended that all of these different forms were manifestations of one and the same nosological entity, manic depressive insanity (Hippius, Peters and Ploog, 1983).

Kraepelin's original definition of manic-depressive insanity included "the whole domain of the so-called periodic or circular insanities" as well as "simple mania, most of the morbid states termed melancholia, and also, a considerable proportion of the amentias." This broad definition was expanded later to include "all cases of affective excess" and ultimately, on the basis of the contributions of Dreyfus (1905) also "involuntional melancholia," a disorder regarded at the beginning as a separate nosological entity because of its prolonged course.

Although the unitary concept of manic-depressive insanity had already been questioned by Jaspers (1913a), it was not until Leonhard's (1957) contributions that a consistent attempt to break down the unitary concept of MDP (manic-depressive psychosis) began (Perris, 1974). By employing a four-dimensional approach with consideration to the end-states of the illness, Leonhard separated a number of distinct disorders within manic-depressive illness. By introducing the concept of "polarity" regarding the formal pattern of the course he separated within the affective psychoses bipolar and unipolar forms. A "bipolar" form means that both manic and depressive episodes occur in the same patient. A "unipolar," originally referred to as "monopolar," form means that there are only "depressive" or only "manic" episodes.

Stimulated by Leonhard's work, two independent comprehensive investigations were carried out, one by Angst (1966) in Switzerland and another by Perris (1966) in Sweden. Results of these studies favored the distinctness of bipolar and unipolar affective psychoses on the basis of "heredofamilial factors" (Angst and Perris, 1968). Similar conclusions were reached by Winokur and Clayton (1967) in the United States. Furthermore, in bipolar patients urinary 3-methoxy-4-hydroxy-phenyl-glycol (MHPG) concentrations (Beckman and Goodwin, 1975) and platelet monoamine oxidase (MAO) activity (Murphy and Weiss, 1972) were found to be significantly lower than in unipolar patients.

In the DAS (Petho, Ban, Kelemen et al., 1984), the diagnosis of affective psychosis is based on the evaluation of 27 variables. They include variables relevant to mood (hyperthymic, dysthymic, irritable); variables relevant to onset (acute, subacute); and variables relevant to the disease picture (simple, multiform). Other, cross-sectional

psychopathological manifestations include distractibility and/or concentration difficulties with disturbance of sleep, appetite and/or sexual behavior. There is no split among perceptual-cognitive, relational-affective and motor-adaptive psychopathological structures. Perceptions, relations and actions are congruent with mood. Accordingly with a shift in the mood state towards elation (hyperthymia) or depression (dysthymia), there is an increase or decrease of speed of thought and an increase or decrease of psychomotor activity. As a rule, affective psychoses do not have an insidious onset. On the other hand, they present with a unipolar or bipolar course with periodically or even rhythmically recurring episodes. There is full remission between episodes.

In the same classification the diagnosis of manic melancholic psychosis (a group of nonsystematic-bipolar disorders) is based on the presence of the manic (or hypomanic) or the melancholic (or subclinical melancholic) syndrome and respectively the melancholic or the manic syndrome in the past. Bipolar manic melancholic psychosis is subdivided into four subtypes on the basis of their course, i.e., manic melancholic psychosis with mania (bipolar I), manic melancholic psychosis with hypomania (bipolar II), manic melancholic psychosis with melancholia (bipolar III) and manic melancholic psychosis with subclinical melancholia (bipolar IV).

Corresponding diagnoses to affective psychoses in the DCR are affective psychoses in the ICD-9 and major affective disorders and cyclothymic disorder in the DSM-III. Similarly corresponding diagnoses to DCR manic melancholic psychosis are manic-depressive psychosis circular types (currently manic, currently depressed, mixed or current condition not specified) in the ICD-9; and bipolar disorders (mixed, manic or depressed and cyclothymic disorder) in the DSM-III.



In the ICD-9, similar to the DCR, the diagnosis of affective psychosis is not restricted to manic-depressive illness with alternating manic and depressive episodes. It is not made, however, unless there is evidence for holothymic mood-congruent evaluations. In contradistinction to the DCR, in the ICD-9 there is a considerable emphasis on accompanying psychopathological symptoms, such as delusions, perplexity, disturbed attitude to self and disordered behavior. Also greater emphasis is placed on suicidal tendency.

DSM-III criteria for major affective disorders correspond to the DCR diagnoses. In certain respects, however, the diagnosis is restricted. Continuous signs of the disorder must be present to a significant degree for at least one week. Patients whose illness does not meet criteria for duration and severity are diagnosed as cyclothymic disorder in DSM-III.

Psychopharmacological contributions favor the distinctness of bipolar and unipolar affective psychoses. The therapeutic effect of lithium salts is superior to other modalities in the prophylactic treatment of manic depressive patients.

The prophylactic effect of lithium salts in bipolar patients has been demonstrated in at least seven placebo-controlled clinical studies involving a total of 400 manic-depressive patients. In these studies lithium, in the daily dosage range of 600 to 1200 mg with serum lithium levels from 0.6 to 1.2 mEq/l, was consistently more effective than placebo in reducing the occurrence of both manic and depressive episodes. According to Prien (1979), the evidence for lithium prophylaxis in depressive episodes is less conclusive than in manic episodes. However, Schou (1979b) found that the relapse rate in tricyclic antidepressant treated bipolar depressed patients was significantly higher (59%) than in lithium treated bipolar patients (35%).

In spite of the superiority of lithium salts over other modalities in the treatment of bipolar, manic-depressive patients, studies on the action mechanism of lithium salts have contributed little to the understanding of manic depressive psychosis. This may be related to the fact that the mechanism of action of lithium salts has not been explained (Baldessarini and Lipinski, 1975; Schou, 1979a). However, there is sufficient evidence to believe that lithium interferes with the release and increases the reuptake of catecholamines at the site of presynaptic neurons (Baldessarini and Yorke, 1970), decreases the sensitivity of postsynaptic catecholamine receptors (Hollister, 1978); and inhibits the release of the NE and/or prostaglandin (PG) E-stimulated cyclic 3,5 adenosine monophosphate (cAMP) (Forrest, 1975; Murphy, Donnelly and Moskowitz, 1973). Other effects of lithium include stimulation of choline transport (Millington, McCall and Wurtman, 1979) with enhancement of the synthesis of acetylcholine, glutamate and  $\gamma$ -aminobutyrate (Gottesfeld, Epstein and Samuel, 1971; Jope and Jenden, 1978); differential activation of phospholipase, and reestablishment of the resting electrolyte balance across the cell membrane (Coppen, Shaw and Mangoni, 1962). It is not known which actions of lithium are responsible for its therapeutic effects in bipolar patients. Some believe that it is its action on the central catecholamine systems (Ahluwalia and Singhal, 1984).

Another possible reason that lithium salts have provided little if any clues for a better understanding of the nature of manic-depressive disorders is that they are far from being specific treatments and are indicated also in the treatment of impulse disorders, episodic violence, emotionally unstable character disorders, premenstrual syndrome and borderline patients (Bernstein, 1983). In spite of other indications

lithium salts remain the specific treatment modality for a well identified diagnostic population within the endogenous psychoses. Many patients stabilized on lithium therapy exhibit rapid relapse into severe mania following cessation of drug treatment (Klein, Brovcek and Greil, 1981; Lapierre, Gagnon and Kokkinidis, 1980; Small, Small and Moore, 1971; Wilkinson, 1979). Nevertheless, not all patients stabilized on lithium therapy relapse rapidly following cessation of therapy and/or not all bipolar manic-depressive patients respond to lithium treatment. The finding that only approximately 65 percent of bipolar patients respond to lithium prophylaxis clearly indicates that bipolar affective psychosis is a biologically heterogeneous diagnostic group. It remains to be seen whether the separation of Bipolar I (depression with mania) from Bipolar II (depression with hypomania) and from Bipolar III (depression with hypomania or mania precipitated by the administration of an antidepressant or electroconvulsive therapy) will improve homogeneity (Spitzer, Endicott and Robins, 1978a and b). On the other hand, recognition of the heterogeneity of the bipolar population could explain why some patients who remain refractory to lithium treatment respond favorably to carbamazepine, while others respond to valproic acid (Lerer, 1985). It remains to be seen whether a relatively high pre-treatment plasma calcium/magnesium ratio (over 2.62) could separate a biologically homogenous and/or nosologically meaningful lithium-responsive bipolar group which is distinct from the carbamazepine and/or valproic acid responders (Carman et al., 1974). In favor of this possibility is the rise in plasma magnesium level in lithium-responsive depressed patients during the initial five days of treatment (Crammer, 1975).

Independent of clinical psychopharmacologic research, genetic psychiatric research has indicated that the density of muscarinic cholinergic (quinuclidinyl benzilate) binding sites in the skin fibroblasts of patients with

manic-depressive psychosis and in their ill relatives is significantly higher than in normal controls. Also, incubation of cells with lithium resulted in a decrease of binding sites into the normal range (Nadi, Nurnberger and Gershon, 1984). Attempts to replicate these findings, however, consistently failed (Lenox et al., 1985; Kelsoe et al., 1985; Gershon et al., 1985). Would they be supported by further evidence, the question remains whether this alleged genetic-biological marker could be linked to a nosologically meaningful subpopulation within manic-depressive psychosis and/or the genetically defined population would be homogenous in terms of responsiveness to lithium salts.

#### Melancholia and Depressions

Of the two cross-sectional psychopathologic syndromes encountered in manic-depressive psychosis, depression is the more frequent. It has been estimated that 100 million people worldwide suffer from a recognizable depression (Ban et al., 1981). A survey carried out from 1967 to 1976 in a community in the United States revealed that 6.8 percent of the respondents were experiencing depression at the time of the survey (period prevalence) and 26.7 (one of four respondents) had experienced symptoms of depression earlier in their lives (lifetime prevalence) (Weissman and Klerman, 1978; Weissman and Myers, 1978a and b). However, not all persons who have experienced depression suffer from a clinically verifiable depressive illness. If those cases that are not depressive illnesses are excluded, the prevalence figures are considerably lower.

The incidence of affective illness in the general population is estimated to be approximately 2 percent (i.e., 1 of 50) with a slightly higher incidence in females (2.5%) than in males (1.8%). Among the relatives of unipolar and bipolar patients, however, the risk for all

mood disorders jumps to between 10 to 20 times the general population rate (Tsuang and Vandermeij, 1980). Accordingly, Winokur and Clayton (1967) found that the risk of brothers and sisters of a person with mood disorder rises from 12 percent if neither parent is ill, through 26 percent if one parent is ill, to 43 percent if both parents are ill. Although the mode of inheritance remains hidden the significant increase in the rate of occurrence of affective disorder among the biological relatives of patients indicate that biological-genetic factors play an important role in the etiology of these illnesses.

#### Separation of Vital Depression

The most important contribution to the clarification of the confounding situation created by the all embracing concept of manic-depressive psychosis (which includes all depressions) was made by Schneider (1920, 1959). By distinguishing between "vital depression" which he considered a medical illness, and other ("non-psychotic") depressive disorders, Schneider opened the paths to our present system of classification of depressions.

The crucial step in the separation of depressive illness from other depressive disorders was the recognition of "depressive personality." Distinct from "vital depression" which is the result of a disease process, depressive personality is a developmental abnormality. As such, it is ill defined in psychopathological terms (Chodoff, 1972). In general, however, people with a depressive personality lack self-confidence, are susceptible to fatigue and dread the unknown. Unlike those with specific illness (unipolar or bipolar), they have been feeling sad, experiencing guilt, and complaining of concentration difficulties for a long time.

Vital depression is an endogenous affective illness which embraces all three psychopathological structures: (1) the perceptual-cognitive,

(2) the relational-affective and (3) the motor-adaptive. It is characterized by "passive-unmotivated" dysphoria and disturbance of vital feelings with the explicit experience of displeasure and discontent leading to a disturbed time sense, poverty of thought, reduced emotional susceptibility and retardation. There are also vegetative symptoms, accompanied by hypochondriasis, corporization and feelings of motor and sensory disturbances. This concept of vital depression, or depressive disease described by Schneider in 1920 differs considerably from Kraepelin's (1921) concept of "depressive states" which are characterized by the triad of sad or anxious mood, thought retardation and decreased drive.

The concept of "psychogenic depressive reaction" was perceived at first as reactions of abnormal personalities to moderate or mild stress, or reactions of normal personalities to severe stress (corresponding to Schneider's concept of neurosis). By this definition "psychogenic depressive reaction" was positioned between "developmental anomalies" and sui generis "depressive illnesses." More recently, with the contributions of Stromgren (1958,1968), it has been recognized that psychogenic depressive reactions are illnesses that may occur in psychotic and non-psychotic forms. Common characteristics of both states are a clearly identifiable precipitating factor, thematic continuity between the trauma and the content of the illness, lack of depressive evaluation and preoccupation with the traumatic life events. Other common characteristics include reactive mood changes and feelings of passivity (Jaspers, 1963, 1974). Within this new frame of reference "psychogenic depressive reactions" are perceived as disorders (illnesses) whether psychotic or not, and are distinct from personality disorders in that activation of an endogenous factor depends on a precipitating life event and not on personality development.

### Empiricistic and Pragmatic Classifications

Kurt Schneider has been considered by some as "the last classicist in psychiatry" (Kisker, 1968). Nevertheless, his classification of "depression" was not unanimously accepted. It remained restricted to the German speaking countries until the late 1970s. Instead, in English speaking countries attention was focused on the rapidly growing British school under the leadership of Aubrey Lewis who in his classic article restated Kraepelin's unitary view. Lewis' (1934) publication was based on a clinical survey of depressive states which provided him with data to conclude that "melancholia" was not a group of disorders but one disease.

For some time Lewis' thesis has dominated British psychiatry. However, during the late 1950s--almost a quarter of a century after the publication of the original paper--the controversy, whether all depressions are the same endogenous disease or constitute different disorders distributed on a continuum, erupted again (Ban, 1981). The resulting research led to some of the empiricistic classifications based on a wide range of descriptive data collected from depressed patients and submitted to multivariate statistical techniques, e.g., factor analysis, cluster analysis, or multiple discriminant analysis. By employing this approach Kiloh and Garside (1963) identified a bipolar factor splitting observations into positive and negative loadings. Endogenous depression (age over 30, depression worse in morning, weight loss 7 lbs. or more) and neurotic depression (responsive to environmental change, self pity, initial insomnia) were differentiated. Similarly, Kendell (1968) identified at the fourth order of analysis, a bipolar factor contrasting psychotic depression and neurotic depression. By employing principal component analysis, he found that the three leading symptoms of neurotic depression were anxiety, tension, and brief duration of illness. Within the same frame of

reference Hamilton and White (1959) discerned that depressed patients with retardation is made up of different population from depressed patients with agitation. Grinker et al. (1961) separated four types of depression: retarded, anxious, hypochondriacal and angry. Overall et al. (1966) distinguished three classes of depression: retarded, anxious, and hostile. Paykel (1972) described four categories of depression: psychotic, anxious, hostile and "depression in the young with personality disorder." Klein (1974a and b) proposed three groups of depression: endogenomorphic, chronic dysphoric, and reactive. Raskin and Crook (1976) identified four classes of depression: agitated, neurotic, endogenous, and "depression with poor pre-morbid personality" (Table X).

Simultaneously with classifications of depression based primarily on cross-sectional psychopathological data, numerous other classifications have been proposed. On entirely pragmatic grounds Kielholz (1972) differentiated among three different groups of depressions: somatogenic, endogenous and psychogenic. Robins and Guze (1972) differentiated between two groups of depression: primary and secondary. Primary depression refers to a combination of signs and symptoms that involve psychomotor and vegetative dysfunctions, dysphoria, hopelessness, worthlessness, guilt, and suicidal preoccupations occurring de novo as a primary disorder of mood. Secondary depression refers to similar signs and symptoms usually with feelings of sadness, inadequacy and hopelessness that occur during the course of a preexisting nonaffective psychiatric disorder or is associated with medical illness. Implied in secondary affective disorder is an antecedent disease. Because of this, secondary depressions may show considerable heterogeneity (Andreasen and Winokur, 1979). This contrasts with primary depression which forms a relatively homogenous group. Even primary depression however, has some



Table X

Authors	Year	Groups
Hamilton and White	1959	Agitated Retarded
Grinker et al.	1961	Type A (Retarded) Type B:(Anxious) Type C (Hypochondriacal) Type D (Angry)
Kiloh and Garside	1963	Endogenous Neurotic
Overall et al.	1966	Retarded Anxious Hostile
Kendell	1968	Psychotic Neurotic
Kielholz	1972	Soma togenic Endogenous Psychogenic
Paykel	1972	Psychotic Anxious Hostile Depression in the Young with Personality Disorder
Robins and Guze	1972	Primary Secondary
Andreasen and Winokur	1972	Pure Spectrum Disease Nonfamilial or Sporadic
Klein	1974	Endogenomorphic Chronic Dysphoric Reactive
Raskin and Crook	1976	Agitated Neurotic Endogenous Depression with Poor Premorbid Personality

Classifications of depression.

heterogeneous features in regard to the course of the disease and the prevailing psychopathologic symptoms (Perris, 1974). When compared with patients suffering from primary depression, patients with secondary depression tend to have a lifelong coping style characterized by depression, make more but less serious suicide attempts, and complain more of hostility, anxiety, somatization and difficulties in falling asleep (Andreasen and Winokur, 1979).

#### Genetic and Experimental Classification

Antecedent-etiological factors are of pivotal importance in genetic classifications in which the concept of "endogenous" is translated into experimental hypotheses in terms of familial incidence of the disease. As such they represent a transition between the empiricistic-pragmatic and experimental classifications of depression. In these essentially two-dimensional classifications genetic hypotheses are tested to explain the heterogeneity of depressive states. In this respect they differ in their emphasis from sui generis psychiatric classifications in which hypotheses, based on a comprehensive four-dimensional model, with consideration of all four developmental stages of the illness, are tested to reveal the proportion of genetic and other contributions.

The prototype, and one of the most frequently referred to genetic classification of depression, is that of Andreasen and Winokur (1979) who distinguish three distinct groups of depressions: pure depression, depression spectrum disease, and nonfamilial depression. Nonfamilial or sporadic refers to a depression which occurs in a person who has a family history of other than affective disorder that may form a spectrum with depression, such as alcoholism or antisocial personality (Baker et al., 1971). Characteristics of depression spectrum disease are early onset

(below 40 years) and female prevalence, while of pure depression, late onset (after 40 years) and equal sex distribution (Winokur, 1973, 1979). Patients with nonfamilial depression have primary rather than secondary depression significantly more often. The incidence of primary and secondary depressions is equal in pure depression and depression spectrum disease (see Appendix VI, Figure 1 and Tables I-III).

An entirely new approach to the classification of depression involves the employment of biochemical measures (Table XI). Included among the most frequently measured biochemical variables are plasma cortisol levels, urinary 3-methoxy-4-hydroxy-phenyl glycol (MHPG--the final metabolic end product of norepinephrine), cerebrospinal fluid homovanillic acid (HVA--the final metabolic end product of dopamine) and 5-hydroxy-indole-acetic acid (5HIAA--the final metabolic end product of serotonin) concentrations, free plasma tryptophan levels (FPT) and platelet monoamine oxidase (MAO) activity. Supplementing these measures are neuroendocrine tests, such as the extensively employed dexamethasone-cortisol suppression (DST), clonidine-growth hormone (GH) release, thyrotropine releasing hormone (TRH)--thyrotropine stimulating hormone (TSH) response and pibedil-homovanillic acid accumulation (PHA), (Ban, 1971). In spite of the sophisticated technology employed, a biochemical approach to classification is essentially one-dimensional, i.e., cross-sectional. One of the essential prerequisites for such a classification is the separation of "trait"-dependent variables from "state" dependent variables. But even if this is attained the problem remains that in a biochemically based classification biochemical hypotheses are tested to explain the heterogeneity of depressive states. In this respect, biochemical classifications differ in emphasis from sui generis psychiatric classifications in which hypotheses, based on a comprehensive four-dimensional model, with consideration to all four developmental stages of the illness, are tested to reveal its biochemical substrate.

Table XI

Biochemical	Neuroendocrine
Serum cortisol	Dexamethasone-cortisol suppression
Urinary MHPG	TSH response to TRH
Cerebrospinal fluid HVA	Clonidine-GH release
Cerebrospinal fluid 5HIAA	Piribedil-HVA accumulation
Free plasma tryptophan	
Platelet MAO	

Biochemical measures and neuroendocrine tests employed in the classification of depressive states.

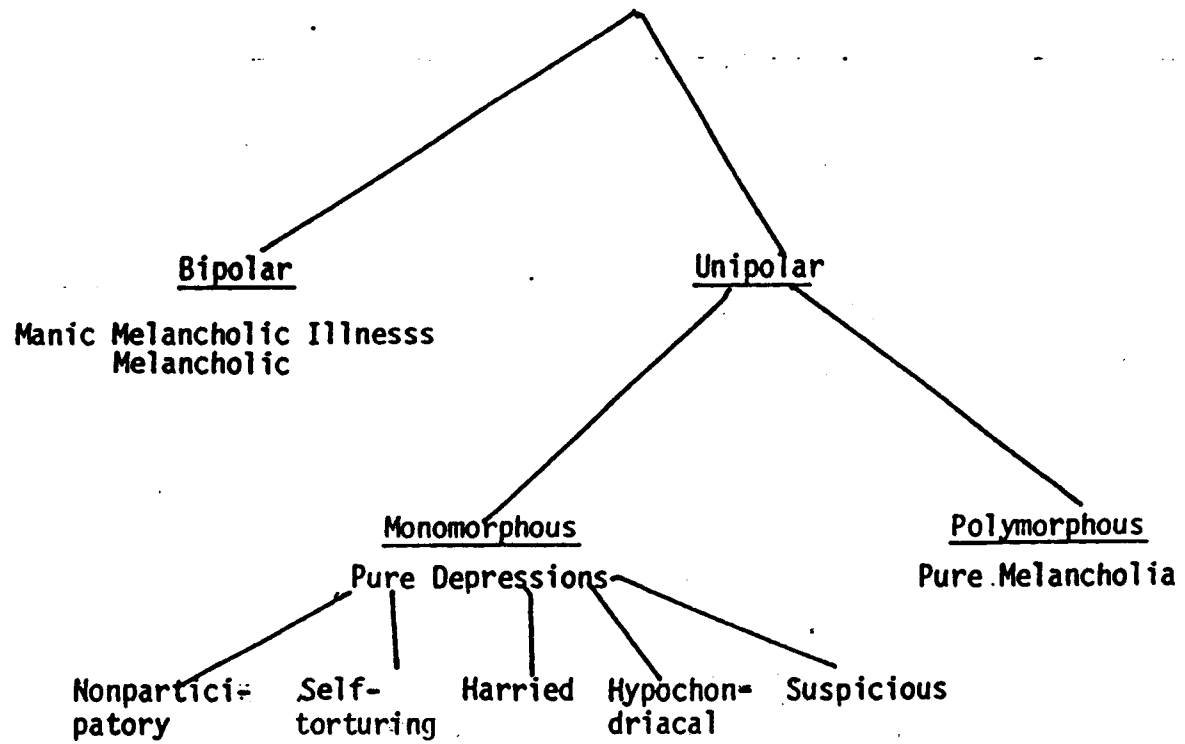
### Nosological Classifications

After a detour of almost 40 years, interest in the nosology of depression and in Schneider's (1920) concept of depressive illness was revived. By combining structural analysis with a holistic approach (i.e., perceiving the patient in his totality and not just as an aggregate of psychopathological symptoms), and with consideration of all four developmental stages of depressive illness, Leonhard (1957) recognized that Schneider's "vital depression" consists of a number of different clinical syndromes. Of these only one, pure melancholia corresponds to some extent with the original concept. However, and in contradistinction to Schneider, he considered the triad of motiveless (incomprehensible) dysthymic mood, psychomotor retardation and thought retardation as the cardinal symptoms of pure melancholia; and perceived the indecisiveness, and feeling of inadequacy (insufficiency) as secondary phenomena to the cardinal-primary manifestations. By shifting the emphasis from cross-sectional psychopathology to the unipolar-bipolar dimension of the course, Leonhard separated the melancholic syndrome of bipolar manic melancholic illness from unipolar pure melancholia, a concept introduced by Lange (1897) and Schou (1927) (Pedersen, Poort and Schou, 1947). Similarly, by recognizing the importance of the overall (holistic) clinical picture, whether simple (monomorphous) or multiform (polymorphous), he separated unipolar pure melancholia from the unipolar pure depressions, i.e., nonparticipatory, harried, hypochondriacal, self-torturing and suspicious. These unipolar pure depressions are prevailingly affective, systematic diseases from a structural point of view, while pure melancholia is a nonsystematic disease in which thought and desire are also obligatorily disturbed. Furthermore, Leonhard called attention to cross-sectional features distinguishing between the bipolar and unipolar forms of depression. He suggested that

bipolar--nonsystematic--forms display a more colorful appearance. Also, they vary not only between the two poles, but in each phase offer different clinical pictures. The same does not apply to the unipolar--systematic--forms in which each individual form is characterized by a syndrome not associated or even transiently related to any other form and recur in patients with a periodic course with the same symptomatology (Figure 8).

The five distinct subtypes of pure depression are named on the basis of their prevailing clinical features. Although they are prevailing affective-mood disorders, in two of them (harried and nonparticipatory) motor-adaptive structures, and in three others (hypochondriacal, suspicious and self-torturing) perceptual-cognitive structures, are also involved. Of the five subtypes, "harried" depression is characterized by motor restlessness associated with marked tension and anxiety with driven (but meager) complaintiveness and poor thematization; while hypochondriacal depression by hypochondriasis and corporization (feeling sick or diseased) with hopeless complaintiveness and homonom bodily hallucinations (bodily misperceptions). Self-torturing depression is characterized by self-condemnation and guilt feelings with loss of self-esteem and lamentativeness; while suspicious depression by suspiciousness, ideas of reference and auditory hallucinations. Nonparticipatory depression is characterized by lack of affective participation and feelings of alientation with abulia and the feeling of loss of feelings referred to as anhedonia. In contradistinction to pure melancholia which usually ends within a limited period of time, in pure depressions, there is a tendency for chronicity. On the other hand, similar to pure melancholia, pure depressions yield to complete remission between episodes, even if the duration of the episodes is prolonged.

Figure 8



Leonhard's (1957) classification of depression.

Irrespective of the nosological classifications described, ICD-9 distinguishes three subtypes of depression and DSM-III five subtypes. The three subtypes of the ICD-9 include manic-depressive psychosis depressed type, manic depressive psychosis circular type but currently depressed, and other nonorganic psychoses depressive type. Corresponding subtypes in DSM-III are bipolar disorder depressed, major depressive disorder single episode, major depressive disorder recurrent, cyclothymic disorder, and atypical depression. There is no correspondence between Leonhard's depressive subtypes, adopted in the DGR, and depressive diagnoses in ICD-9 or DSM-III.

#### Psychopharmacology and the Depressions

The two major groups of drugs primarily used in the treatment of depressive disorders are cyclic antidepressants and monoamine oxidase inhibitor (MAOI) antidepressants.

#### Cyclic Antidepressants

Differential responsiveness to therapeutically effective cyclic (tricyclic) antidepressants brought to attention the heterogeneity within the depressive population. Although there is sufficient evidence to support the contention that the overall therapeutic effectiveness of tricyclic antidepressants is greater than individual psychotherapy, group, or other social therapeutic methods, tricyclic antidepressants exert a therapeutic effect only in 65 to 70 percent of depressed patients during acute and maintenance phases of treatment. Response rates have remained essentially the same with the new generation of cyclic antidepressants. Included among these



substances are drugs with specificity towards the norepinephrine system, such as maprotiline, the serotonin system, such as fluvoxamine, fluoxetine, citalopram and trazodone, or the dopamine system, such as nomifensine. Included also are antidepressants in which monoamine uptake inhibition (characteristic of antidepressants) is combined with dopamine receptor blockade (characteristic of antipsychotics), such as amoxapine. There are indications that response rate can be improved by adjusting the dose on the basis of monitored blood levels to attain a therapeutic range.

Considering that the usefulness of cyclic antidepressants in prophylactic treatment is questionable, that approximately 25 percent of depressed patients respond to nonspecific-placebo treatment, and another 25 percent spontaneously remit within three to four weeks, it is difficult to determine the actual percentage of depressed patients who are cyclic antidepressant responsive (Ban, 1974). To identify this population numerous clinical studies have been designed. In a comprehensive review of these studies Bielski and Friedel (1976) revealed that patients with endogenous depression, characterized by psychomotor retardation, anorexia, weight loss, and sleep disturbance are the ones with a favorable therapeutic response. Delusions, and neurotic, hysterical and/or hypochondriacal traits, considerably decrease the response rate.

In the absence of a well identified biologically homogenous depressive population which is responsive to cyclic antidepressants, it is unlikely that valid inferences can be made about the biological substrate of depression from the action mechanism of these drugs. Regardless of their clinical relevance, however, research designed to elucidate the action mechanism of cyclic antidepressants has contributed to the development of modern neuropharmacology and to a better understanding of the neurochemistry of the brain.

By now there is substantial evidence that the therapeutic action of cyclic antidepressants cannot simply be attributed to monoamine reuptake inhibition,  $\alpha$ -adrenergic receptor blockade, and/or immediate increase in available monoamine concentrations at the synaptic cleft (Carlsson et al., 1966, 1969; Segal, Kuczenski and Mandell, 1974; Snyder and Yamamura, 1977; Voigtlander, 1976). It is more likely that therapeutic changes result from the decrease in sensitivity of the noradrenergic receptor system associated with a decrease in norepinephrine (NE) turnover rate and activity (firing rate) of noradrenergic neurons in the locus coeruleus; and/or the increase in serotonin (5HT) receptor sensitivity in the hippocampus and geniculate bodies (Karobath et al., 1976). In spite of the blocking effect of muscarinic acetylcholine and histamine receptors (Kofata, 1979; Richelson, 1979), it is commonly held that the crucial mechanism in the action of cyclic antidepressants is the "down regulation" of the  $\beta_2$ -receptor coupled NE-sensitive adenylate cyclase system in specific brain regions. A frequently used argument in favor of this contention is that the time course of this down-regulation in both human and animal studies parallels the delayed onset of therapeutic effect. Another frequently used argument in favor of the "down regulation" hypothesis is that it is a common feature of all effective treatment modalities, including electroconvulsive therapy (ECT), of depressive states. Nevertheless, because the therapeutic indications for ECT are not restricted to depression and they include some of the schizophrenias and manias (Small et al., 1985), supersensitivity of  $\beta_2$ -receptors cannot be considered a valid hypothesis for the pathomechanism of depression even if down regulation of  $\beta_2$ -receptors is an important step in the action mechanism of cyclic antidepressants.

While attention is focused on the NE system in relationship to the action mechanism of cyclic antidepressants, clinical neurophysiological

studies revealed a significant relationship between the changes in the tonic components of rapid eye movement (REM) sleep (i.e., latency time and number of periods), regulated by cholinergic mechanisms, and therapeutic response (Kupfer and Foster, 1972). Furthermore, an increase in REM latency and REM suppression after a loading dose of 50 mg of amitriptyline was predictive of a favorable outcome with a high level of probability (Kupfer et al., 1979). Considering that there is no habituation of changes seen in the tonic components of REM sleep while there is habituation to changes seen in the phasic components, one may speculate, that in the antidepressant effect of amitriptyline, cholinergic mechanisms play a more important role than catecholaminergic mechanisms (responsible for the regulation of the phasic components of REM sleep). In favor of this is the correlation between amitriptyline blood levels and the tonic components (but not the phasic components) of REM sleep; and the significantly greater sensitivity to arecoline, a muscarinic cholinergic agent to increase REM latency in depressed patients than in normal controls (Sitaram et al., 1980).

These new findings revived interest in Selbach's (1961) contention about the action mechanism of the prototypical cyclic antidepressant, imipramine. According to Selbach imipramine exerts its effect in three successive stages. The first, is characterized by trophotropic actions (feeling of tiredness, decrease of blood pressure), the second by lability (tremor, fluctuation in blood pressure), and the third by ergotropic effects (elevation, increased interest). Or in other words, imipramine has an effect on autonomic regulation and produces an imbalance in which the parasympathetic (trophotropic)-cholinergic system is more strongly inhibited than the sympathetic (ergotropic)-catecholaminergic system as reflected in the ergotropic manifestations. The finding that there is a fall in plasma

cortisol level with all forms of effective treatment of depressive states (Ban, 1974), is in keeping with the importance of anticholinergic effects in the action mechanism of cyclic antidepressants, since anticholinergic substances, such as atropine, block the circadian rise in plasma cortisol (that is commonly seen in depression). In keeping also are the findings of some of the original reports with the dexamethasone suppression test (DST). According to these reports patients whose morning rise of cortisol can be suppressed by atropine-like substances, have a favorable response to cyclic antidepressants (McLeod, Carroll and Davies, 1970), while "non-suppressors" have not (McLeod, 1972).

#### Monoamine Oxidase Inhibitors

The second most frequently employed group of drugs used to treat depressed psychiatric patients are the MAOIs. They comprise a structurally heterogeneous group of drugs with the common characteristics of inhibiting the activity of the intracellular (mitochondrial) enzyme, monoamine oxidase (MAO), responsible for the oxidative deamination of biogenic amines, such as norepinephrine (NE), dopamine (DA), and serotonin (5HT) to pharmacologically inactive acidic derivatives. Because a prerequisite for the therapeutic effect of these drugs is a minimum of 80 percent inhibition of MAO activity, it is assumed that this action is intrinsically linked to their therapeutic effect in depression.

The origin of MAOIs was in substances used to treat tuberculosis. Substitution of one of the hydrogen atoms in the hydrazine moiety of isoniazid by an isopropyl group resulted in iproniazid, the first clinically employed MAOI antidepressant. Both isoniazid and iproniazid, used as tuberculostatic agents, produced euphoria. Nevertheless, only with iproniazid was the "euphoria" associated with MAO inhibiting properties (Flaherty,

1952; Zeller et al., 1952). However, it was not until the late 1950s that three independent teams of psychiatrists were able to demonstrate the antidepressant effects of the drug (Crane, 1957; Kline, 1958, Scherbel, 1960). While Brodie, Pletscher and Shore (1956) revealed an actual rise in brain monoamines after iproniazid administration, and an actual decrease in brain monoamines after reserpine administration, Loomer, Saunders and Kline (1957) contrasted the iproniazid-induced elevation of mood with the reserpine-induced depression.

Iproniazid was withdrawn from clinical use because of hepatotoxic effects. It was replaced by various MAOI hydrazine preparations such as isocarboxazid, mebanazine, nialamide and phenelzine and by various non-hydrazine compounds, such as tranlycypromine, a phenylcyclopropylamine, and pargyline, a propargylamine used primarily to treat hypertension (Biel, Horita and Drukker, 1964).

Considerable difficulties have been encountered in establishing the therapeutic indications for MAOIs in depressive states. Some clinicians regard MAOI antidepressants as the secondary choice of treatment in depression and prescribe them only when a cyclic antidepressant has failed. There is sufficient clinical experience, however, for using a MAOI as primary therapy for patients with at least two cross-sectional depressive syndromes. One, referred to as "atypical" depression (Sargent, 1961), is characterized by hyperphagia, hypersomnolence, waves of lethargy, reversed diurnal variation and hyperactivity (Quitkin, Rifkin and Klein, 1979). Another is characterized by anxiety, fatigue, phobia and numerous somatic complaints (Robinson et al., 1973). It remains to be determined whether these cross-sectional clinical syndromes, delineated by careful clinical observations, represent nosologically meaningful diagnostic categories.

The recent upsurge of interest in MAOI antidepressants is probably the result of purification and characterization of the enzyme MAO from the brains of animals and man (Youdim, 1978); and the evidence that mitochondrial MAO in the CNS exists in more than one form (Johnstone, 1968). It is probably also related to the advent of new drugs, such as clorgyline (Barbeau, 1978) and deprenyl (Knoll, 1978) which are selective inhibitors of enzyme forms referred to as Type A and Type B (Gershon, 1978). Of the two enzymes, Type A is primarily responsible for the deamination of 5-hydroxytryptamine (Tripton and Mantle, 1978) frequently implicated in the pathomechanism of depression, and Type B for the deamination of benzylamine and phenylethylamine (Magyar and Knoll, 1977). It is the activity of the Type B enzyme that is measured in the platelet and that is predominant in the primate brain. In spite of extensive research, the only tangible result is an increased Type B enzyme activity in premenopausal women with depression (Klaiber et al., 1979). It is not known, however, to what extent this patient population is therapeutically responsive to the administration of MAOI antidepressants. Furthermore, because some clinical manifestations seen in patients with hysteroid dysphoria (Klein, 1974), a population characterized by increased appetite and need for sleep, correspond with manifestations of amphetamine withdrawal (the result of derangement in the regulation of phenylethylamine structures), the possibility has been raised that hysteroid dysphoric patients may show a favorable therapeutic response to deprenyl or other Type B MAOIs.

#### Pharmacotherapy of Depression

While there is substantial evidence for a differential therapeutic response within the depressive population to both cyclic and MAOI antidepressants, there is little information, based on well designed studies,

on the effect of either cyclic or MAOI antidepressants in the different depressive subpopulations. Consequently, there is no convincing evidence that cyclic or MAOI antidepressants, or any of the other treatment modalities-- psychological, behavioral, physical and/or pharmacological--can produce favorable changes in patients with "depressive personality" (Schneider, 1959). The same applies to "hostile depression" and "depression in the young with personality disorder" (Paykel, 1972), "chronic dysphoria" (Klein, 1974), "depression with poor premorbid personality" (Raskin and Crook, 1976), and possibly also to the "hostile depression syndrome" of Overall et al. (1966). For psychogenic depressive reactions, a number of different treatment modalities, psychological and pharmacological, have been tried, but because of the usually short duration of these disorders and their high susceptibility to placebo treatment, it is difficult to decide whether anyone of the treatment modalities is superior to the others. Included among these disorders are neurotic depression (Kiloh and Garside, 1963; Kendell, 1968; Raskin and Crook, 1976), also referred to as anxious depression (Overall et al., 1966; Paykel, 1972), psychogenic depression (Kielholz, 1972) and reactive depression (Klein, 1974). The same does not apply to psychogenic affective (depressive) psychosis in which psychotherapy, behavior therapy and treatment with anxiolytic sedatives or MAOI antidepressants are not indicated, while treatment with cyclic antidepressants alone usually does not suffice and needs to be combined with the administration of an antipsychotic. In a considerable proportion of patients not even this is sufficient and pharmacotherapy needs to be replaced by electroconvulsive treatment. To some extent the same applies to depression spectrum disease in which treatment with cyclic antidepressants usually does not suffice and need to be supplemented or replaced by an antipsychotic to attain a favorable therapeutic response (Andreasen and Winokur, 1979).

In the treatment of vital depression (Schneider, 1920), also referred to as endogenous depressions (Kiloh and Garside, 1963; Kielholz, 1972; Raskin and Crook, 1976), psychotic depression (Kendell, 1968; Paykel, 1972), primary depression (Robins and Guze, 1979), endogenomorphic depression (Klein, 1974) and pure depression (Andreasen and Winokur, 1972), a number of different antidepressants have been tried. While there is substantial reason to believe that there is a differential therapeutic response to antidepressants within the vital-endogenous depressive population, indicating that endogenous depression consists of a biologically heterogeneous population, there is little information based on properly designed studies on the effect of different treatment modalities in the different subpopulations. Consequently, there are indications but no convincing evidence that in Leonhard's (1979) nonsystematic depressive population (i.e., bipolar depression and unipolar pure melancholia), cyclic antidepressants alone are usually not sufficient and need to be supplemented with lithium salts. Further, there are indications that among the five subtypes of pure (systematic) depressions only two--nonparticipatory (usually referred to as retarded) and self-torturing (may be referred to as suicidal)--show a favorable therapeutic response to treatment with cyclic antidepressants. But one of these two subtypes (suicidal depression) seems to respond more consistently and reliably to electroconvulsive treatment.

Therapeutic responsiveness to cyclic antidepressants in the other three subtypes of pure depression is more questionable. In hurried (usually referred to as agitated) depression, treatment with cyclic antidepressants usually does not suffice and need to be combined with antipsychotics, to attain behavioral control. Hypochondriacal traits decrease therapeutic responsiveness, and the administration of a cyclic antidepressant may even



increase the complaints of patients with hypochondriacal depression. On the other hand, anxiolytic sedatives seem to alleviate suffering and are frequently combined with cyclic antidepressants in the treatment of hypochondriacal depression. Similar to hypochondriacal traits, suspiciousness decreases therapeutic responsiveness and the administration of a cyclic antidepressant may even aggravate the content disorder of thought and psychotic symptomatology of patients with suspicious (usually referred to as psychotic or delusional) depression. On the other hand, antipsychotics effectively control psychotic symptomatology and are frequently combined with cyclic antidepressants in the treatment of suspicious depression. Considering the dopamine receptor blocking properties of 7-OH amoxapine, one of the hydroxylated metabolites of amoxapine, and the distinct possibility that dopaminergic structures play a role in psychotic symptomatology, amoxapine has been tried in a limited number of patients with suspicious-delusional (psychotic) depression and in a limited number of patients with hurried-agitated depression. In both subtypes the therapeutic response was favorable in the majority of patients (Anton and Sexauer, 1983; Ragheb and Ban, 1984).

Although diagnostic classifications based exclusively on biochemical measures are of questionable value, there are indications that some of the biochemical data become meaningful and interpretable within a four-dimensional classification of depressive states. Thus, both platelet MAO activity and urinary MHPG concentrations have been found to be significantly lower in bipolar than in unipolar depression (Schildkraut et al. 1978a and b; Murphy and Weiss, 1972). This is in line with the findings that cyclic antidepressants are superior to MAOI antidepressants in their therapeutic effect in patients with bipolar depression. It is also consistent with the clinical impression that treatment with imipramine is superior to treatment with amitriptyline in the same patients. On the other hand, there is sufficient evidence that

patients with relatively higher urinary MHPG concentration respond more favorably to amitriptyline than to imipramine (Maas, Fawcett and Dekirmenjian, 1972; Schildkraut, 1973).

It remains to be seen whether hysteroid dysphoria (Klein, 1974) is characterized by high platelet MAO activity. Also, whether premenopausal women with high platelet MAO activity (Klaiber et al., 1979) show a more favorable therapeutic response to MAOI than cyclic antidepressants. Similarly, it remains to be seen whether the high MAO group, consisting of patients with depressive anxiety states, which has been found to be responsive to treatment with monoamine oxidase inhibitors would correspond with neurotic depression, referred to as dysthymic disorders in the DSM-III (Robinson et al., 1973). Recent findings, indicating a linear relationships between 24 hour urinary free cortisol excretion and high MAO activity and high MAO activity and DST nonsuppression (Schatzberg et al., 1983), are at variance with this contention.

There is no evidence that low CSF-HVA concentrations (signifying a low dopamine turnover rate in the CNS) will identify patients with "vital depression," but there are indications that it might correspond with the diagnostic subtype of unipolar depression referred to as retarded or non-participatory (Post et al., 1978; Van Praag, 1977). Similarly, although there is no evidence that low CSF-5HIAA concentrations (signifying low serotonin turnover rate in the CNS) will identify patients with "endogenous depression," there are indications that low 5HIAA concentrations especially if associated with low CSF magnesium levels (Banki et al., 1985), may correspond with the diagnostic subtype of unipolar depression referred to as suicidal or self-torturing (Asberg, Thoren and Trackman, 1976; Lidberg et al., 1985). It remains to be seen whether these new diagnostic end-points

can be translated into differential therapeutic responsiveness to antidepressants accessible for clinical use. If they are valid, nomifensine, a dopaminergic substance should be more efficacious than other cyclic antidepressants in nonparticipatory depression. Also, fluoxetine, fluvoxamine, trazodone, and citalopram, all serotonergic substance, should be more efficacious than other cyclic antidepressants in the treatment of self-torturing depression.

Finally and more recently, there are indications that DST nonsuppression might correspond with the diagnostic subtype of unipolar depression, referred to as psychotic (delusional) or suspicious (Rothschild et al., 1983). The delusional-psychotic symptoms in these patients are attributed to the hypercortisolemia induced increase in dopaminergic activity. Hypercortisolemia was found to be associated with DST nonsuppression (Schatzberg et al., 1983) and dexamethasone, similar to other steroids, was found to produce pronounced increases of unconjugated dopamine levels in human plasma as well as specific areas (such as the nucleus accumbens) in the rat brain (Rothschild et al., 1983). This is in line with the findings that patients with suspicious depression require a combination of a cyclic antidepressant and an anti-psychotic or a dibenzoxazepine, such as amoxapine, which through its hydroxylated metabolite combines antidepressant with antipsychotic effects.

Simultaneously with the recognition of the possible underlying pathomechanism of suspicious-delusional depression, a family genetic study has provided support for the validity of this diagnostic subtype of unipolar depression. In the study of Prusoff et al. (1983), the relatives of delusional probands were 1.5 times more likely to have major depression than were the relatives of the nondelusional probands and 3.5 times more likely to have major depression than the relatives of normal controls. More important, there was some evidence for specificity of transmission; 37% of the

depressed relatives of the delusionals had delusional depression themselves compared to 19 percent of the relatives of the nondelusionals.

### Mania and Euphorias

The other cross-sectional syndrome encountered in manic-depressive illness is mania. It is considerably less frequent than depression, although there are no reliable figures on its incidence and/or prevalence.

One of the best description of the pure manic syndrome was given by Jaspers (1963). According to him the syndrome in its pure form is characterized by "a primary, unmotivated and superabundant hilarity and euphoria, by psychic changes towards a flight of ideas and an increase in possible associations." This superabundant hilarity or "feeling of delight in life" is accompanied by "an increase in instinctual activities; increased sexuality; increased desire to move about; pressure of talk and pressure of activity." The massive associations at the patient's disposal make him look witty and sparkling but "render him at the same time superficial and confused." Furthermore, "physically and mentally patient feels that he is extremely healthy and strong. He thinks his abilities are outstanding. With unflinching optimism he will contemplate all things around him, the whole world and his own future in the rosiest of lights. Everything is as bright and happy as can be. His ideas and thoughts all agree on this point most harmoniously; to any other idea he is wholly inaccessible."

Pure mania in the ideal form is extremely rare. Therefore, as early as 1899 Weygandt separated a number of components, such as hilarity

(affective), flight of ideas (cognitive) and pressure of movements (adaptive) which he considered the structural elements of mania. Integrating these structural elements in different possible constellations he identified a number of different syndromes, such as the syndrome of "unproductive mania" which consists of hilarity and pressure of movement with retardation of thought and the syndrome of "manic stupor" which consists of hilarity and retardation of movement with retardation of thought.

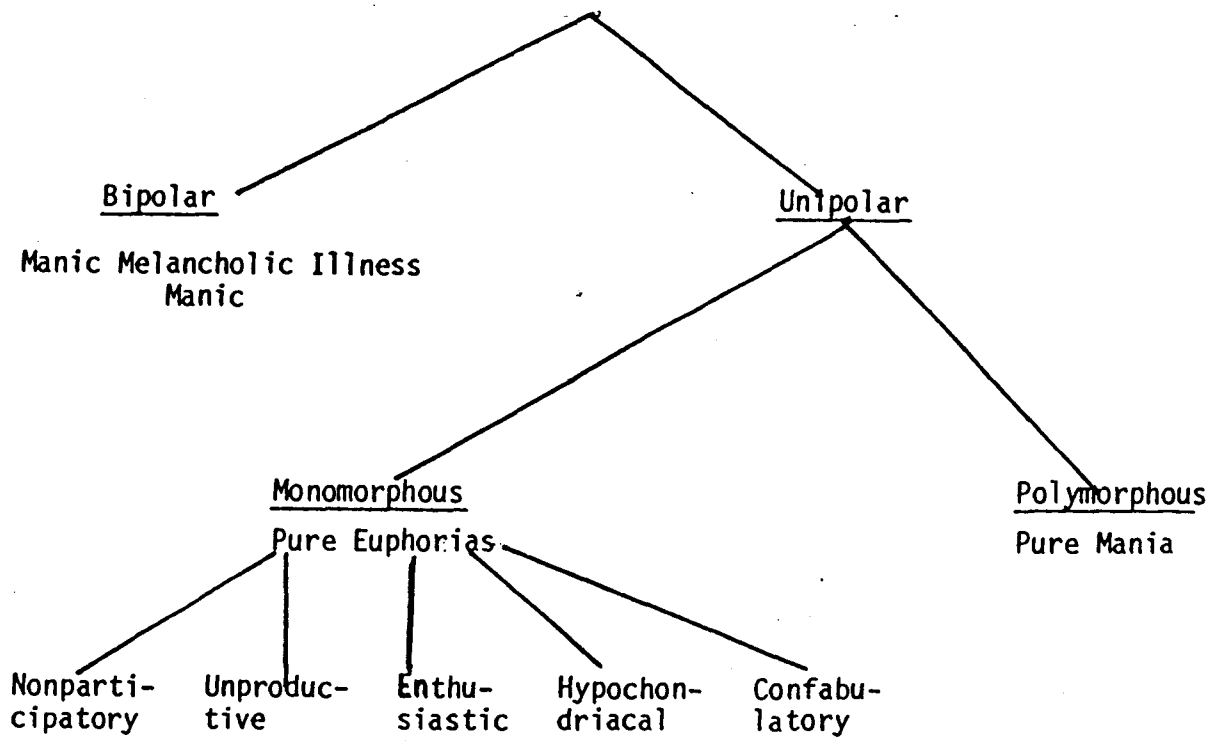
By combining structure analysis with a holistic approach, Leonhard (1979) recognized that the illness referred to as mania consists of a number of different clinical syndromes of which only one, pure mania corresponds to some extent with the original concept. However, and in contradistinction to Weygandt, he considered the triad of motiveless (incomprehensible) elated mood, psychomotor excitation and flight of ideas with pressured speech as the cardinal symptoms of pure mania. The extreme decisiveness with premature decisions and exaggerated self-esteem with feelings of competence were perceived as secondary phenomena to the cardinal-primary symptoms. By shifting the emphasis to the unipolar-bipolar dimension Leonhard separated the manic syndrome of bipolar manic melancholic illness from unipolar pure mania. Similarly, by recognizing the importance of the overall clinical picture, whether simple (monomorphous) or multifold (polymorphous), he separated unipolar pure mania from unipolar pure euphorias, i.e., nonparticipatory, unproductive, hypochondriacal, enthusiastic and confabulatory. These unipolar pure euphorias are prevailing affective diseases, while pure mania is a disease in which thought and desire are also obligatorily disturbed. Furthermore, Leonhard brought to attention cross-sectional distinguishing features between the bipolar and the unipolar forms of mania. He suggested that the bipolar forms display a more colorful appearance. They vary not only between the two poles, but in each phase offer

different clinical pictures. The same does not apply to the unipolar form which is characterized by a syndrome not associated or even transiently related to any other forms and recurs in patients with a periodic course with the same symptomatology (Figure 9).

The five distinct subtypes of pure euphoria are named for their prevailing clinical features. Affective-mood changes prevail in all subtypes. However, in two of them, i.e., in unproductive and nonparticipatory, motor-adaptive structures and in three of them, i.e., enthusiastic, hypochondriacal and confabulatory, perceptual-cognitive structures are also affected. Of the five subtypes unproductive euphoria is characterized by motiveless feeling of happiness with radiant facial expression and poor thematization; hypochondriacal euphoria by hypochondriasis with homonom bodily hallucinations and cheerful complaintiveness; enthusiastic euphoria by exaggerated self-esteem with excessive happiness and a desire to make others happy; confabulatory euphoria by confabulations with recounting happy experiences and lively talkativeness; and nonparticipatory euphoria by lack of feelings of sympathy with impoverishment of emotions and will. Pure mania usually ends within a brief period of time, but pure euphorias tend to be chronic. On the other hand, similar to pure mania, pure euphorias completely remiss between episodes, even if the duration of the episodes is prolonged.

ICD-9 distinguishes three types of mania and DSM-III two types. The three types of the ICD-9 include manic depressive psychosis manic type, manic depressive psychosis circular type but currently manic, and other non-organic psychosis excitative type. Corresponding types in the DSM-III are bipolar disorder manic and cyclothymic disorder. There is no correspondence between Leonhard's manic subtypes, adopted in the DCR and manic diagnoses in the ICD-9 and DSM-III.

Figure 9



Leonhard's (1979) classification of euphorias.

In spite of substantial evidence that antipsychotics are equally as effective as lithium salts in controlling an acute manic episode, there is an increasing consensus that lithium salts are the treatment of choice in manic patients. Nevertheless, it is unwise to undertake treatment with lithium before some behavioral control and cooperation is attained by the parenteral administration of an antipsychotic drug, because of the metabolic imbalance created by the frequently insufficient food, fluid, and in particular salt intake (Ban and Hollender, 1981; Shaw, 1979). Another important observation is that a considerable proportion of patients with a manic syndrome do not respond to either lithium salts or antipsychotic drugs given within the therapeutic dosage range. Some of these patients remain refractory even to combined treatment.

The differential therapeutic response to lithium salts and/or antipsychotics favors the contention that patients with a manic syndrome are a biologically heterogeneous population. Nevertheless, no systematic attempt has been directed to identify the patient population showing a favorable response to lithium salts and/or antipsychotics. There are indications, however, that the lithium responsive population is the one which displays a nonsystematic picture, i.e., pure mania, with prevailing manifestations in the perceptual-cognitive, relational-affective and motor-adaptive psychopathological structures simultaneously, while the lithium refractory population is the one which displays systematic pictures, i.e., pure euphorias with prevailing manifestations in two of three psychopathological structures. In view of the insufficient therapeutic response in a considerable proportion of patients several different experimental therapeutic approaches



have been tried. Included among them are treatment with the serotonin agonist, fenfluramine (Murphy, Campbell and Costa, 1978) and treatment with serotonin antagonists such as methylsergide, cinanserin and p-chloro-phenylalanine (Ananth, 1976). Included also are treatment with  $\beta$ -adrenergic blockers, such as oxprenolol and propranolol (Atsmon and Blum, 1978; Volk et al., 1972); treatment with anticonvulsants such as carbamazepine and valproic acid (Okuma, Kishimoto and Inone, 1973); and treatment with methyl-dopa, a false norepinephrine neurotransmitter (Mosher, Klerman and Greany, 1966). All these experimental approaches are of questionable clinical value. None of them has been validated in properly designed clinical experiments.

Substantial evidence indicates that reserpine, a *Rauwolfia* alkaloid, is a therapeutically effective agent in a substantial proportion of patients. To attain optimal therapeutic effects dosages as high as 20 mg per day may need to be prescribed. There are some indications that the effectiveness of reserpine is restricted to bipolar patients and to patients with pure mania. However, in the course of reserpine treatment there might be a shift to depression from mania in bipolar patients (Ban, 1969). Since the same does not apply to patients with pure mania, reserpine may be a useful agent for the separation of bipolar mania from pure unipolar mania.

Because reserpine, with therapeutic effect in mania, has central cholinomimetic properties, while imipramine, with therapeutic effect in depression, exerts central anticholinergic effects, it is hypothesized that a given affective state may represent a balance between central cholinergic and adrenergic activity, with depression being a disease of cholinergic and mania a disease of adrenergic dominance (Janowsky et al., 1972). In favor of these contentions are the findings that physostigmine, a substance that interferes with the breakdown of acetylcholine via enzyme inhibition, has

rapidly controlled mania in a clinical study, and induced depression in marijuana intoxicated patients. In favor also is the finding that physostigmine-induced depression can be reversed by the administration of atropine, a standard anticholinergic drug (Ban, 1974).

In view of the differential therapeutic response to drugs in manic patients it seems that the manic syndrome consists of a biologically heterogenous population. Because drugs with different action mechanisms have been shown to produce favorable therapeutic effects in some patients, there is no good reason to believe that studying the action mechanism of these drugs will provide clues for a better understanding of the pathomechanism of "mania."

### Schizophrenic Psychoses

#### From Dementia Praecox to Schizophrenia

The first clinical description of patients, who were to be diagnosed later as schizophrenic, was in Morel's (1853) *Etude Cliniques* in which he described "young mental patients" with a particular kind of sudden degeneration. However, it was only seven years later in 1860 (in his *Traite des Maladies Mentales*) that he termed this "sudden immobilization of all the faculties" as "démence précoce."

The concept of "démence précoce" remained dormant until Kraepelin (1893), in the fourth edition of his textbook, brought together the syndromes of hebephrenia, described by Hecker (1871), catatonia, or tension insanity described by Kahlbaum (1874), and dementia paranoïdes (which was singled out by him from the vast range of paranoïas, under the heading of "psychological degeneration processes"). Subsequently in the fifth edition (1896) he characterized this "group of clinical conditions" by its "peculiar destruction of internal connections of the personality and a marked damage of emotional life." Because patients belonging to this group of illnesses

showed considerable resemblance to what Morel (1852, 1860) described under the term "démence précoce," Kraepelin adapted the term "dementia praecox" and used it three years later in 1899, to designate a single disease progressing towards "psychic enfeeblement" that manifests in three forms--hebephrenic, catatonic and paranoid. In the seventh edition (1904) of the textbook, the paranoid type of dementia praecox included Magnan's (1893) "délire chronique." In the eighth edition (1909-1915), a distinction was made between the paranoid form of dementia praecox proper and other "paranoid deteriorations" referred to as "paraphrenias" (Pichot, 1983). In the paraphrenias, in contradistinction to dementia praecox disorders of emotion and volition, even if present, are not marked. To comply with the new definition, "délire chronique" was transferred to the paraphrenias (Pichot, 1983). For Kraepelin this separation remained valid on clinical grounds. It was Mayer (1921) who later subsumed paraphrenias under the heading of the schizophrenias.

Thus, in the eighth edition of his textbook, Kraepelin put forward a completely different subdivision of the group of disorders he subsumed under "dementia praecox." The new classification distinguished among 10 different forms, i.e., dementia simplex, silly deterioration (lappische Verblödung), depressive deterioration, depressive deterioration with delusional formations, circular forms, agitated form, periodic form, catatonia, paranoid form and schizophasia. It was also in the eighth edition that Diem's (1903) concept of "dementia simplex" was adapted and in which "silly deterioration" was substituted for "hebephrenia."

The changes proposed in the eighth edition remained isolated from the main stream of psychiatry. Instead, it is the classification from the fifth edition which distinguishes three forms--hebephrenic, catatonic and paranoid--that is usually attributed to Kraepelin. This classification and diagnostic approach was operationalized by Landmark (1982).

By replacing Kraepelin's nosological hypothesis by a pathogenetic one and the term "dementia praecox" with the term "schizophrenia," Bleuler (1911) confirmed and consolidated the concept. He defined schizophrenias as a "group of psychoses," characterized "by a specific type of thinking, feeling and relation to the external world" which "appears in no other disease in this particular fashion." Accordingly, Bleuler distinguished between the "fundamental" and the "accessory" symptoms of schizophrenia and asserted that the fundamental symptoms--loosening of associations, inappropriateness of affect, ambivalence and autism (referred to as the four-A's)--are exclusive to schizophrenia, while the accessory symptoms occur in other psychiatric conditions as well. Furthermore he assumed that the "primary symptoms" of schizophrenia--disturbance of associations, affective changes (possibly), hallucinations (possibly), stereotypes and physical disorders (such as vasomotor and pupillary changes)--were the direct expressions of the brain disease, while the secondary symptoms were derived from the primary pathological phenomena (see Appendix XVII, Table I). With consideration to "fundamental" and "accessory," as well as "primary" and "secondary" symptoms Bleuler distinguished among four types of schizophrenia, simple, paranoid, hebephrenic and catatonic.

In the DAS, based on the DCR (Petho, Ban, Kelemen et al., 1984), substantiation of a diagnosis of schizophrenia is carried out by the evaluation of 10 variables. The variables include symptoms which can be present in any psychosis (delusions, hallucinations) and variables which are specific to schizophrenia, such as catathymic evolution of symptoms, and dissociation among perceptual-cognitive, relational-affective

and motor-adaptive functions (split). The other variables are: formal thought disorder that disturbs comprehensibility (primary incoherence, tangential thinking, blocking, derailment, desultory thinking and/or onomatopoesis), affective changes (blunted, inadequate and/or inappropriate) and personality changes (abandonment of habits, change in life style, incomprehensibility of behavior and/or autistic behavior). Additional prerequisites are clear consciousness, the absence of holothymic evaluations, and the consistent presence of psychopathology for at least two weeks.

Diagnoses corresponding to schizophrenic psychoses of the DCR are schizophrenic psychoses in ICD-9 and schizophrenic disorders and schizophreniform disorders in DSM-III.

In ICD-9 the diagnosis of schizophrenic psychoses is not restricted to disorders running a protracted, deteriorating or chronic course. It is not made however, unless there is, or has been evidence during the same illness for a characteristic disturbance of thought, perception, mood, conduct or personality. In contradistinction to the DAS criteria, however, in ICD-9 considerable emphasis is placed on disorders of the ego, such as the sense of being controlled by alien forces and that one's thoughts, feelings and acts are known to or shared by others. There is also greater emphasis placed on explanatory delusions, e.g., that natural or supernatural forces are at work and responsible for patient's clinical state.

DSM-III criteria of schizophrenic disorders correspond also with DAS criteria. In certain respects, however, the diagnosis is restricted in that the illness needs to occur before age 45 and continuous signs of the disorder must be present for at least six months. When the duration of illness is longer than two weeks but shorter than six months, the diagnosis in DSM-III is schizophreniform disorder.

In spite of its high, almost 1 percent prevalence rate in the general population--and the recognition that the lifetime risk for children of schizophrenics is approximately 15 times higher than that of the 0.86 percent in the general population--there are no generally accepted criteria for the diagnosis of schizophrenia (Tsuang and Vandermeij, 1980). The most frequently employed clinical and/or research criteria were summarized by Berner et al. (1983) in Diagnostic Criteria for Schizophrenic and Affective Psychoses. They included Schneider's (1957) First Rank Symptoms, the St. Louis Criteria (Feighner et al., 1972), the New Haven Schizophrenia Index (Astrachan et al., 1972), the Flexible System for the Diagnosis of Schizophrenia (Carpenter, Strauss and Bartko, 1973), the Present State Examination Criteria (Spitzer, Endicott and Robins, 1978a and b), Taylor and Abrams Criteria (Taylor and Abrams, 1978; Taylor, Redfield and Abrams, 1981), the French Empirical Criteria (Pull, Pull and Pichot, 1981), and the Vienna Research Criteria (Berner and Katschnig, 1983) (see Appendix VII, Tables II to V). In view of the difficulties encountered in identifying generally acceptable criteria for the diagnosis of schizophrenia and contributions of recent investigations, especially by Pope and Lipinski (1978), Koehler (1979), Pope et al. (1980) and Berner (1982), it has been suggested that schizophrenic symptoms have "no differential diagnostic weight for distinguishing between schizophrenia and cyclothymia" (referring to affective psychoses) (Berner et al., 1983). If this assumption could be substantiated by further evidence, Jaspers' (1913, 1946) hierarchical diagnostic principle would be reversed. Or in other words, diagnosis would not be determined by the pathology at the "deepest level" and therefore in case of the presence of both affective and schizophrenic symptoms the presence of schizophrenic symptoms would not outweigh the presence of affective ones.

From Schizophrenia to the Schizophrenias

The first information on the natural course of schizophrenia dates back to Kraepelin (1899, 1919) who described dementia praecox as a disease which as a rule is progressive particularly in regard to emotional deterioration. In a few cases the process may come to a standstill. Some of the symptoms may even disappear. Far more commonly, however, the outcome is profound deterioration. Accordingly, Kraepelin's figures for a group of inpatients at the Heidelberg Hospital showed that of the 12.6 percent who had a complete remission first, 8.5 percent relapsed three to six years later and only 4.1 percent remained well. The figure of 12.6 percent could be raised to 13.3 percent by adding to it all the cases with only a mild defect and to 17 percent by extending it to all the cases that would live a more or less socially adjusted life independent of the degree of defect (Hoenig, 1967). On the other hand, 70 percent of Kraepelin's dementia praecox patients deeply deteriorated.

The three crucial figures of Kraepelin on the natural course of schizophrenia are full recovery, 4.1 percent; social remission, 17 percent; and deterioration, 70 percent. It is interesting to note the little variation in these figures during the prepsychopharmacological era. Thus, Evensen (1904) in his first study reported 15 percent social remissions, a figure somewhat lower than Kraepelin's. His sample consisted of male schizophrenics younger than twenty-six years first admitted to the Gastaud Hospital between 1887 and 1896. The evaluation was based on a five- to fifteen-year follow-up. After a similar follow-up period on a sample of 815 schizophrenic patients discharged from the Gastaud Hospital between 1915 and 1929, Evensen (1936) found that 23 percent of the patients were self-supportive or in social remission. This was a modest improvement to

his own and also to Kraepelin's earlier figures. Similar to Kraepelin's are Langfeldt's (1937) figures based on a seven- to thirteen-year follow-up study of 100 schizophrenic patients. In his sample, 66 percent were uncured or worse (just 4 percent less than in Kraepelin's) and 17 percent were completely recovered. When this 17 percent was broken down further, however, 14 percent consisted of patients with an atypical--so-called schizophreniform--clinical picture. Taking off the 14 percent of patients with schizophreniform psychoses leaves 3 percent full remission, which is only slightly lower than Kraepelin's figure (Hoenig, 1967).

The observation that schizophrenic disorders do not always follow an unfavorable course led Langfeldt (1937, 1939, 1956, 1960, 1969) to the identification of criteria which could distinguish between a bona fide "process schizophrenia" with a bad prognosis and "schizophreniform psychoses" with a good prognosis. This separation has been substantiated by the work of Stephens, Shaffer and Carpenter (1982) and Vaillant (1964).

Recognition that schizophrenic disorders do not always follow a deteriorating course led to the distinction between schizophrenic and schizophreniform psychoses by Langfeldt (1939, 1956). Recognition that schizophrenic disorders do not always follow a similar course led to the differentiation of continuous schizophrenia, periodical (recurrent) schizophrenia and shift-like progressive schizophrenia by Snezhnewski (Nadzharov, 1967; Snezhnewski and Vartanian, 1971).

Langfeldt's and Snezhnewski's contributions are based on a three-dimensional model of schizophrenia with careful consideration to the first three developmental stages. Most recently, Crow (1980) on pragmatic grounds but with consideration to findings in clinical psychopharmacology and brain imaging, proposed that distinction should be made within the schizophrenias



between a Type I syndrome, characterized by positive symptoms, i.e., abnormal psychological features such as delusions, hallucinations and thought disorder, and a Type II syndrome, characterized by negative symptoms, i.e., diminished or absent normal functions, such as flattening of affect, poverty of speech and loss of volition.

It should be noted that Kraepelin (1919), who developed the concept of schizophrenia by pooling together a number of different clinical syndromes on the basis of their time course, was not unaware of the heterogeneity within the schizophrenic population. He distinguished among nine different end-states of the disease, ranging from severe deterioration with flattened affect, through prevailing confusion of speech, complex hallucinatory experiences or systematized delusions to mild, nonspecific impairment, or full remission (see Appendix VIII, Table I).

The most important contribution to our understanding of these heterogeneous end-states of "schizophrenia" are those of Kleist (1923, 1960) and Leonhard (1957, 1979). In the course of a four dimensional analyses of psychopathological symptoms, course of illness and outcome pictures in a large number of schizophrenic patients, both Kleist and Leonhard have concluded that schizophrenia consists of two distinct populations (groups of disorders) referred to as typical (Kleist) or systematic (Leonhard) and atypical or nonsystematic, and that, each population consists of a number of different illnesses, which have different end-states (subtypes). The two populations, but not the different end-states, are easily distinguishable on the basis of the course of the schizophrenic process. In the nonsystematic schizophrenias, the intermittent periodicity resembles manic depressive illness, and in the systematic schizophrenias, the "down-hill" course resembles organic dementias. Since Kleist (1960) believed that each subtype is the result of a specific impairment in a different neurological system, he asserted

that the schizophrenias are diseases of the brain which may affect several different neurological systems (atypical), or are confined (localized) to one neurological system (typical) (Table XII). Leonhard, on the other hand, emphasized possible genetic differences among the subtypes, and the functional rather than the morphological nature of the various disorders (Table XIII).

There was little, if any, interest in this complex classification of schizophrenias prior to, and immediately following, the introduction of neuroleptics. Prior to this was probably due to the lack of effective treatment, while after the introduction of neuroleptics it was probably due to the belief that neuroleptics are the treatment of choice for all schizophrenics. With the recognition that not every schizophrenic benefits equally well from neuroleptics and that long-term neuroleptic administration may induce serious adverse effects such as tardive dyskinesia, skin pigmentation and ocular changes, there has been a resurgence of interest in Leonhard's classification of chronic schizophrenias (Ban, 1982). Much impetus for the revival was attributed to Fish (1958a and b, 1962, 1964a and b) who classified a chronic schizophrenic population on the basis of Leonhard's criteria. He found the subtypes to be of clinical relevance and useful in the identification of patients therapeutically responsive to neuroleptics. Further interest in Leonhard's system was generated by Astrup (1959, 1962, 1979). He employed a special test battery, consisting of word associations, motor-conditional reflex, defensive finger withdrawal and several other tests, and was able to identify differences in performance and in level of deterioration among different subtypes of schizophrenia. Furthermore, Ey (1958, 1959) in France and Sarro Burbano (1957) in Spain found no difficulties in employing Leonhard's classification in their patients.

Table XII

Diagnostic Categories	Typical	Atypical
Hebephrenias	Silly hebephrenia Depressive hebephrenia Apathetic hebephrenia Autistic hebephrenia	
Catatonias	Negativistic catatonia Proskinetetic catatonia Akinetic catatonia Stereotyped catatonia Parakinetic catatonia Speech-inactive catatonia Speech-prompt catatonia	Iterative catatonia
Paranoias	Progressive somatopsychosis Progressive autopsychosis Progressive confabulosis Phantasiophrenia Progressive influence psychosis Progressive inspiration psychosis	
Paraphrenias		Circumscribed delusional psychosis Progressive signification psychosis Progressive self-reference psychosis
Confusiophrenias	Incoherent schizophrenia  Paralogical schizophrenia Schizophasia	Shift-like confused schizophrenia

Kleist's (1923, 1957) classification of schizophrenias; 26 subtypes, belonging to five categories and two major (typical and atypical) groups of disorders. Adapted from Silveira's (1961) presentation at the Third World Congress of Psychiatry.

Table XIII

Nonsystematic	Schizophrenias		
	Paraphrenias	Systematic Hebephrenias	Catatonia
Affect-laden paraphrenia	Phonemic	Autistic	Parakinetic
Cataphasia	Hypochondriacal	Eccentric	Proskinetik
Periodic catatonia	Confabulatory	Shallow	Speech-prompt
	Expansive	Silly	Speech-inactive
	Fantastic		Manneristic
	Incoherent		Negativistic

Leonhard's (1957, 1979) classification of schizophrenias.

However important Leonhard's classification is, it is difficult to apply because of the practical problems involved in using a complicated system. In an effort to simplify the task, Fish (1964b) devised a guide for the assignment of patients to specific subtypes. Recently another guide has been developed by Ban (1982) (see Appendix IX, Tables I and II).

#### Nonsystematic vs Systematic Schizophrenias

Within Leonhard's (1979) classification of endogenous psychoses non-systematic and systematic schizophrenias represent two distinctly different groups of disorders. Nonsystematic schizophrenias are characterized by rapid onset, multiform clinical manifestations, intermittent episodic course and relatively favorable outcome with usually mild defect and relatively good working ability. In contrast, systematic schizophrenias are characterized by insidious onset, simple clinical manifestations, processual-progressive course and usually unfavorable outcome with moderate to marked defect and considerably impaired working ability. Another distinguishing feature of the two populations is "double-entry bookkeeping," which if present designates a systematic population. In patients of the non-systematic population the whole personality is transformed by the psychosis while affective responses remain relatively well preserved (Ban, Guy and Wilson, 1984a).

Furthermore, the two schizophrenic populations differ also in respect to cross-sectional psychopathology, and not only in terms of onset, course and outcome. Prevalent among the varied (diffuse) psychopathological manifestations in patients with nonsystematic schizophrenia are dysthymic and/or hyperthymic mood changes, hallucinations, emotionally loaded delusions and/or multiform catatonic activity. Outcome is characterized by residual symptoms such as blunted affect, circumstantial or vague speech,

impaired role functioning, peculiar behavior, social withdrawal and/or unusual social experiences. In contrast, prevalent among the specific (circumscribed) psychopathological manifestations in patients with systematic schizophrenias are hallucinations with or without hallucinatory excitements, delusions without emotional loading and/or simple catatonic activity, such as ambitendency, automatic obedience, cooperation in movements, mannerisms, mutism, negativism, parakinesis, posturing, proskinesis, rigidity, stereotypy, and/or waxy flexibility. Outcome is characterized by clinical and/or personality defect.

#### Systematic Schizophrenias

Within Leonhard's conceptual framework, acute psychotic exacerbations may be seen as dissociations among three psychopathological structures-- perceptual-cognitive, emotional-affective, and motor-adaptive--with each exacerbation resulting in a gradual "regression" and transition from a higher to a lower level of functioning in one of the structures.

Thus, primarily on the basis of the course of the illness, Leonhard distinguished between a systematic and a nonsystematic schizophrenic population. By employing a structure analysis of the clinical features, he divided the systematic population into three categories. They are catatonias (disorders with prevailing motor-adaptive psychopathologies), paraphrenias (disorders with prevailing perceptual-cognitive psychopathologies) and hebephrenias (disorders with prevailing relational-affective psychopathologies).

Finally, by careful phenomenological exploration of the subjective experiences of his patients and meticulous psychopathological assessment of their objective manifestations, Leonhard identified 16 subtypes within the systematic population. There are six catatonic (parakinetic, proskinetik, speech-prompt, speech-inactive, manneristic and negativistic), six paraphrenic

(phonemic, hypochondriacal, confabulatory, expansive, fantastic and incoherent) and four hebephrenic (autistic, eccentric, shallow and silly) subtypes (Table XIV).

#### Systematic Catatonias

The six subtypes of systematic catatonia represent different stages in the level of deterioration in motor-adaptive structures. It includes patients with a relative excess and a relative deficiency in activities. Relative excess of activity may appear as unnatural-awkward voluntary and jerky involuntary expressive movements with facial grimacing in parakinetic catatonia; obedient answering but talking beside the point (Vorbeireden) with an empty facial expression in speech prompt catatonia; and autonomic obedience with a monotonous mumbling speech in proskinetetic catatonia. In contrast, the relative deficiency of activity appears as impoverished speech, such as mutism or delayed and slow replies in speech-inactive catatonia; impoverished involuntary motor activity, such as waxy flexibility or stiff movements and posturing in manneristic catatonia; and an active striving against all attempts at making contact in negativistic catatonia. Thus, among the systematic catatonias negativistic catatonia seems to be the opposite of proskinetetic catatonia, manneristic catatonia the opposite of parakinetic catatonia, and speech-inactive catatonia the opposite of speech-prompt catatonia.

In the differentiation among the subtypes of the catatonic category, most revealing are psychopathological symptoms related to speech. Thus, speech-prompt catatonics respond promptly and without delay. However, they do not show spontaneous loquaciousness and their voluble speech in responding to questions lacks meaningful content. While negativistic catatonics may give partial answers, manneristic catatonics frequently do not talk at all.

Table XIV

Catatonia	Paraphrenias	Hebephrenias
<u>Parakinetic</u>	<u>Phonemic</u>	<u>Autistic</u>
Continuous parakinesis	Phonemic-delusional hallucinations	Extreme autism
Increase in expressive and reactive movements	Complains about content of hallucinations	Off-putting verbal responses
Jerky-choppy pattern of speech	Even mood with blunting of emotions	A mood of displeasure and discontent
<u>Speech Prompt</u>	<u>Hypocondriacal</u>	<u>Eccentric</u>
Replies promptly	Bodily-heteronom-hallucinations	Affected behavior
Adversion	Complains about hearing voices	Querulous complaintativeness
Hardly speaks spontaneously	Unpleasant--dissatisfied mood	Dysthymia or depressed mood
<u>Proskinetik</u>	<u>Expansive</u>	<u>Shallow</u>
Persistence of movements	Systematized delusions of grandeur	Extreme emotional impoverishment
Mumbling, murmuring and verbigeration	Demonstrative mannerisms correspond with delusions	Episodic hallucinatory excitement
<u>Speech inactive</u>	Euphoria	Carefree euphoria
Delayed verbal replies	<u>Confabulatory</u>	<u>Silly</u>
Perplexed	Continuous confabulations	Immature
Continuous whispering to hallucinatory experiences	Falsification of memory	Alogical thinking
<u>Manneristic</u>	Elated mood	Contented, mildly cheerful mood
Stiff postures with maintenance of position	<u>Fantastic</u>	
Decrease of automatisms	Visual, often scenic hallucinations	
Talks little or not at all	Fantastic experiences	
<u>Negativistic</u>	Contented mood	
Negativism	<u>Incoherent</u>	
Negativistic excitement	Hallucinatory rich autism	
Partial answers	Cannot be distracted from hallucinations	
	Primary incoherence	

Three prevailing characteristics of each of the 16 subtypes of systematic schizophrenia. Adapted from Ban, Guy and Wilson (1984a).



There is a jerky pattern of speech with short ungrammatical sentences in parakinetic catatonia; murmuring, and verbigeration in proskinetic catatonia; and a continuous whispering to hallucinatory experiences in speech-inactive catatonia. Although opposition (Gegenhalten) is seen in manneristic catatonia, cooperation (Mitmachen) and grasping (Mitgehen) are exclusive for proskinetic catatonia. Abnormal postures, such as generalized rigidity, waxy flexibility (Haltungsverharren), and the so-called "psychological pillow," a manifestation of opposition, are pathognomonic for manneristic catatonia; waxy flexibility may also occur in speech prompt catatonia. Abnormal spontaneous movements are widespread in this category; grimacing is characteristic of parakinetic catatonia; handling and intertwining of proskinetic catatonia; stereotypes of proskinetic and manneristic catatonia and impulsive action of manneristic and negativistic catatonia. While speech prompt and proskinetic catatonics turn toward the examiner in an exaggerated manner (adversion), speech-inactive catatonics turn away (aversion), although true negativism is present only in negativistic catatonia.

Differential characteristics among the systematic catatonias are almost exclusively based on the differential motor and speech patterns of the subtypes. Pathognomonic of the negativistic subtype is the association of blunted affect with negativistic excitement, and of the manneristic subtype the association of hard mannerisms with well retained affectivity and lack of hallucinatory and delusional experiences.

#### Systematic Paraphrenias

The six subtypes of paraphrenia represent different levels of deterioration in perceptual-cognitive structures. The subtypes are on a continuum of severity from phonemic and hypochondriacal through expansive, confabulatory and fantastic to incoherent. With the increase in formal disorder of

thinking, there is a corresponding decrease in working ability. Further, there is a shift in affectivity from blunting (phonemic), through depression (hypochondriacal) to meaningless euphoria (expansive, confabulatory and fantastic). Accordingly, in phonemic paraphrenia, verbal hallucinations commenting on, or talking to the patient are associated with a somewhat "wooly" thinking, while in incoherent paraphrenia, representing the opposite end of the continuum, massive auditory hallucinations are accompanied by confusion of thinking, incoherence of speech and disordered behavior. In hypochondriacal paraphrenia, the subtype closest to phonemic paraphrenia, verbal hallucinations, fragmented into disconnected phrases, are associated with bizarre bodily hallucinations and a corresponding irritable, morose, and dissatisfied mood, while in fantastic paraphrenia, the subtype closest to incoherent paraphrenia, the severe derailment of thinking falls only somewhat short of conceptual disorganization. The patient's mental life is almost totally occupied by fantastic delusions and mixed (auditory, visual, bodily, and not infrequently scenic) hallucinations. Compared to the fantastic paraphrenic who lives in a world without boundaries of life and death (also without time and space), the expansive paraphrenic lives in the physical world of man. Their haughty pose and corresponding grandiose delusions distinguish these patients from the confabulatory paraphrenic, whose vivid and detailed descriptions of alleged experiences appear as fairy tales, especially when experienced as if they happened in dreams.

Fish (1964b) has brought to attention that even in the paraphrenias auditory hallucinations and/or delusions are not obligatory psychopathological symptoms. Expansive and confabulatory paraphrenics do not hear hallucinatory voices; incoherent paraphrenics do not develop delusions. If persecutory delusions develop in phonemic and hypochondriacal paraphrenic patients they are never

primary, but secondary to their hallucinatory experiences. The nature and content of hallucinations differ in the various subtypes of the paraphrenic category. Hypochondriacal paraphrenics are seen to speak to voices at times; incoherent paraphrenics speak to voices all the time. Furthermore, fantastic paraphrenics often reveal, that they can hear and understand what birds and inanimate objects say. Visual, scenic, and mass hallucinations, as well as delusional misidentifications, are characteristic psychopathological symptoms of patients with fantastic paraphrenia. Sexual bodily hallucinations are characteristic psychopathological symptoms of patients with hypochondriacal paraphrenia. Grandiose delusions are not encountered exclusively in expansive paraphrenia; they may also be present, in confabulatory and fantastic paraphrenia. On the other hand fantastic delusions are only present in fantastic and possibly confabulatory paraphrenia. Patients belonging to the different paraphrenic subtypes differ in their affect and mood. In phonemic paraphrenia there is slight blunting of emotional responses; in hypochondriacal paraphrenia blunted emotional responses are associated with a somewhat depressed mood; and in expansive, confabulatory and fantastic paraphrenia with euphoria. Probably most important, however, is that in phonemic and hypochondriacal paraphrenics the formal thought disorder is usually less severe than in expansive paraphrenics; and while in confabulatory and fantastic paraphrenics there is an interference with thinking in incoherent paraphrenics goal directed processing of ideas is not present at all.

Differential characteristics among the systematic paraphrenias are almost exclusively based on the nature of hallucinatory and/or delusional experiences. Supplementing these are differences in the quality (formal disorder) of patient's thinking and affective (mood) state.

### Systematic Hebephrenias

While the six subtypes of paraphrenia represent different levels of deterioration of perceptual-cognitive structures, the four subtypes of hebephrenia represent different levels of deterioration in emotional-affective structures. On the other hand, similar to the paraphrenias, the four hebephrenic subtypes are on a continuum of severity, as reflected in working ability, from autistic and eccentric through shallow to silly. Parallel with the continuum, there is a shift in mood from depressed and irritable (autistic and eccentric) to cheerful and contented (shallow and silly).

Among the four subtypes, autistic hebephrenia is characterized by active avoidance of all contact, off-putting verbal responses and stiff face; eccentric hebephrenia by soft mannerisms, senseless stealing, and hypochondriacal and querulous complainativeness; shallow hebephrenia by lack of initiative and apathetic indifference and silly hebephrenia by inane giggling, spiteful tricks and restless behavior. In spite of the extreme flatness of affect and lack of initiative, there are episodic hallucinatory excitements in patients with shallow hebephrenia. In the same way as senseless hoarding is indicative of eccentric hebephrenia, hallucinatory excitement is indicative of shallow hebephrenia.

Differentiation among the systematic hebephrenias is almost exclusively based on the primary characteristics of the illness, such as immature behavior (silly), emotional impoverishment (shallow), soft mannerisms (eccentric) and empty autism (autistic). At least two of these subtypes display episodic irritability and/or aggression (silly and autistic) and at least two subtypes, episodic hallucinatory behavior (shallow and autistic).

### Nonsystematic Schizophrenias

In his monograph on the Classification of Endogenous Psychoses, Leonhard (1957, 1979) asserts that the nonsystematic schizophrenias are one of the five

major groups of disorders within the endogenous psychoses and that "systematic and nonsystematic schizophrenias have essentially nothing to do with each other." In contrast to the systematic schizophrenias which show no polarity, systematic schizophrenias are bipolar disorders which share common features with the cycloid psychoses, a group of bipolar disorders perceived by Leonhard as being on the continuum between the phasic-affective type of psychoses and the schizophrenic type of psychoses.

Nonsystematic schizophrenias consist of three distinct disorders: cataphasia, affect-laden paraphrenia and periodic catatonia. In cataphasia, also referred to as schizophasia, there is a striking dissociation between the disordered or confused speech and thought, and the well-preserved behavior with an appropriate affective response (Kleist and Schwab, 1950). The clinical picture is analogous to schizophasia described independently by Kraepelin (1913) and Kleist (1930, 1939). Kraepelin pointed out a severe confusion of linguistic expressions despite well ordered behavior, while Kleist emphasized the presence of neologisms and word-confusion, which rarely appear in Kraepelin's description. Thus, in patients with cataphasia behavior is characteristically more coherent than speech and responses to questions more understandable than spontaneous speech production. While some patients with cataphasia may display agitation, pressure of speech, confusion, asyntaxis, paralogia, paragrammatism and/or neologisms, other patients may be taciturn and mute and exhibit a dull and empty facial expression. Depending on the prevailing manifestations cataphasia is subtyped into an excited and an inhibited form.

In affect-laden paraphrenia, which corresponds with Kraepelin's (1919) paraphrenia systematica and Kleist's (1947, 1957) progressive reference psychosis, pathology of affectivity plays a central role. Delusions or disorder of thought content are secondary to the pathologically-changed affect.

Verbalization of the delusional material may lead to irritability, enthusiasm, or, in some cases, to threatening verbal, attitudinal or physical behavior. Thus, in contradistinction to cataphasia, in affect-laden paraphrenia there are primary affective changes (anxiety, irritability, ecstasy) and secondary delusions (reference, grandeur, fantastic, mixed) with a paralogical (or logical) systematized (or non-systematized) delusional structure. Pathognomonic of affect-laden paraphrenia is the fluctuating affective state with emotionally charged delusions, i.e., strong delusional dynamics. Prevailing manifestations are anxiety, irritability, delusions of reference and fantastic delusions; or ecstatic mood and grandiose delusions; or a fluctuating affective state with mixed delusions. Depending on the prevailing clinical features affect-laden paraphrenia is subtyped into an anxious, an ecstatic and a bipolar form.

In periodic catatonia, the third disorder of nonsystematic schizophrenias, motor behavior is primarily disturbed. There is an unusual mixture of excitatory and inhibitory symptoms, associated with episodic hyperkinesia or hypokinesia. In extreme cases there is akinetic stupor. Characteristically there is a decrease or increase of expressive and/or reactive movements with a loss of harmony of natural movements. Other manifestations include parakinesia, motor and postural stereotypy, impulsive acts, negativism, hyperkinesia, hypokinesia, akinesia and/or mixed kinesia. Depending on the prevailing clinical features periodic catatonia is subtyped into an excited, an inhibited and a mixed form.

There is a strong similarity between the three disorders of nonsystematic schizophrenia and cycloid psychoses; cataphasia resembling confusion psychosis, affect-laden paraphrenia resembling anxiety-elation psychosis and periodic catatonia resembling motility psychosis. The signal

difference between the two groups of disorders is related to outcome with full recovery in cycloid psychoses and residual symptoms in the nonsystematic schizophrenias (Ban, Guy and Wilson, 1984a).

In ICD-9 all schizophrenic disorders are grouped under schizophrenic psychoses without distinguishing between the groups of nonsystematic and systematic schizophrenias. Within this all embracing group of disorders there are ten different types of schizophrenic illnesses described. Of these ten types, there is some correspondence between the simple and hebephrenic types of ICD-9 and the hebephrenic category of Leonhard; the catatonic type of ICD-9 and the catatonic category including periodic catatonia of Leonhard; the paranoid type of ICD-9 and the paraphrenic category of Leonhard; schizoaffective type of ICD-9 and affect-laden paraphrenia of Leonhard. While Leonhard's classification has no corresponding diagnoses for latent schizophrenia, residual schizophrenia, other schizophrenia and unspecified schizophrenia, ICD-9 has no corresponding diagnoses for cataphasia and for any one of the 16 subtypes of systematic schizophrenia (which are adapted in the DCR).

Similar to ICD-9, in DSM-III also, all schizophrenic psychoses are grouped under schizophrenic disorders without distinguishing between the groups of nonsystematic and systematic schizophrenias. In contradistinction to ICD-9, however, within this all embracing group of disorders there are only five different types of schizophrenic illnesses. Of these five types, there is some correspondence between the disorganized type of DSM-III and hebephrenic category of Leonhard; catatonic type of DSM-III and catatonic category, including periodic catatonia of Leonhard; and paranoid type of DSM-III and paraphrenic category including affect-laden paraphrenia of Leonhard. While Leonhard's classification has no corresponding diagnoses for the

undifferentiated and residual type, DSM-III has no corresponding diagnoses for cataphasia and for anyone of the 16 subtypes of systematic schizophrenia.

### Treatment of Schizophrenic Disorders

#### Pharmacotherapy vs Other Treatments

Progress in clinical psychopharmacology has focused attention on the heterogeneity of the schizophrenic population. It has also revealed that schizophrenia consists of at least two major groups of disorders. Research in clinical therapeutics, however, has not gone beyond the unitary concept of schizophrenia. One possible reason for this is that for the therapeutic management of the majority of schizophrenic patients, pharmacotherapy offers higher reliability, easier accessibility, greater simplicity and fewer hazards than any other treatments known today. Pharmacotherapy is certainly the treatment of choice for acute and chronic schizophrenics in the community where uncontrolled pathological behavior may be unacceptable. It is also usually the most effective means of shortening the patient's stay in the hospital and of preventing future readmissions (Lehmann, 1975).

By now the superiority of pharmacotherapy over physical treatments--insulin-induced hypoglycemia and electroconvulsive therapy (ECT)--has been shown convincingly (Heinrich, Kretschmar and Kretschmar, 1972). However, ECT may still be tried if schizophrenic patients fail to improve after three months or more on pharmacotherapy. Similarly, there is substantial evidence to believe that pharmacotherapy is superior to individual psychotherapy, group psychotherapy, and milieu therapy (May, 1968). Nevertheless, a combination of these therapies with pharmacological treatment may be more effective than pharmacotherapy alone, especially during the rehabilitation and maintenance phases of treatment (Hogarty et al., 1973). The same applies



to behavior therapy which has been found useful primarily in the treatment of chronic institutionalized schizophrenics (Lieberman, 1971).

The pharmacological agents most specifically effective in schizophrenia are the neuroleptic drugs, also referred to as antipsychotics or major tranquilizers.

#### Pharmacotherapy with Antipsychotic-Neuroleptics

With the rapidly growing number of neuroleptics it has become increasingly important that every new neuroleptic should have a better therapeutic index and/or a different therapeutic profile than chlorpromazine, or any of the other clinically used neuroleptic drugs. These therapeutic expectations have not been fulfilled. To date all attempts to establish differential clinical effects among neuroleptics have fallen short. In spite of this, clinical observation indicates that a particular patient, unaffected by a specific neuroleptic, may respond to another neuroleptic.

There are no predictors of therapeutic responsiveness to neuroleptics; and there is no evidence for a relationship between biochemical changes and therapeutic effects. There are indications however, that there is a relationship between the changes in the principal urinary metabolites of indoleamines and catecholamines and the side effects induced by neuroleptics. Decrease in VMA is frequently associated with hypotensive manifestations, increase in 5HIAA with gastroenteral side effects, and increase in HVA with akinetic or akinetic-hypertonic symptoms (Ban, 1973).

It is disappointing that there are no reliable clinical predictors of therapeutic responsiveness to neuroleptics. In one study, thioridazine was found to be therapeutically more consistently effective in patients with a poor premorbid adjustment (Judd et al., 1970), while in another chlorpromazine

was found to be more consistently effective in patients with a good premorbid adjustment (Klein and Rosen, 1973). Similarly, in one study (Goldberg, Klerman and Cole, 1965) the "withdrawal dimension" could be affected by neuroleptic drugs only, while in another, the "negative (withdrawal) symptoms" such as blunted affect, poverty of speech, and social withdrawal were found to respond to social therapies (Wing, Leff and Hirsch, 1973). Since the "florid symptoms" of schizophrenia correspond with Schneider's (1957) "first rank symptoms" (thought insertion, thought broadcasting, thought withdrawal, delusional perceptions, delusions of control, auditory hallucinations), the possibility has been raised that it is the "first rank symptoms" which can be controlled by neuroleptic drugs only. Nevertheless, Abrams and Taylor (1973) found no relationship between the presence of "first rank symptoms" and therapeutic responsiveness to neuroleptics.

In spite of the facts, that the percentage of "symptom free" schizophrenic patients has not been increased by the introduction of neuroleptic drugs and that the therapeutic changes have been confined to a shift from the prevalence of "psychotic" to the prevalence of "residual symptoms" (Kelly and Sargent, 1965), there is an impressive consensus that the treatment of choice for schizophrenia is pharmacotherapy with neuroleptics (Cawley, 1967). The lack of increase in "symptom free" schizophrenic patients corresponds with the findings that the rate of remission has remained essentially unchanged during the past 55 years (Kraepelin, 1899; Simon et al., 1965), although the discharge rate from hospitals has considerably increased. The increased discharge rate from hospitals, regardless of the presence of psychopathological symptoms, may explain the higher social remission rates found by Gross, Huber and Schuttler (1971) and Hoenig and Hamilton (1966)--51 and 55 percent respectively--in their

(eight- and four-year follow-up) studies carried out after the introduction of new drugs. Nevertheless, the fact remains that social recovery in Achte's (1961) four-year follow-up study on patients admitted between 1953-1955, i.e., prior to the introduction of neuroleptics, is higher (65%) than in these two reports.

#### Neuroleptics and Etiological Speculations

One of the most important contributions to schizophrenia research which has resulted from psychopharmacologic progress is the verification that schizophrenia consists of a biologically heterogenous population. In view of this it is paradoxical that the most extensively explored biochemical hypothesis, the DA excess hypothesis, deals with "schizophrenia" instead of one or another subtype of the schizophrenias.

#### Dopamine Excess or Deficiency

The finding that "clinical potencies" (mg/kg therapeutic dose requirements of neuroleptics) correlate well with binding affinities at DA<sub>2</sub> receptors prompted several laboratories to search for alterations in the levels of DA and/or DA receptors in post-mortem brains of schizophrenic patients. As a result, a significantly increased number of DA<sub>2</sub> receptors (Owen et al., 1978), as well as a 50 percent increase in DA content was found in schizophrenic brains (Bird et al., 1977). There are indications, however, that the increase in the number of DA<sub>2</sub> receptors may be related to prior treatment with neuroleptic drugs.

In favor of the hypothesis that DA excess is related to the psychopathology in schizophrenic patients are the findings that schizophrenic psychopathology may be precipitated and/or aggravated by the administration of DA releasers, such as methylphenidate or ethanol. In favor also is that the therapeutic effects of neuroleptics may be potentiated by adding

substances which interfere with the formation and/or action of DA to the treatment regime such as alphas-methyl-para-tyrosine (a specific tyrosine hydroxylase inhibitor) or alphas-methyl-dopa (a non-specific dopa decarboxylase inhibitor) (Snyder, 1976). On the other hand and in variance with the DA excess hypothesis are the findings that the time of onset of amphetamine psychosis (which serves as the model psychosis for schizophrenia) coincides more closely with DA depletion than with increased DA availability. In variance also are the findings that in some schizophrenic patients, amphetamine administration alleviates psychotic symptomatology and in others it enhances the therapeutic effect of neuroleptics (Fukuda and Mitsuda, 1979; Van Kammen et al., 1982).

#### Prostaglandin: Deficiency or Excess

In keeping with the DA excess hypothesis, however, is the prostaglandin (PG) deficiency hypothesis of schizophrenia. The link between the two is prolactin, a potent stimulator of PG synthesis. Since the release of prolactin is controlled by DA, the neuroleptic-induced DA receptor blockade produces prolactin excess and an increase in PG synthesis.

The hypothesis that schizophrenia is a PG deficiency disease is based on observations that schizophrenic patients are relatively resistant to pain and inflammation and are free of rheumatoid arthritis, a disorder in which PG plays an important role. In favor of the hypothesis are findings that PG antagonists, e.g., chloroquine, quinine, quinacrine, may, in high doses, induce schizophrenic-like states, and that therapeutically effective neuroleptics stimulate the production of prolactin while drugs which precipitate or aggravate schizophrenia, e.g., levodopa, cortisol, suppress secretion and/or block prolactin effects (Horrobin, 1977). Further, in two pilot studies, penicillin, which mobilizes dihomogamma-linolenic acid (DGLA)--the rate limiting step in PGE<sub>1</sub> synthesis--has shown some therapeutic effects in chronic schizophrenic patients (Chouinard, Annable and Horrobin, 1978).

Conversely, it has been suggested that schizophrenia is a disease of PG excess, i.e., the result of an excessive release of PGE<sub>1</sub> into the hypothalamus with an accompanying elevation of temperature (Feldberg, 1976). Although Falloon et al. (1978) found no evidence that paracetamol-- a substance which reduces PGE<sub>1</sub> levels--had any therapeutic effect in acute schizophrenic patients, Gjessing (1953) reported febrile episodes in two-thirds of his special group of catatonic patients.

#### Endorphins: Excess or Deficiency

The  $\beta$ -endorphin excess hypothesis is in keeping with the PG deficiency hypothesis. Terenius et al. (1976) found elevated  $\beta$ -endorphin levels in the CSF of schizophrenic patients and  $\beta$ -endorphin was shown to block the mobilization of DGLA and the formation of PGE<sub>1</sub> resulting in a diametrically opposite effect to that of prolactin on PG synthesis. Because successful neuroleptic treatment decreased CSF  $\beta$ -endorphin concentrations, a positive relationship was suggested between CSF endorphin concentrations and schizophrenic psychopathology. Further, because naloxone, by occupying endorphin receptors, has reversed  $\beta$ -endorphin induced catatonia (in animals), the possibility has been raised that naloxone may have antischizophrenic properties. However, the initial favorable therapeutic effects of intravenous naloxone administration could be replicated only in two out of eight clinical experiments.

Conversely, it has been suggested that decreased availability of  $\beta$ -endorphin to the cerebral opiate receptor sites is responsible for schizophrenic psychopathology (Jacquet and Marks, 1976). Within this frame of reference, schizophrenic psychopathological symptoms are perceived as the result of a deficiency in the production of an endogenous neuroleptic peptide which can be replaced by exogenous neuroleptic drugs. In favor of

this hypothesis is the opiate receptor binding property of endorphins and neuroleptics and the finding that, of all CNS regions, the striatum has the highest opiate-binding capacity. In favor, also were the findings that, in at least three schizophrenic patients, intravenous  $\beta$ -endorphin administration produced a reduction (and/or disappearance) of auditory hallucinations, paranoid ideation and pathological pressure of thought (Kline et al., 1977). The controversy regarding the role of endorphins in schizophrenic psychopathology is far from being resolved (Petho et al. 1982; Volavka et al., 1977).

#### Neuroleptics: Long-term Effects

The origin of the DA excess hypothesis of schizophrenia is in the recognition of the role of dopaminergic structures in the action mechanism of neuroleptic drugs. The PG and endorphin hypotheses are secondary elaborations and based on the assumption that schizophrenia is one disease and that the pathomechanism of this disease is related to structures which are affected by antipsychotic drugs.

On the other hand, the fact remains that neuroleptics have considerably transformed the prevailing manifestations of schizophrenic disease. While this transformation was not sufficient to significantly change the distribution of subtypes from the late 1930s to the early 1980s (Ban, Guy and Wilson, 1984a), it was sufficient to discharge patients from the hospital into the community. This, in turn, has resulted in an increase in fertile marriages among community-based schizophrenics (Erlenmeyer-Kimling et al., 1969). Implicit in these fertility gains relevant to the general population is a small, but important shift in the structure of the gene pool. This, of course, is not expected to lead to an abrupt rise in the incidence

of schizophrenia. What can be foreseen, however, is the gradual accumulation of alleles, the gradual dispersion of alleles throughout larger segments of the population and an eventual increase in the proportion of persons who may be affected.

Irrespective of its possible social consequences, long-term treatment with neuroleptics may produce serious adverse effects. While skin pigmentation occurs in less than 0.1 percent of all patients treated with phenothiazines for a period of two years or more (Lehmann and Ban, 1974), the estimated incidence of ocular changes is as high as 20 to 35 percent in patients receiving phenothiazines over an extended period. The prevalence of tardive dyskinesia, the most serious long-term complication, ranges from 0.5 to 40 percent (Ban, 1979).

One possible way to reduce the occurrence of these complications is through a more discriminate use of neuroleptic drugs. While there is little, if any, evidence that patients with different types of schizophrenia, as classified by DSM-III or ICD-9, would respond differentially to neuroleptics, there are indications for differential therapeutic responsiveness to neuroleptics in Leonhard's different subtypes.

#### Neuroleptics and Leonhard's Classification

The possible relationship between therapeutic responsiveness and Leonhard's subtypes within the schizophrenias was first recognized by Astrup (1959) and demonstrated by Fish (1964a). In a survey including 474 chronic schizophrenic patients Fish found that in both the nonsystematic and systematic schizophrenic populations catatonic patients responded less favorably than the others, and within the systematic population hebephrenic patients responded less favorably than paraphrenics.

There seems to be also a relationship between therapeutic dose requirements and Leonhard's subtypes (Ban, Guy and Wilson, 1984b). In a survey of 768 patients, carried out in eight countries it was found that mean daily dosages in the nonsystematic and systematic populations were similar while within the nonsystematic population mean daily dosages of patients with cataphasia were more than twice that in affect-laden paraphrenia and almost four times that in periodic catatonia. The difference among the three groups was statistically significant ( $p \leq 0.01$ ). While there was little difference in mean daily dosages among the three systematic schizophrenic categories, there was a wide variation in mean daily dosages among the subtypes within each category. Of the four paraphrenic subtypes, mean daily dosages were highest in the phonemic and the incoherent, and lowest in the expansive and confabulatory subtypes. Of the four hebaphrenic subtypes mean daily dosages were highest in the eccentric and lowest in the speech-inactive and parakinetic subtypes. In spite of the great variations in dosage, only in the paraphrenic and catatonic categories did the difference in dosage requirements among the subtypes, reach the accepted level of statistical significance ( $p \leq 0.05$ ). The findings that among the paraphrenic subtypes those with exclusively auditory hallucinations (phonemic and incoherent) were receiving the highest dosages of neuroleptics, while the nonhallucinatory subtypes (expansive and confabulatory) were receiving the lowest mean daily dosages may have important heuristic implications. The same applies to the recognition that among the catatonic subtypes those with an excess of movements (parakinetic and proskinetic) were receiving relatively low mean daily dosages of neuroleptics, while those with a deficiency of movements, such as the manneristic and negativistic were receiving relatively high dosages.



In keeping with the contention of differential therapeutic responsiveness in different subtypes are the observations in a patient with the diagnosis of periodic catatonia (febrile catatonia), a nonsystematic subtype, in whom an increase in neuroleptic dosage was associated with exacerbation, a decrease in dosage with amelioration, and discontinuation of medication with remission of psychopathological symptoms (Kelwala and Ban, 1981a). In another case report, on two patients with diagnoses of shallow hebephrenia, a systematic subtype, discontinuation of neuroleptic medication for an extended period (Kelwala and Ban, 1981b) had no detectable effect. Thus, in two shallow hebephrenic patients, the usefulness of maintaining neuroleptic treatment was questionable, while in a patient with periodic catatonia neuroleptic treatment seemed to have a negative therapeutic effect.

The notion that neuroleptic treatment in certain patients may not merely be ineffective but may actually be harmful received further substantiation by a survey of 24 patients treated with lithium/neuroleptic combinations. A common characteristic of these patients was that they had previously shown insufficient therapeutic response to neuroleptic drugs alone. Analyses of data revealed that 9 of 10 patients of the nonsystematic population exhibited a favorable therapeutic response to the combination, while 9 of 14 systematic patients showed no response or an unfavorable therapeutic response. In addition, 5 of the 24 patients developed neurotoxicity during the course of treatment, 2 of 5 patients with the diagnosis of silly hebephrenia and 1 each with the diagnoses of expansive, fantastic and confabulatory paraphrenia. While 5 of the 14 patients with systematic schizophrenia manifested neurotoxicity, none of the 14 patients with nonsystematic schizophrenia, predominantly affect-laden paraphrenia, developed

a similar undesirable response to the lithium/neuroleptic combination (Prakash, Kelwala and Ban, 1982).

Probably most important, however, are indications of a possible relationship between chronic adverse effects and Leonhard's subtypes (Guy, Ban and Wilson, 1985). No patient with the diagnosis of expansive and confabulatory paraphrenia (belonging to a paraphrenic subtype without hallucinations) developed tardive dyskinesia in the course of treatment. The highest incidence of tardive dyskinesia among the catatonic subtypes was encountered in parakinetic catatonia, a subtype receiving relatively low mean daily dosages of neuroleptics. Furthermore, the incidence of tardive dyskinesia was significantly ( $p \leq .001$ ) lower in the nonsystematic than in the systematic patient group.

It is a disappointing fact that in spite of all effective treatments and psychopharmacologic progress the distribution of Leonhard subtypes in 768 chronic hospitalized patients contributed by nine centers, located in eight countries, representing four continents, remained similar in the early 1980s (Ban, Guy and Wilson, 1984a), to the distribution of the subtypes in hospitalized populations of similar size in the late 1930s (Leonhard, 1957) and early 1960s (Astrup, 1979). In all three samples the number and percent of systematic schizophrenics was higher than the nonsystematic schizophrenics. The number and percent of affect-laden paraphrenics was higher than the other two nonsystematic types, and the number and percent of phonemic paraphrenics was higher than the other five systematic paraphrenic subtypes. Furthermore, despite the differences in treatment in the eight countries there were statistically significant correlations among the eight countries regarding the distribution of the six paraphrenic, four hebephrenic and six catonic subtypes (Ban, Guy and Wilson, 1984a).

It is a common contention that psychopharmacology opened unforeseen possibilities for progress in schizophrenia research. A re-evaluation of current concepts of "schizophrenia" with special emphasis on the different disease forms represented by the different "end-states," could open unforeseen possibilities for psychopharmacologic progress with a shift of emphasis from studying therapeutic efficacy, based on statistical probabilities, to the identification of therapeutically-responsive schizophrenic patients to specific treatment modalities.

Recognition of the different diseases through their end-states could lead to the identification of schizophrenic populations (subtypes) particularly responsive to substances such as reserpine or molindone, antipsychotics with properties distinct from traditional chlorpromazine-type of neuroleptics. It could also lead to a definition of schizophrenic populations which may benefit from the administration of benzodiazepines (e.g., alprazolam, diazepam),  $\beta$ -adrenergic receptor blockers (e.g., propranolol), or MAOIs (e.g., phenelzine or tranylcypromine). In 1960, Flach et al. noted the significant decrease in urinary calcium excretion in those paranoid schizophrenic and depressed patients who showed a favorable therapeutic response to the tricyclic antidepressant, imipramine, or electroshock (Flach, 1964). It remains to be seen whether this antidepressant responsive schizophrenic population represents a distinct subtype within Leonhard's classification of schizophrenias.

### Cycloid Psychoses

Recognition of the difficulties encountered in the separation of "affective" and "schizophrenic" psychoses yielded the identification of "cycloid psychoses."

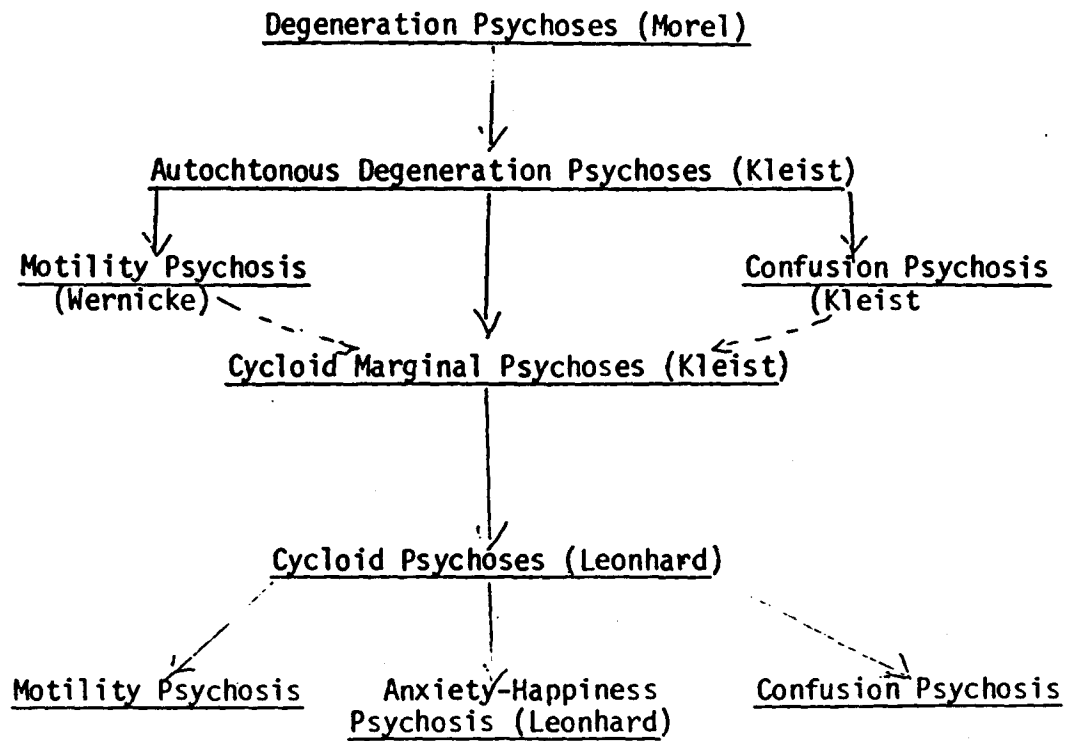
In his textbook on "The Classification of Endogenous Psychoses," Leonhard (1957) pooled together three different forms of psychoses: motility psychosis (Wernicke, 1894, 1900; Kleist, 1912; Funfgeld, 1936), confusion psychosis (Kleist, 1928) and anxiety-happiness (elation) psychosis (Leonhard, 1934, 1939) under the heading of cycloid psychoses. He separated cycloid psychoses from the phasic and schizophrenic psychoses and defined them as a group of remitting bipolar disorders which resemble the phasic psychoses in their course and the nonsystematic schizophrenic psychoses in their content. Leonhard (1960) noted the great similarity in contents between the nonsystematic schizophrenias and cycloid psychoses. He also emphasized, however, the essential difference between these two groups of disorders. Only cycloid psychoses displayed complete recovery from each phase. In this respect they resemble phasic (affective) psychoses to the extent, that if full recovery is not achieved the possibility of misdiagnosis needs to be considered. Chronic courses are exceptionally rare. If they occur, however, cycloid psychoses "lose their tension" after repeated periods of hospitalization.

Conceptual development of cycloid psychoses dates back to the work of the 19th century French school (Fish, 1964; Brockington, Perris and Meltzer, 1982). Legrain (1886) and Magnan (1893) recognized that within Morel's (1860) "degeneration psychoses" (psychoses that are the result of a degenerative process within a given family) there were illnesses with an acute or subacute onset (Legrain, 1886), which followed a phasic, episodic course (Magnan, 1893) with a full remission between episodes. The concept was further elaborated by Schroder (1926) who referred to this group of disorders as "metabolic psychoses" in order to highlight their episodic nature. Gaupp (1926) called them "mixed (combinierten) psychoses" because

of the mixture of "schizophrenic" cross-sectional psychopathology with a longitudinal-course resembling manic-depressive illness. The separation of two distinct illnesses from this mixed group of psychoses, motility psychoses (Wernicke, 1894) and confusion psychosis (Kleist, 1928), yielded the concepts of "autochthonous degeneration psychoses" and "cycloid marginal psychoses" (which include both motility and confusion psychoses) in the work of Kleist (1921, 1928). Subsequently, the identification of a third distinct illness, anxiety-happiness psychosis (Leonhard, 1934), resulted in the present concept of cycloid psychosis which includes motility, confusion and anxiety-happiness psychoses (Leonhard, 1957) (Figure 10), (see Appendix X, Tables I-III).

In his lecture at the Royal Edinburgh Hospital for Nervous and Mental Disorders on the 27th of June 1960, Leonhard (1961) defined cycloid psychoses, as a group of acute, reversible psychoses which do not fulfill the criteria of schizophrenic or manic depressive illness. He reasserted that cycloid psychoses, appear in three different bipolar forms of illness, motility psychosis, confusion psychosis and anxiety-happiness psychosis, each consisting of contrasting clinical states which may occur at different times, but are never present simultaneously. Thus, the prevailing manifestations of motility psychosis are hyperkinesia or akinesia. In contradistinction to periodic catatonia, however, there is never an admixture of hyperkinesia and akinesia. Confusion psychosis in the excited phase is characterized by incoherent thinking, misidentifications and pressure of speech. In the inhibited phase pressure of speech is replaced by a decrease in verbalization. The third disorder, anxiety-happiness psychosis, is manifest with prevailing anxiety or elation (happiness).

Figure 10



Cycloid psychoses: development of the concept.

A desire to make others happy is pathognomonic of happiness psychosis. In cycloid psychoses there is no overlap between the two opposite poles in anyone of the three illnesses. On the other hand, the three cycloid psychoses are not sharply separated from each other. The same applies to the differentiation of cycloid psychoses from the non-systematic schizophrenias: motility psychosis from periodic catatonia, confusion psychosis from cataphasia and anxiety-happiness psychosis from affect-laden paraphrenia. Not infrequently the final diagnosis must be withheld and decided upon on the basis of the outcome of the illness, i.e., full recovery in cycloid psychoses and partial remission in the nonsystematic schizophrenias (Table XX).

The concept of cycloid psychosis was further elaborated in the work of Perris (1973, 1974) who put forward an operational definition for this diagnosis. According to Perris, to qualify for a diagnosis of cycloid psychosis, the patient must have affective symptoms (mood swings) associated with confusion, delusions of reference, motility disturbances, ecstasy and/or pan-anxiety. He shifted the emphasis from paranoid anxiety or motility extremes to acute onset, polymorphic (multiform) symptomatology and confusion. Of particular importance is the polymorphic clinical picture with all sorts of symptoms jumbled, suggesting the presence of several different disorders, none of which is dominant or persistent. The clinical picture may shift from one syndrome to another, and there is never a fully developed stable manic, depressive, or paranoid syndrome.

The shift of emphasis in the definition of cycloid psychosis is possibly responsible for the difference in reported prevalence rates between Leonhard's (1957) study carried out in Frankfurt from 1938 to 1942 and subsequently in Berlin and the study of Cutting, Clare and Mann (1978),

Table XX

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<u>First Dimension</u> Cross-sectional Psychopathology (Symptomatology)	Hyperkinesia or akinesia Incoherent thinking Pressure of talk with misidentifications Retardation with ideas of reference Anxiety with ideas of reference and/or significance Elation (happiness) with expansive ideas and the desire to make others happy
<u>Second Dimension</u> Onset - Etiology	Endogenous with acute or subacute onset
<u>Third Dimension</u> Course of Illness	Episodic-remitting Bipolar
<u>Fourth Dimension</u> Outcome Picture	Full recovery

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Leonhard's (1969) diagnostic criteria of cycloid psychosis.



carried out in London on patients admitted to the Maudsley professorial unit from 1955 to 1964. In the Frankfurt-Berlin study (Leonhard's criteria) out of 1537 patients 837 were schizophrenic, 282 manic-depressive and 418 cycloid. In the London study (Perris' criteria) out of 2500 admissions only 73 or 3% of all admissions and 8% of all psychotic admissions were cycloids. Cycloid psychosis was the fourth most common psychotic diagnosis in the Maudsley series, after depressive psychosis (18%), schizophrenia (16%) and organic conditions (10%). The different definitions, used in the two cohorts, might also explain why in the German sample the most frequently occurring cycloid disorder was anxiety-happiness psychosis (178 patients) followed by confusion psychosis (142 patients) and motility psychosis (98 patients), while in the British sample the least numerous subgroups were the ones with manifestations of ecstasy (7 patients) and pan-anxiety (30 patients).

In spite of the differences in the frequency of occurrence in the two studies, results of the survey carried out by Cutting, Clare and Mann (1978) favor Leonhard's contention that cycloid psychosis is a nosologically distinct category within the endogenous psychoses. In a follow-up examination of 90 percent of their 73 cycloid patients, they found that compared with other psychoses, the cycloids had the highest recovery rate (90%), the highest proportion of patients with at least one remission and the highest admission and episode rates (.28 and 0.30/year, respectively). They spent more time in hospitals than depressed or manic patients (.86 months/year, compared with .24 and .46 respectively), but much less than schizophrenic patients (2.52 months/year). The distinctiveness of cycloids on outcome measures was also substantiated in the study of Brockington et al (1982). In a series of 233 patients, they found that 90 percent of 30

cycloids fully recovered, while only 67 percent of the whole group showed a similar response. When compared with schizophrenia, the cycloids fared even better; 92 percent of the 24 cycloids given a CATEGO diagnosis of schizophrenia made a full recovery compared with the 59 percent in the 102 noncycloid CATEGO schizophrenics.

In the DCR (Petho, Ban, Kelemen et al., 1984) substantiation of a diagnosis of cycloid psychosis is based on the evaluation of 16 variables. The diagnosis is essentially made on the basis of Leonhard's principles, although Perris' criteria, such as acute or subacute onset, polymorphic-fluctuating symptomatology, mood swings and thematic incoherence, are also considered. Attention is focused on the presence of protopathic change of Gestalt, in spite of the recognition that in Conrad's (1958) work this is pathognomonic of schizophrenic psychopathology and not of cycloid psychosis. Furthermore insofar as outcome is concerned personality changes are considered to be an acceptable alternative to full recovery.

Cycloid psychosis is not an accepted diagnostic category either in ICD-9 or in DSM-III. Contrary to the common belief that patients with this diagnosis are subsumed under schizophrenic disorders, schizoaffective type in ICD-9 and schizoaffective disorder in DSM-III, there is substantial evidence to believe that this is not the case. However, there is a fair concordance between cycloid psychoses in two series of patients, i.e., 134 patients in the Hetherne series (Cooper et al., 1972) and 119 patients in the Camberwell series (Wing et al., 1968) and Kasanin's (1933) acute schizoaffective psychosis (Kappa = .42 and .37 respectively). However, Brockington et al. (1982) found that of the 108 patients meeting Kendall's study criteria for schizoaffective psychosis (Kendell and Brockington, 1980), only 20 patients (19%) met Perris' (1974) criteria for cycloid psychosis. On the basis of these findings

Brockington, Meltzer and Perris (1982) asserted that "it is obviously a mistake to regard cycloid psychosis as a synonym for schizoaffective disorders." The same applies to manic-depressive psychosis. In spite of all the similarities between cycloid and manic-depressive psychosis, "there was a negligible overlap between these two disease concepts" in the Netherne series.

In two clinical studies in which the correspondence between cycloid psychoses and hospital diagnoses was explored, no consistent relationship was found. In the clinical study of Cutting, Clare and Mann (1978) the hospital diagnosis (based on ICD-9) of 73 cases of cycloid psychosis were: schizophrenia in 33, schizoaffective in 20, affective in 11 and atypical psychoses in 9 patients. Similarly, the diagnosis of 30 cycloid patients in the clinical study of Brockington et al. (1982) were schizophrenia (including schizoaffective schizophrenia) in 18, mania in 7, depressive psychosis in 4 and puerperal psychosis in 1 patient. In the same study, CATEGO classification was S+ in 18, M+ in 5, O+ in 3, P+ in 3 and D+ in 1 patient. RDC diagnoses were schizoaffective depression in 11, schizoaffective mania in 6, both in 1, schizophrenia in 7 and mania in 5 patients; and DSM-III diagnoses were depression with mood incongruent psychotic features in 10, with mood congruent features in 6, schizophreniform psychosis in 5 and schizophrenia in 2 patients. On the basis of these findings Brockington et al. (1982) conclude that "in terms of the ICD and CATEGO systems, a majority had some form of schizophrenia, while in terms of the two American systems a majority had mood-incongruent or schizoaffective depression or mania."

Finally, it should be noted that Fish (1964) considered cycloid psychosis as one of four different kinds of atypical psychoses. The other three are

atypical manic depressive psychoses, psychogenic reactions and epileptoid psychoses. He contends that the differentiation of cycloid psychoses from the other forms of atypical psychoses is an essential prerequisite for meaningful research on these disorders.

Differential characteristics of the three cycloid psychoses were described by Leonhard (1957, 1961), Fish (1962, 1964) and Petho, Ban, Kelemen et al. (1984).

### Confusion Psychosis

The separation of confusion psychosis from confused manias dates to Wernicke (1900) who referred to confusion psychosis as "periodic maniacal autopsychosis" or "agitated confusion." A quarter of a century later the first comprehensive description of confusion psychosis was given by Kleist (1928). Consolidation of the concept is attributed to Fünfgeld (1936). He was the first to explore the possible hereditary pattern of this disorder.

In the original formulation, confusion psychosis is a pure thinking disorder, an illness in which thinking is exclusively affected while affectivity and psychomotor activity are preserved. The thinking disorder in the excited phase of the illness is expressed as "incoherence" or in less severe cases as "incoherence of thematic choice" also referred to as "digressive thematic choice." Thus, for example if asked to differentiate between a tree and a bush, the patient responds by describing the berry bushes at home. If asked to differentiate between giving and lending, patient responds by speaking about gifts and celebrations. Other characteristics of the excited phase are compulsive speech, intrusion of abnormal contents, mis-identifications, ideas of reference and sensory (most frequently auditory) illusions.

The thinking disorder in the inhibited phase of the illness is expressed in the form of inhibited thinking associated in the more severe form with mutism and in the less severe form with impoverished speech. Other characteristics of the inhibited phase are perplexity, ideas of reference and hallucinations (auditory, visual and somatic).

Ideal--pure--form of confusion psychosis rarely occurs. In the majority of patients the manifestations of confusion psychosis are present in association with features of motility psychosis and/or anxiety-happiness psychosis.

In the differential diagnosis mania and catatonic schizophrenia should be considered. Confusion psychosis, in the excited phase, shares with mania pressure of speech. In contradistinction to mania, however, distractibility and flight of ideas are absent, while misidentifications are frequent.

The signal difference between confusion psychosis in the inhibited phase and catatonic schizophrenia is the perplexed and anxious mood. It is present in patients with confusion psychosis, but absent in patients with stuporous catatonia.

#### Motility Psychosis

The first description of hyperkinetic and akinetic motility psychoses dates to Wernicke (1896). He did not regard these syndromes, however, as two different forms of an independent disease but regarded them as syndromes found in a number of different illnesses. It was Kleist's (1928) contribution to formulate a nosological conception and to separate motility psychosis from periodic catatonia and other catatonic schizophrenias.

In the original formulation motility psychosis was a pure psychomotor disorder, an illness in which psychomotor activity was exclusively affected while thinking and affectivity were preserved. The psychomotor disorder in the excited phase of the illness was manifested in the form of "hyperkinesia." The increase of motor activity was quantitative in nature. It

affected both, expressive and reactive movements. Hyperkinetic patients related to all events in their environment and displayed a great deal of expressive and reactive movements, such as facial expressions and gestures.

The psychomotor disorder in the inhibited phase of the illness was manifested in the form of "hypokinesia" or in the most severe cases, in the form of "akinesia." Like in the hyperkinetic phase, the decrease of motor activity was quantitative in nature and affected the expressive and reactive movements. Lack of reactive and expressive movements characterizes akinesia. If akinesia is present, even the necessary reactions to external events and bodily needs may be absent. In milder cases there is rigid posturing and facial expression but the continued presence of voluntary motions.

Ideal--pure--form of motility psychosis rarely occurs. In the majority of patients manifestations of motility psychosis are present in association with features of confusion psychosis and/or anxiety-happiness psychosis.

In the differential diagnosis, mania and periodic catatonia should be considered. Motility psychosis, however, differs from mania by the lack of pressure of speech. Instead, speech is characterized by short phrases followed by long pauses.

The signal difference between motility psychosis and periodic catatonia is that in motility psychosis the pathology is restricted to the quantitative aspects of psychomotricity, while in periodic catatonia psychomotor activity is affected not just quantitatively but also qualitatively. If a patient shows changes in both directions these follow one another in case of motility psychosis and do not occur simultaneously. In contrast, the simultaneous presence of hyperkinetic and akinetic pathology is indicative of periodic catatonia.

### Anxiety-Happiness Psychosis

The identification of a separate "anxiety psychosis" and a separate "expansive autopsychosis with autochthonous ideas" dates to Wernicke (1900). The first comprehensive description of anxiety-happiness, also referred to as anxiety-elation, psychosis was formulated by Leonhard (1934, 1957) considerably later.

In the original formulation anxiety-happiness psychosis was a pure disorder of affectivity. In other words, it was an illness in which affectivity was exclusively affected while thinking and psychomotor activity remained preserved. The disorder of affectivity in the anxiety phase was manifested as anxiety accompanied by mistrust, self-references, hypochondriacal ideas, feelings of inferiority, sensory illusions and the feeling of being influenced.

The disorder of affectivity in the happiness phase of the illness manifested as ecstasy accompanied by ideas of happiness and occasionally by sensory illusions and ideas of reference.

Ideal--pure--form of anxiety-happiness psychosis rarely occurs. In the majority of patients manifestations of anxiety-happiness psychosis are present in association with features of motility psychosis and/or confusion psychosis (Table XXI).

### Differential Characteristics

In the DCR (Petho, Ban, Kelemen et al., 1984) cycloid psychoses consist of three major diagnoses (confusion psychosis, motility psychosis and anxiety-happiness psychosis) and each disorder consisted of two subtypes. Thus, confusion psychosis may appear as inhibited or agitated confusion psychosis, motility psychosis as hyperkinetic or akinetic motility psychosis and anxiety-happiness psychosis as anxiety or happiness psychosis.

Table XXI.

Manifestations	Confusion Psychosis	Motility Psychosis	Anxiety- Happiness Psychosis	Manic Psychosis	Catatonic Schizophrenias
Thinking affected	+	-	-	+	+
Psychomotricity affected	-	+	-	+	+
Affectivity affected	-	-	+	+	-
Pressure of speech	+	-	-	+	-
Flight of ideas	-	-	-	+	-
Speech: short phrases followed by long pauses	-	+	-	-	-
Perplexed and/or anxious mood	+	+	+	-	-
Misidentifications	+	-	-	-	-
Quantitative changes of psychomotricity	-	+	-	+	+
Qualitative changes of psychomotricity	-	-	-	-	+

Schematic presentation of the dominant features (+) which differentiate confusion, motility and anxiety-happiness psychoses from manic psychosis and the catatonic schizophrenias. A (-) does not imply the absence of the particular manifestation.



Each diagnosis is characterized by eight symptoms and within these eight symptoms each subtype is characterized by four. Two of the eight symptoms, i.e., one symptom for each subtype are considered to be pivotal symptoms and their presence obligatory for the diagnosis. Thus, a prerequisite for the diagnosis of confusion psychosis is the presence of inhibited or agitated confusion, for motility psychosis, the presence of hyperkinesia or hypokinesia, and for anxiety-happiness psychosis, the presence of anxiety or ecstasy. In addition for the diagnosis of inhibited confusion psychosis, the presence of inhibited thinking and/or decreased talkativeness and/or mutism is also necessary; and for the diagnosis of agitated confusion psychosis, the presence of thematic incoherence and/or increased talkativeness and/or misidentifications. Similarly, for the diagnosis of akinetic motility psychosis the presence of decreased expressive, reactive and/or voluntary motor activity is required and for the diagnosis of hyperkinetic motility psychosis, the presence of increased expressive, reactive and/or voluntary activity. Finally for the diagnosis of anxiety psychosis the presence of ideas of reference, and/or delusional perceptions and/or feelings of inferiority is mandatory; and for the diagnosis of happiness psychosis, the presence of ideas of happiness and/or desire to make others happy and/or exaggerated self-esteem.

Corresponding diagnostic categories in ICD-9 and DSM-III have not been identified. It is likely, however, that confusion psychosis is usually diagnosed as acute schizophrenic episode in ICD-9 and schizophrenic disorder disorganized type in DSM-III, motility psychosis as schizophrenic psychosis catatonic type in ICD-9 and schizophrenic disorder catatonic type in DSM-III, and anxiety-happiness psychosis as schizophrenic psychosis paranoid or schizoaffective type in ICD-9 and schizophrenic disorder paranoid type or schizoaffective disorder in DSM-III. However, since cycloid psychoses

usually display multiform (polymorphic) symptoms they may be diagnosed as schizophrenic psychosis, affective psychosis, other nonorganic psychosis or paranoid state in ICD-9; similarly they may be diagnosed as schizophrenic disorder, affective disorder, psychotic disorder not elsewhere classified or paranoid disorder in DSM-III.

#### Therapeutic Considerations

Because a diagnostic formulation is a prerequisite for treatment and/or for the study of the effectiveness of different treatment modalities, cycloid psychoses have no generally accepted therapy which is based on findings in properly designed and conducted clinical studies. In spite of this there is sufficient evidence that patients with cycloid psychoses show a differential response to antipsychotics, antidepressants and mood-stabilizer lithium salts. The same applies to the three different forms and the six subtypes.

A pattern frequently seen in the pharmacotherapy of cycloid psychoses is that of a patient who become depressed when treated with an antipsychotic-neuroleptic, increasingly psychotic when treated with an antidepressant, and develop a toxic confusional state when given lithium salts. The prototype of such patients was a 24-year-old woman with a hyperkinetic motility psychosis. She was brought to hospital because of alleged erotic advances to unknown men in public. During the initial period of hospitalization she displayed severe hyperkinesia with stamping of feet, squinting and grimacing. When questioned she responded with excessive movements but with short phrases followed by long pauses. The provisional diagnosis of mania was made and haloperidol was prescribed. As a result, excessive movements ceased and were replaced by severe akinesia. Because the akinesia was so severe that patient stopped responding to bodily needs, medication was discontinued. Discontinuation of haloperidol resulted in a shift back to the hyperkinetic

state. Lithium was prescribed, but it had to be stopped because of the confusional state it induced even when below therapeutic blood levels. After approximately 12 weeks of unsuccessful therapeutic attempts with various neuroleptics, the patient promptly responded to electroconvulsive treatment. Remission was complete and there was no recurrence of psychosis during a three-year follow-up period.

Although there are no verified findings, there are indications that a considerable proportion of patients with cycloid psychosis are treated with ECT, lithium salts and/or different drug combinations, i.e., anti-depressant-antipsychotic, anxiolytic-antidepressant, lithium-antipsychotic, and antidepressant-lithium. In the absence of recognized treatment, ECT remains the most effective and reliable method among the various treatment modalities employed.

## CONCLUSIONS

In this monograph the historical development of a four-dimensional classification of functional psychoses was outlined. The presentation was restricted to the evolution of concepts with emphasis on the extension of the diagnostic information from cross-sectional psychopathology to all developmental stages of psychiatric illness.

The proposed classification is firmly rooted in cross-sectional psychopathological symptoms. It differs from syndromatological classifications in that the clinical syndromes are not studied in isolation but in the nosological context of the total longitudinal picture of the illness. The nosological entities described do not fulfill all the criteria of a "disease" (Jaspers, 1959, 1963). However, a nosological approach was employed to prevent confounding the biological correlates of any particular stage (cross-sectional syndrome) of a disease with the central biological mechanism of the illness.

Inclusion of "psychogenic" psychoses (Faergeman, 1963) represents an extension of the original concept of functional psychoses from exclusively "productive" (endogenous) to "reactive" illnesses. In "productive" illness, "a process takes its course, leading to a progressive alteration in the psychic constitution," without external cause. In "reactive" illness, "a preexisting abnormal constitution reacts in an abnormal way to external events only to revert to its earlier state when these events cease" (Hoenig, 1984). However, the fact remains that even in case of psychogenic (reactive) psychoses only "the contents of the pathological states are meaningfully connected with the initial experience" (Jaspers, 1913, 1974). In other words, understanding these disorders on the basis of a traumatic life event relates to the content of these psychoses but does not extend to understanding their forms.

The adoption of Leonhard's (1957) subtypes in the classification of "endogenous-productive" illnesses is based primarily on clinical observations. In favor that the subtypes are valid diagnoses are the findings that in their course functional psychoses display increasingly differentiated features. This is at variance with Conrad's (1958) contention that progressive stages of one and the same illness are represented in the different syndromes (Fish, 1961). None of these observations exclude the possibility that a state of over-arousal (Kornetsky and Mirsky, 1966; Weil-Melherbe and Szara, 1971) might play a central role in the pathophysiology of all subtypes or developmental stages of schizophrenias and desynchronization of the circadian rhythm (Halberg, 1968; Mellerup and Rafaelsen, 1979; Pflug and Tolle, 1971) of all affective disorders.

General paralysis, a disease produced by the effects of *treponema pallidum* on the brain, may appear as several distinctly different syndromes. Because of this, general paralysis has become a specter against "subtyping" in psychiatry. Within a three-dimensional model of diagnosis all patients with the same diagnosis and regardless of their early manifestations, display, a similar syndrome, i.e., dementia. In other words, it is dedifferentiation which results in dementia, the common final syndrome in all patients with general paralysis, a systemic neurological disease; while it is differentiation which results in subtypes, or distinct syndromes in patients with functional psychoses. Consequently, diagnostic evaluation of these disorders must proceed in a step-wise fashion and encounter an increasingly larger proportion of the illness, i.e., onset, cross-sectional syndrome, course and outcome.

Description of psychopathological symptoms is usually the first step in diagnostic evaluation. This is followed by the identification of "psychosyndromes" which are based on the profiles of simultaneously present psychopathological forms. Considering that localization of psychopathological events (symptoms) in the brain has failed in spite of many attempts, a

purely syndrome-based approach to classification of psychiatric disorders has little to offer concerning an understanding of these illnesses.

An alternative to the syndrome based approach to the classification of psychiatric disorders is the nosology based approach. By accepting the "nosological postulate" it is assumed that each psychiatric illness, characterized by a specific psychopathologic syndrome, has a characteristic course with a predictable outcome even if, for the time being, its etiology is not known.

### Cross-sectional Psychopathology

Analyses of cross-sectional psychopathological syndromes in the different psychiatric illnesses have brought to attention distinct differences in the affected psychopathological structures. These differences appear in the general and special characteristics of the different disease pictures. Accordingly, manifestations related to systemic (organic) disease display psychopathological symptoms which are primarily related to "integrational" functions, such as "disorders of consciousness," "memory impairment," "disorientation" and/or "deterioration of personality," while manifestations of functional (psychogenic and endogenous) psychoses display psychopathological symptoms which are primarily related to "perceptual-cognitive," "relational-affective" and "motor-adaptive" functioning. In the affective disorders psychopathological symptom development is related to mood (holothymic or mood congruent); and in both affective and cycloid disorders psychopathological symptoms related to cognitive, affective and adaptive functioning are in harmony, i.e., in-keeping with each other. The same does not apply to schizophrenic disorders, where symptom development is unrelated to mood and is based on catathymic (emotional) mechanisms;

and where psychopathological symptoms related to cognitive, affective and adaptive functioning are dissociated, i.e., split from each other. Nevertheless, in both schizophrenic and affective disorders, nonsystematic illnesses are characterized by multiform (polymorph), and systematic illnesses by simple (monomorph) clinical pictures.

Among the functional psychoses, delusional psychoses, paraphrenic schizophrenias and confusion psychoses display psychopathological symptoms which are primarily related to perceptual-cognitive functioning. Other diagnoses with psychopathological symptoms related to perceptual-cognitive functioning include affect-laden paraphrenia (delusions with strong delusional dynamics), psychogenic paranoid psychosis (ideas of reference), unproductive euphoria and harried depression (restricted thinking or poverty of thought), hypochondriacal euphoria and hypochondriacal depression (hypochondriasis), confabulatory euphoria (confabulations) and suspicious depression (suspiciousness).

Among the endogenous psychoses, both affective and cycloid psychoses display psychopathological symptoms which are primarily related to relational-affective functioning. However, in affective disorders hyperthymic (elated) or dysthymic (depressed) mood is the dominant clinical feature, while in cycloid psychoses it is perplexed mood, i.e., a mood of puzzlement or uncertainty. Other diagnoses with psychopathological symptoms related to relational-affective functioning include psychogenic affective psychoses (exaltation or depression) and the systematic hebephrenias (emotional indifference and blunted effect).

Finally, among the schizophrenic psychoses, systematic catatonias, cataphasia and periodic catatonia display psychopathological symptoms which are primarily related to motor (including speech)-adaptive functioning.



Other diagnoses with psychopathological symptoms related to motor-adaptive functioning include motility psychosis (hyperkinesia or hypokinesia), harried depression (restlessness), autistic hebephrenia (autism) and eccentric hebephrenia (soft mannerisms).

It remains to be seen to what extent the cross-sectional psychopathological syndromes will fulfill expectations regarding predictability of course and outcome of a psychiatric disease. But even if such expectations are fulfilled, the question remains whether corresponding changes in the brain with the proposed nosological categories can be identified by the presently available biochemical, neurophysiological and/or brain imaging techniques.

#### Form of Onset

Cross-sectional syndromes are based on the simultaneous presence of different psychopathological forms. Considering that only the content of these manifestations are understandable through patients' developmental history, relevant anamnestic information for nosological diagnosis is restricted to the description of the onset (acute, subacute or chronic) of the illness and information, whether criteria of an exogenous reaction, biological reaction in case of systemic disease and psychogenic reaction in case of psychic trauma, are fulfilled.

Because form of onset provides for only three possibilities (acute, subacute and insidious), different forms of onset become meaningfully interpretable only with consideration of information regarding subsequent developmental stages of the disease. However, in case of functional psychoses, an insidious onset indicates systematic schizophrenic disease, although in the differential diagnosis chronic interpretative delusional psychosis needs to be entertained. Furthermore, while a

biological reaction with few exceptions, produces psychopathological symptoms indicative of organicity, such as disorder of consciousness, memory disturbance, disorientation and/or deterioration of personality, a psychological reaction may display psychopathological features resembling organic (dissociative) or endogenous (affective or paranoid) syndromes. Consequently for a diagnosis of psychogenic affective or paranoid psychosis consideration needs to be given to the third developmental stage or the course of the disease.

### Course of Illness

In nosological diagnoses, there is a shift in emphasis from developmental history to course of illness, i.e. whether the disorder follows a recurrent, possibly rhythmic, or continuous, possibly downhill course. However, neither "recurrent" and "rhythmic" nor "continuous" and "downhill" should be interchangeably used, because "rhythmic recurrence" is restricted to cycloid and affective psychoses and the nonsystematic schizophrenias, while a "continuous downhill" course is present only in the systematic schizophrenias and chronic delusional psychoses.

Recognition of the importance of the unipolar-bipolar dimension in relationship to mood states, but including also other aspects of relational-affective and motor-adaptive functioning, opened the possibility for the separation (within the affective psychoses) of unipolar and bipolar illnesses. It led to the recognition that not only affective psychoses but also cycloid psychoses and nonsystematic schizophrenias may follow a unipolar or bipolar course. Furthermore, recognition of the relationship between disease picture and course of illness, multiform picture-bipolar course and simple picture-unipolar course, prompted re-evaluation of cross-sectional

psychopathological syndromes. This in turn yielded to the identification of numerous subtypes within the schizophrenias and the affective psychoses.

#### Outcome or End-State

Outcome is the final developmental stage of psychiatric illness and the ultimate validation of four-dimensional diagnoses is through their "outcome features." Outcome features range from full "recovery" from the illness to residual psychopathology. In between the two extremes are full "remissions" between episodes of the illness and subclinical manifestations, such as maladjustment and/or personality changes. In contradistinction to the conventional, we have used the term "residual," to denote irreversible "end-states," characterized by distinct psychopathological syndromes (subtypes). These develop in disorders with a continuous course, such as systematic schizophrenias and chronic delusional psychoses. The opposite to residual psychopathology is full recovery, a prerequisite for a final diagnosis of psychogenic and acute delusional psychoses. Full recovery, however, does not imply protection against recurrence of the same or another psychiatric illness.

Full remission is the characteristic outcome feature of affective and cycloid psychoses. The "symptom" free periods (remissions) are between the symptomatic episodes in disorders which follow an episodic-recurrent course. While as a rule residual psychopathology is absent, it is not infrequent to see personality changes after recurrent episodes of cycloid psychoses and maladjustment after prolonged episodes of affective disorders, e.g., euphorias, depressions.

Although nonsystematic schizophrenias follow a recurrent episodic course, full remissions are not encountered between episodes. Instead, there

are personality changes with maladjustment, and not infrequently, distinct psychopathological symptoms.

#### Effect of Pharmacotherapy

There is substantial evidence to believe that among the different treatment modalities for the functional psychoses, pharmacotherapy is significantly superior to other treatment modalities. Still, the question remains: to what extent has the introduction of psychotropic drugs changed the four developmental stages of the different illnesses?

Insofar as form of onset, i.e., the first developmental stage is concerned, there is no reason to believe that it has been affected by the introduction of psychotropic drugs. Primary prevention is still outside the scope of clinical psychopharmacology. There is no indication that the onset of functional psychoses can be prevented and/or that the form of the onset modified by any of the available psychotropic drugs.

The same applies also to outcome that has not shown essential change that can be attributed to the introduction of modern pharmacotherapies. Accordingly, residual psychopathology remains the characteristic outcome of systematic schizophrenias and chronic delusional psychoses and full recovery of psychogenic and acute delusional psychoses. There are full remissions between recurrent episodes of affective and cycloid psychoses and partial remissions between recurrent episodes of unsystematic schizophrenias. In spite of all pharmacotherapeutic advances, however, recurrent episodes may still result in personality change in cycloid psychoses, maladjustment in affective psychoses, and residual psychopathology in unsystematic schizophrenias.

Pharmacotherapy induced changes are restricted to the second and third developmental stages, i.e., cross-sectional psychopathology and

course of illness in the functional psychoses. During the second developmental stage (cross-sectional syndrome), it is well established that neuroleptics, cyclic antidepressants and lithium salts can significantly decrease the intensity or severity of schizophrenic, depressive and manic clinical manifestations. In case of episodic disorders, they can also shorten the duration of the active phase of manifest psychopathology. There are only indications, however, that the same drugs during the third developmental stage (course of illness), can significantly increase the duration of the interval between episodes and maintain patients in remission. Considering that not all patients, respond equally well to treatment and that treatment and especially maintenance-prophylactic treatment with these drugs can result in chronic adverse effects, efficacy studies with psychotropic drugs should be designed in a manner that they could identify the therapeutically responsive population within the different diagnostic groups. It may also be necessary to shift the emphasis of efficacy studies from the second to the third developmental stage, that is, from control of symptoms to maintenance of remission.

Irrespective of their impact on treatment, the new drugs have focused attention on the heterogeneity of psychiatric populations within the generally accepted (ICD-9 and DSM-III) diagnostic categories. Also, that within each diagnostic group some patients respond while others remain refractory to the same therapeutic approach. To date there are no established biological markers for any of the diagnoses and there are no indications that any of the accessible biochemical and/or neurophysiological measures will increase the biological homogeneity of diagnostic groups in terms of therapeutic responsiveness to psychotropic drugs.

We do not necessarily believe that in the proposed classification specific cerebral changes will show greater correspondence (parallel) with diagnosis-specific changes in the different psychopathological structures than in other currently used classifications. We are more inclined to agree with Jaspers' early (1910, 1963) contention that all research "up to now has only brought us closer to finding such parallel events, but they have nowhere actually been found." On the other hand, we firmly believe that the psychopathological syndromes are integral parts of distinct psychiatric illnesses within the functional psychoses. We also believe that a careful analysis of psychopathological syndromes within the context of their developmental pattern of onset, course and outcome, can provide for biologically more homogeneous populations than the populations derived by any other methods.

We hope that in the proposed classification the conceptual development of different illnesses subsumed under functional psychoses, is properly reflected. The conceptualizations presented evolved in the course of a historical process which has integrated numerous clinical observations into distinct clinical pictures. Because the diagnostic groups have not been generated by generally accepted empiricistic and/or experimental methods, their validity will have to be established in carefully designed clinical research.

APPENDIX

APPENDIX I  
MULTIAXIAL SYSTEMS OF CLASSIFICATIONS



The development and various forms of multiaxial classifications were presented by Helmchen in a paper entitled *Multiaxial Systems of Classifications*, published in the *Acta Psychiatrica Scandinavica* (61: 43-55) in 1980. The five multiaxial classifications presented in tables I-V are adapted from this paper.

Table II

- 
- I. Symptomatology**
- A. Symptoms in the strict sense
    - 1.0 Mood swings
      - 1.1 manic
      - 1.2 depressive
  - B. Personality disturbances
    - 17.0 Uncommunicative, reserved, timid, of solitary inclination
    - 17.1 autistic
- II. Severity**
- 1. Neurosis
  - 2. Psychosis
- Single criterion for delineation:  
reality evaluation
- III. Etiology**
- 1.0 Somatogenic
    - 1.1 histogenic = "organic"
  - 2.0 Psychogenic
    - 2.1 external conflict
  - 3.0 Characterogenic
  - 4.0 Cryptogenic = cause unknown
- IV. Course**
- 1.0 Diseases (processes, dynamic developments)
    - 1.1 isolated episode
    - 1.2 periodic course
    - 1.3 progressive course
  - 2.0 Abnormalities (relatively static, habitual states)
    - 2.1 disturbances of development
      - oligophrenia
    - 2.2 defects
      - dementia
- 

Ottosson and Perris' (1973) model of a multi-axial system of classification distinguishes among four axes: (1) Symptomatology, (2) Severity, (3) Etiology and (4) Course. (Based on Ottosson JO and Perris C: Multi-dimensional classification of mental disorders. Psychol. Med. 3: 238-243, 1973).

Table III

Axis	Criteria
1. Symptomatology	-Type of symptoms -Pattern of symptom groups, syndrome
2. Time	-Age of onset -Speed of onset (acuteness) -Course (intermittent, chronic) -Duration -Outcome
3. Etiology	-Disposition, familial -Disposition, personality type -Precipitation, psychoreactive -Precipitation, somatic -Precipitation, therapeutic -Fixation, psychoreactive -Fixation, social -Fixation, therapeutic
4. Intensity	-Of most of the criteria on the above-mentioned axes 1-3 -Of the consequences of the criteria on the above-mentioned axes 1 and 2
5. Certainty	-Of each of the criteria on the above-mentioned axes 1-3 -Of verbal diagnosis -Of coded diagnosis

Helmchen's (1975) model of a multi-axial system of classification distinguishes among five axes: (1) Symptomatology, (2) Time, (3) Etiology, (4) Intensity and (5) Certainty. (Based on Helmchen H: Schizophrenia: Diagnostic concepts in the ICD-8. In Lader MH ed.: Studies in Schizophrenia. Brit. J. Psychiat. Spec. Publ. No. 10: 10-18, 1975).

Table IV

- 
1. Psychiatric condition  
1st psychiatric condition  
2nd psychiatric condition  
3rd psychiatric condition
  2. Underlying cause or precipitating factor
  3. Mental subnormality  
educationally subnormal  
subnormal  
severely subnormal
  4. Additional physical illness or handicap
- 

Wing et al's (1968) model of a multi-axial system of classification distinguishes among four axes: (1) Psychiatric condition, (2) Underlying cause or precipitating factor, (3) Mental subnormality and (4) Additional physical illness or handicap. (Based on Wing L, Bramley C, Hailey A, and Wing JK: Camberwell cumulative psychiatric case register. Part I: time and methods. Soc. Psychiat. 3: 116-123, 1968).

Table V

- 
1. Symptoms
  2. Previous duration and course of symptoms
    - A. Duration
      - 1) long-term - first onset more than 2 years ago
      - 2) moderate duration - first onset between 2 months and 2 years ago
      - 3) recent onset - first onset less than 2 months ago
    - B. Course
      - 1) continuous - symptoms constant since onset
      - 2) fluctuating - period(s) of partial remission since onset
  3. Associated factors
    - A. Environmental stresses (e.g. death in family, financial problems)
    - B. Physical illness
      - 1) with central nervous system effects (e.g. central nervous system syphilis)
      - 2) other (e.g. pneumococcal pneumonia)
    - C. Drug or alcohol abuse
    - D. Other associated factors (specify)
  4. Personal relationships
    - A. Very good - frequent and close personal contacts
    - B. Good
    - C. Fair - occasional or troubled personal contacts
    - D. Poor
    - E. Very poor - rare personal contacts or withdrawn
  5. Work function (includes paid work, house work, or schoolwork as student)
    - A. Very good - works regularly and effectively
    - B. Good
    - C. Fair - works part-time and/or with limited effects
    - D. Poor
    - E. Very poor - works rarely or never, or works ineffectively
- 

Strauss' (1975) model of a multi-axial system of classification distinguishes among five axes: (1) Symptoms, (2) Previous duration and course of symptoms, (3) Associated factors, (4) Personal relationship and (5) Work function. (Based on Strauss JS: A comprehensive approach to psychiatric diagnosis. *Amer. J. Psychiat.* 132: 1193-1197, 1975).

APPENDIX II  
PHARMACOTHERAPY OF FUNCTIONAL PSYCHOSES

Antipsychotic-neuroleptics (Table I and II) and monoamine uptake inhibitor tricyclic and non-tricyclic antidepressants (Tables III and IV) employed in treatment.

Table I

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I. Phenthiazines	Chlorpromazine
II. Thioxanthenes	Thiothixene
III. Dibenzoxazepines	Loxapine
IV. Butyrophenones	Haloperidol
V. Diphenylbutylpiperidines	Pimozide
VI. Indole Derivatives	Molindone

---

Six structurally different groups of neuroleptic-antipsychotics with prototype drugs.



Table II

1-11	12-22	23-31
Haloperidol	Promazine	Methylperidol
Chlorpromazine	Clothiapine	Oxypertine
Levomepromazine	Loxapine	Mesoridazine
Thioridazine	Pimozide	Alimenzazine
Fluphenazine	Carpipramine	Trifluoperidol
Perphenazine	Perazine	Clopenthixol
Thiothixene	Reserpine	Molindone
Trifluoperazine	Floropipamide	Spiperone
Sulpiride	Fluspirilene	Moperone
Clozapine	Butaperazine	
Propericiazine	Flupenthixol	

Thirty-one neuroleptics employed in eight countries presented in rank order of frequency of use. (Adapted from Ban TA, Guy W and Wilson WH: Pharmacotherapy of chronic hospitalized schizophrenics: diagnosis and treatment. *Psychiatric Journal of the University of Ottawa* 9: 191-195, 1984).

Table III

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Dibenzazepines	Imipramine
Dibenzodiazepines	Dibenzepin
Dibenzocycloheptadiens	Amitriptyline
Dibenzocycloheptatriens	Protriptyline
Dibenzothiepines	Prothiadene
Dibenzoxepines	Doxepin
Dibenzoxazepines	Amoxapine
Anthracenes	Melitracene
Anthridines	Propazepine
Acridans	Dimethacrine

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Ten structurally different groups of tricyclic antidepressants with prototype drugs. (Adapted from Ban TA: Psychopharmacology of Depression. Karger, Basel, Munchen, Paris, London, New York and Sydney, 1981.)

Table IV

---

Dibenzobicyclo-Octadienes	Maprotiline
Carboxylic Acid Esters, Amides and Amidoximes	Alaproclate
Arylalkyl and Arylcycloalkylamines	Fluvoxamine
Phenoxyalkylamines	Viloxazine
Diaryl and Diaryloxy Derivatives	Fluoxetine
Arylbicyclic Compounds	Citalopram
Oxazoles, Imidazoles and Triazoles	Trazodone
Benzpyrazoles and Benzimidazoles	Clodazone
Condensed Indoles	Tandamin
Quinolines and Tetrahydroiso- quinolines	Nomifensin

---

Ten structurally different cyclic (non-tricyclic) antidepressants with prototype drugs. (Adapted from Ban TA: Psychopharmacology of Depression. Karger, Basel, Munchen, Paris, London, New York and Sydney, 1981.)

APPENDIX III  
INTERNATIONAL CLASSIFICATION OF DISEASES  
9th Edition

Descriptive diagnoses relevant to functional psychoses from the 9th edition of the International Classification of Diseases (ICD-9) (Table 1).

Table 1

---

Other Psychoses (295-299)

295. Schizophrenic psychoses

A group of psychoses in which there is a fundamental disturbance of personality, a characteristic distortion of thinking, often a sense of being controlled by alien forces, delusions which may be bizarre, disturbed perception, abnormal affect out of keeping with the real situation, and autism. Nevertheless, clear consciousness and intellectual capacity are usually maintained. The disturbance of personality involves its most basic functions which give the normal person his feeling of individuality, uniqueness and self-direction. 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 schizophrenic person's thoughts and actions in ways that are often bizarre. He may see himself as the pivot of all that happens. Hallucinations, especially of hearing, are common and may comment on the patient or address him. Perception is frequently disturbed in other ways; there may be perplexity, irrelevant features may become all-important and, accompanied by passivity feelings, may lead the patient to believe that everyday objects and situations possess a special, usually sinister, meaning intended for him. In the characteristic schizophrenic disturbance of thinking, peripheral and irrelevant features of a total concept, which are inhibited in normal directed mental activity, are brought to the forefront and utilized in place of the elements relevant and appropriate to the situation. Thus thinking becomes vague, elliptical and obscure, and its expression in speech sometimes incomprehensible. Breaks and interpolations in the flow of consecutive thought are frequent, and the patient may be convinced that his thoughts are incongruous. Ambivalence and disturbance of volition may appear as inertia, negativism or stupor. Catatonia may be present. The diagnosis "schizophrenia" should not be made unless there is, or has been evident during the same illness, characteristic disturbance of thought, perception, mood, conduct, or personality--preferably in at least two of these areas. The diagnosis should not be restricted to conditions running a protracted, deteriorating, or chronic course. In addition to making the diagnosis on the criteria just given, effort should be made to specify one of the following subdivisions of schizophrenia, according to the predominant symptoms.

Includes: schizophrenia of the types described in 295.0-295.9 occurring in children

Excludes: childhood type schizophrenia (299.9)  
infantile autism (299.0)

Table 1 (continued)

## 295.0 Simple type

A psychosis in which there is insidious development of oddities of conduct, inability to meet the demands of society, and decline in total performance. Delusions and hallucinations are not in evidence and the condition is less obviously psychotic than are the hebephrenic, catatonic and paranoid types of schizophrenia. With increasing social impoverishment vagrancy may ensue and the patient becomes self-absorbed, idle and aimless. Because the schizophrenic symptoms are not clear-cut, diagnosis of this form should be made sparingly, if at all.

## Schizophrenia simplex

Excludes: latent schizophrenia (295.5)

## 295.1 Hebephrenic type

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, accompanied by giggling or self-satisfied, self-absorbed smiling, or by a lofty manner, grimaces, mannerisms, pranks, hypochondriacal complaints and reiterated phrases. Thought is disorganized. There is a tendency to remain solitary, and behaviour seems empty of purpose and feeling. This form of schizophrenia usually starts between the ages of 15 and 25 years.

## Hebephrenia

## 295.2 Catatonic type

Includes as an essential feature prominent psychomotor disturbances often alternating between extremes such as hyperkinesia and stupor, or automatic obedience and negativism. Constrained attitudes may be maintained for long periods: if the patient's limbs are put in some unnatural position they may be held there for some time after the external force has been removed. Severe excitement may be a striking feature of the condition. Depressive or hypomanic concomitants may be present.

Catatonic:  
agitation  
excitation  
stupor

Schizophrenic:  
catalepsy  
catatonia  
flexibilitas cerea

## 295.3 Paranoid type

The form of schizophrenia in which relatively stable delusions, which may be accompanied by hallucinations, dominate the clinical picture. The delusions are frequently of persecution but may take other forms (for example of jealousy, exalted birth, Messianic mission, or bodily change). Hallucinations and erratic behaviour may occur; in some cases conduct is seriously disturbed from

Table 1 (continued)

the outset, thought disorder may be gross, and affective flattening with fragmentary delusions and hallucinations may develop.

#### Paraphrenic schizophrenia

Excludes: paraphrenia, involuntional paranoid state (297.2)  
paranoia (297.1)

#### 295.4 Acute schizophrenic episode

Schizophrenic disorders, other than those listed above, in which there is a dream-like state with slight clouding of consciousness and perplexity. External things, people and events may become charged with personal significance for the patient. There may be ideas of reference and emotional turmoil. In many such cases remission occurs within a few weeks or months, even without treatment.

#### Oneirophrenia

Schizophreniform:  
attack  
psychosis, confusional type

Excludes: acute forms of schizophrenia of:  
catatonic type (295.2)  
hebephrenic type (295.1)  
paranoid type (295.3)  
simple type (295.0)

#### 295.5 Latent schizophrenia

It has not been possible to produce a generally acceptable description for this condition. It is not recommended for general use, but a description is provided for those who believe it to be useful; a condition of eccentric or inconsequent behaviour and anomalies of affect which give the impression of schizophrenia though no definite and characteristic schizophrenic anomalies, present or past, have been manifest.

The inclusion terms indicate that this is the best place to classify some other poorly defined varieties of schizophrenia.

#### Latent schizophrenic reaction

Schizophrenia:  
borderline  
prepsychotic  
prodromal

Schizophrenia:  
pseudoneurotic  
pseudopsychopathic

Excludes: schizoid personality (301.2)

#### 295.6 Residual schizophrenia

A chronic form of schizophrenia in which the symptoms that persist from the acute phase have mostly lost their sharpness. Emotional response is blunted



Table 1 (continued)

and thought disorder, even when gross, does not prevent the accomplishment of routine work.

Chronic undifferentiated schizophrenia  
 Restzustand (schizophrenic)  
 Schizophrenic residual state

#### 295.7 Schizoaffective type

A psychosis in which pronounced manic or depressive features are intermingled with schizophrenic features and which tends towards remission without permanent defect, but which is prone to recur. The diagnosis should be made only when both the affective and schizophrenic symptoms are pronounced.

Cyclic schizophrenia  
 Mixed schizophrenic and affective psychosis  
 Schizoaffective psychosis  
 Schizophreniform psychosis, affective type

#### 295.8 Other

Schizophrenia of specified type not classifiable under 295.0-295.7.

Acute (undifferentiated)  
 schizophrenia

Atypical schizophrenia  
 Coenesthopathic schizophrenia

Excludes: infantile autism (299.0)

#### 295.9 Unspecified

To be used only as a last resort.

Schizophrenia NOS  
 Schizophrenic reaction NOS  
 Schizophreniform psychosis NOS

### 296 Affective Psychoses

Mental disorders, usually recurrent, in which there is a severe disturbance of mood (mostly compounded of depression and anxiety but also manifested as elation and excitement) which is accompanied by one or more of the following: delusions, perplexity, disturbed attitude to self, disorder of perception and behaviour; these are all in keeping with the patient's prevailing mood (as are hallucinations when they occur). There is a strong tendency to suicide. For practical reasons, mild disorders of mood may also be included here if the symptoms match closely the descriptions given; this applies particularly to mild hypomania.

Table 1 (continued)

Excludes: reactive depressive psychosis (298.0)  
 reactive excitation (298.1)  
 neurotic depression (300.4)

296.0 Manic-depressive psychosis, manic type

Mental disorders characterized by states of elation or excitement out of keeping with the patient's circumstances and varying from enhanced liveliness (hypomania) to violent, almost uncontrollable excitement. Aggression and anger, flight of ideas, distractibility, impaired judgement, and grandiose ideas are common.

Hypomania NOS  
 Hypomanic psychosis  
 Mania (monopolar) NOS  
 Manic disorder

Manic psychosis  
 Manic-depressive psychosis or  
 reaction:  
 hypomanic  
 manic

Excludes: circular type if there was a previous attack of depression  
 (296.2)

296.1 Manic-depressive psychosis, depressed type

An affective psychosis in which there is a widespread depressed mood of gloom and wretchedness with some degree of anxiety. There is often reduced activity but there may be restlessness and agitation. There is a marked tendency to recurrence; in a few cases this may be at regular intervals.

Depressive psychosis  
 Endogenous depression  
 Involutional melancholia

Manic-depressive reaction, depressed  
 Monopolar depression  
 Psychotic depression

Excludes: circular type if previous attack was of manic type (296.3)  
 depression NOS (311)

296.2 Manic-depressive psychosis, circular type but currently manic

An affective psychosis which has appeared in both the depressive and the manic form, either alternating or separated by an interval of normality, but in which the manic form is currently present. (The manic phase is far less frequent than the depressive).

Bipolar disorder, now manic

Excludes: brief compensatory or rebound mood swings (296.8)

296.3 Manic-depressive psychosis, circular type but currently depressed

Circular type (see 296.2) in which the depressive form is currently present.

Bipolar disorder, now depressed

Table 1 (continued)

Excludes: brief compensatory or rebound mood swings (296.8)

296.4 Manic-depressive psychosis, circular type, mixed

An affective psychosis in which both manic and depressive symptoms are present at the same time.

296.5 Manic-depressive psychosis, circular type, current condition not specified

Circular type (see 296.2) in which the current condition is not specified as either manic or depressive.

296.6 Manic-depressive psychosis, other and unspecified

Use this code for cases where no other information is available, except the unspecified term, manic-depressive psychosis, or for syndromes corresponding to the descriptions of depressed (296.1) or manic (296.0) types but which for other reasons cannot be classified under 296.0-296.5.

Manic-depressive psychosis:  
NOS  
mixed type

Manic-depressive:  
reaction NOS  
syndrome NOS

296.8 Other

Excludes: psychogenic affective psychoses (298.-)

269.9 Unspecified

Affective psychosis NOS  
Melancholia NOS

297 Paranoid States

Excludes: acute paranoid reaction (298.3)  
alcoholic jealousy (291.5)  
paranoid schizophrenia (295.3)

297.0 Paranoid state, simple

A psychosis, acute or chronic, not classifiable as schizophrenia or affective psychosis, in which delusions, especially of being influenced, persecuted or treated in some special way, are the main symptoms. The delusions are of a fairly fixed, elaborate and systematized kind.

297.1 Paranoia

A rare chronic psychosis in which logically constructed systematized delusions have developed gradually without concomitant hallucinations or the

Table 1 (continued)

Excludes: brief compensatory or rebound mood swings (296.8)

296.4 Manic-depressive psychosis, circular type, mixed

An affective psychosis in which both manic and depressive symptoms are present at the same time.

296.5 Manic-depressive psychosis, circular type, current condition not specified

Circular type (see 296.2) in which the current condition is not specified as either manic or depressive.

296.6 Manic-depressive psychosis, other and unspecified

Use this code for cases where no other information is available, except the unspecified term, manic-depressive psychosis, or for syndromes corresponding to the descriptions of depressed (296.1) or manic (296.0) types but which for other reasons cannot be classified under 296.0-296.5.

Manic-depressive psychosis:  
NOS  
mixed type

Manic-depressive:  
reaction NOS  
syndrome NOS

296.8 Other

Excludes: psychogenic affective psychoses (298.-)

269.9 Unspecified

Affective psychosis NOS  
Melancholia NOS

297 Paranoid States

Excludes: acute paranoid reaction (298.3)  
alcoholic jealousy (291.5)  
paranoid schizophrenia (295.3)

297.0 Paranoid state, simple

A psychosis, acute or chronic, not classifiable as schizophrenia or affective psychosis, in which delusions, especially of being influenced, persecuted or treated in some special way, are the main symptoms. The delusions are of a fairly fixed, elaborate and systematized kind.

297.1 Paranoia

A rare chronic psychosis in which logically constructed systematized delusions have developed gradually without concomitant hallucinations or the

Table 1 (continued)

schizophrenic type of disordered thinking. The delusions are mostly of grandeur (the paranoiac prophet or inventor), persecution or somatic abnormality.

Excludes: paranoid personality disorder (301.0)

#### 297.2 Paraphrenia

Paranoid psychosis in which there are conspicuous hallucinations, often in several modalities. Affective symptoms and disordered thinking, if present, do not dominate the clinical picture and the personality is well preserved.

Involitional paranoid state  
Late paraphrenia

#### 297.3 Induced psychosis

Mainly delusional psychosis, usually chronic and often without florid features, which appears to have developed as a result of a close, if not dependent, relationship with another person who already has an established similar psychosis. The delusions are at least partly shared. The rare cases in which several persons are affected should also be included here.

Folie a deux

Induced paranoid disorder

#### 297.8 Other

Paranoid states which, though in many ways akin to schizophrenic or affective states, cannot readily be classified under any of the preceding rubrics, nor under 298.4

Paranoia querulans

Sensitiver Beziehungswahn

Excludes: senile paranoid state (297.2)

#### 297.9 Unspecified

Paranoid:  
  psychosis NOS  
  reaction NOS  
  state NOS

#### 298 Other nonorganic psychoses

Categories 298.0-298.8 should be restricted to the small group of psychotic conditions that are largely or entirely attributable to a recent life experience. They should not be used for the wider range of psychoses in which environmental factors play some (but not the major) part in aetiology.

Table 1 (continued)

## 298.0 Depressive type

A depressive psychosis which can be similar in its symptoms to manic-depressive psychosis, depressed type (296.1) but is apparently provoked by saddening stress such as a bereavement, or a severe disappointment or frustration. There may be less diurnal variation of symptoms than in 296.1, and the delusions are more often understandable in the context of the life experience. There is usually a serious disturbance of behaviour, e.g., major suicidal attempt.

Reactive depressive psychosis  
Psychogenic depressive psychosis

Excludes: manic-depressive psychosis, depressed type (296.1)  
neurotic depression (300.4)

## 298.1 Excitative type

An affective psychosis similar in its symptoms to manic-depressive psychosis, manic type, but apparently provoked by emotional stress.

Excludes: manic-depressive psychosis, manic type (296.0)

## 298.2 Reactive confusion

Mental disorders with clouded consciousness, disorientation (though less marked than in organic confusion) and diminished accessibility often accompanied by excessive activity and apparently provoked by emotional stress.

Psychogenic confusion  
Psychogenic twilight state

Excludes: acute confusional state (293.0)

## 298.3 Acute paranoid reaction

Paranoid states apparently provoked by some emotional stress. The stress is often misconstrued as an attack or threat. Such states are particularly prone to occur in prisoners or as acute reactions to a strange and threatening environment, e.g., in immigrants.

Bouffee delirante

Excludes: paranoid states (297.-)

## 298.4 Psychogenic paranoid psychosis

Psychogenic or reactive paranoid psychosis of any type which is more protracted than the acute reactions covered in 298.3. Where there is a diagnosis of psychogenic paranoid psychosis which does not specify "acute" this coding should be made.

Protracted reactive paranoid psychosis

Table 1 (continued)

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**298.8 Other and unspecified reactive psychosis**

Hysterical psychosis	Psychogenic stupor
Psychogenic psychosis NOS	

**298.9 Unspecified psychosis**

To be used only as a last resort, when no other term can be used.

Psychosis NOS

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Descriptive ICD-9 diagnoses relevant to functional psychoses.

APPENDIX IV

DIAGNOSTIC AND STATISTICAL MANUAL OF THE  
AMERICAN PSYCHIATRIC ASSOCIATION

3rd Edition



Operationalized Axis I diagnoses relevant to functional psychoses from the 3rd edition of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-III) (Table I); and information relevant to Axes II, IV and V (Tables II, III and IV).

Table 11

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Schizophrenic Disorders

Diagnostic criteria for a Schizophrenic Disorder

- A. At least one of the following during a phase of the illness:
- (1) bizarre delusions (content is patently absurd and has no possible basis in fact), such as delusions of being controlled, thought broadcasting, thought insertion, or thought withdrawal
  - (2) somatic, grandiose, religious, nihilistic, or other delusions without persecutory or jealous content
  - (3) delusions with persecutory or jealous content if accompanied by hallucinations of any type
  - (4) auditory hallucinations in which either a voice keeps up a running commentary on the individual's behavior or thoughts, or two or more voices converse with each other.
  - (5) auditory hallucinations on several occasions with content of more than one or two words, having no apparent relation to depression or elation
  - (6) incoherence, marked loosening of associations, markedly illogical thinking, or marked poverty of content of speech if associated with at least one of the following:
    - (a) blunted, flat, or inappropriate affect
    - (b) delusions or hallucinations
    - (c) catatonic or other grossly disorganized behavior
- B. Deterioration from a previous level of functioning in such areas as work, social relations, and self-care.
- C. Duration: Continuous signs of the illness for at least six months at some time during the person's life, with some signs of the illness at present. The six-month period must include an active phase during which there were symptoms from A, with or without a prodromal or residual phase, as defined below.

Prodromal phase: A clear deterioration in functioning before the active phase of the illness not due to a disturbance in mood or to a Substance Use Disorder and involving at least two of the symptoms noted below.

Residual phase: Persistence, following the active phase of the illness, of at least two of the symptoms noted below, not due to the disturbance in mood or to a Substance Use Disorder.

Table I (continued)

Prodromal or Residual Symptoms

- (1) social isolation
  - (2) marked impairment in role functioning as wage-earner, student, or homemaker
  - (3) markedly peculiar behavior (e.g., collecting garbage, talking to self in public, or hoarding food)
  - (4) marked impairment in personal hygiene and grooming
  - (5) blunted, flat, or inappropriate affect
  - (6) digressive, vague, overelaborate, circumstantial, or metaphorical speech
  - (7) odd or bizarre ideation, or magical thinking, e.g., superstitiousness, clairvoyance, telepathy, "sixth sense," "others can feel any feelings," overvalued ideas, ideas of reference
- D. The full depressive or manic syndrome (criteria A and B of major depressive or manic episode), if present, developed after any psychotic symptoms, or was brief in duration relative to the duration of the psychotic symptoms in A.
- E. Onset of prodromal or active phase of the illness before age 45.
- F. Not due to any Organic Mental Disorder or Mental Retardation.

## 295.1 Diagnostic Criteria for Disorganized Type

A type of Schizophrenia in which there are:

- A. Frequent incoherence
- B. Absence of systematized delusions
- C. Blunted, inappropriate or silly affect.

## 295.2. Diagnostic Criteria for Catatonic Type

A type of Schizophrenia dominated by any of the following:

- (1) catatonic stupor (marked decrease in reactivity to environment and/or reduction of spontaneous movements and activity) or mutism
- (2) catatonic negativism (an apparently motiveless resistance to all instructions or attempts to be moved)
- (3) catatonic rigidity (maintenance of a rigid posture against efforts to be moved)
- (4) catatonic excitement (excited motor activity apparently purposeless and not influenced by external stimuli)
- (5) catatonic posturing (voluntary assumption of inappropriate or bizarre posture)

Table A-11 (continued)

## 295.3 Diagnostic criteria for Paranoid Type

A type of Schizophrenia dominated by one or more of the following:

- (1) persecutory delusions
- (2) grandiose delusions
- (3) delusional jealousy
- (4) hallucinations with persecutory or grandiose content

## 295.9 Diagnostic criteria for Undifferentiated Type

- A. A type of Schizophrenia in which there are: Prominent delusions, hallucinations, incoherence, or grossly disorganized behavior.
- B. Does not meet the criteria for any of the previously listed types or meets the criteria for more than one.

## 295.6 Diagnostic criteria for Residual Type

- A. A history of at least one previous episode of Schizophrenia with prominent psychotic symptoms.
- B. A clinical picture without any prominent psychotic symptoms that occasioned evaluation or admission to clinical care.
- C. Continuing evidence of the illness, such as blunted or inappropriate affect, social withdrawal, eccentric behavior, illogical thinking, or loosening of associations.

## Paranoid Disorders

## Diagnostic criteria for Paranoid Disorder

- A. Persistent persecutory delusions or delusional jealousy.
- B. Emotion and behavior appropriate to the content of the delusional system.
- C. Duration of illness of at least one week.
- D. None of the symptoms of criterion A of Schizophrenia, such as bizarre delusions, incoherence, or marked loosening of associations.
- E. No prominent hallucinations.
- F. The full depressive or manic syndrome (criteria A and B of major depressive or manic episode) is either not present, developed after any psychotic symptoms, or was brief in duration relative to the duration of the psychotic symptoms.
- G. Not due to an Organic Mental Disorder.

Table 1 (continued)

---

297.10 Diagnostic criteria for Paranoia

- A. Meets the criteria for Paranoid Disorder
- B. A chronic and stable persecutory delusional system of at least six months' duration.
- C. Does not meet the criteria for Shared Paranoid Disorder.

297.30 Diagnostic criteria for Shared Paranoid Disorder

- A. Meets the criteria for Paranoid Disorder
- B. Delusional system develops as a result of a close relationship with another person or persons who have an established disorder with persecutory delusions.

298.30 Diagnostic criteria for Acute Paranoid Disorder

- A. Meets the criteria for Paranoid Disorder
- B. Duration of less than six months.

297.90 Atypical Paranoid Disorder

This is a residual category for Paranoid Disorders and classified above.

Psychotic Disorders Not Elsewhere Classified

295.40 Diagnostic criteria for Schizophreniform Disorder

- A. Meets all of the criteria for Schizophrenia except for duration.
- B. The illness (including prodromal, active, and residual phases) lasts more than two weeks but less than six months.

298.80 Diagnostic criteria for Brief Reactive Psychosis

- A. Psychotic symptoms appear immediately following a recognizable psychosocial stressor that would evoke significant symptoms of stress in almost anyone.
- B. The clinical picture involves emotional turmoil and at least one of the following psychotic symptoms:
  - (1) incoherence or loosening of associations
  - (2) delusions
  - (3) hallucinations
  - (4) behavior that is grossly disorganized or catatonic

Table I (continued)

- 
- C. The psychotic symptoms last more than a few hours but less than two weeks, and there is an eventual return to the premorbid level of functioning. (Note: The diagnosis can be made soon after the onset of the psychotic symptoms without waiting for the expected recovery. If the psychotic symptoms last more than two weeks, the diagnosis should be changed.)
  - D. No period of increasing psychopathology immediately preceded the psychosocial stressor.
  - E. The disturbance is not due to any other mental disorder, such as an Organic Mental Disorder, manic episode, or Factitious Disorder with Psychological Symptoms.

#### 295.70 Schizoaffective Disorder

The term Schizoaffective Disorder has been used in many different ways since it was first introduced, and at the present time there is no consensus on how this category should be defined. Some of the cases that in the past were diagnosed as Schizoaffective Disorder would in this manual be diagnosed as Schizophreniform Disorder, Major Depressive or Bipolar Disorder with Mood-congruent or Mood-incongruent Psychotic Features, or Schizophrenia with a superimposed Atypical Affective Disorder. Future research is needed to determine whether there is a need for this category, and if so, how it should be defined and what its relationship is to Schizophrenia and Affective Disorder.

The category is retained in this manual without diagnostic criteria for those instances in which the clinician is unable to make a differential diagnosis with any degree of certainty between Affective Disorder and either Schizophreniform Disorder or Schizophrenia. Before using the Schizoaffective Disorder category, the clinician should consider all of the diagnoses noted in the first paragraph above, particularly Major Affective Disorders with Psychotic Features.

#### 298.90 Atypical Psychosis

This is a residual category for cases in which there are psychotic symptoms (delusions, hallucinations, incoherence, loosening of associations, markedly illogical thinking, or behavior that is grossly disorganized or catatonic) that do not meet the criteria for any specific mental disorder.

#### Affective Disorders

##### Diagnostic criteria for a manic episode

- A. One or more distinct periods with a predominantly elevated, expansive, or irritable mood. The elevated or irritable mood must be a prominent part of the illness and relatively persistent, although it may alternate or intermingle with depressive mood.

Table I (continued)

- 
- B. Duration of at least one week (or any duration if hospitalization is necessary), during which, for most of the time, at least three of the following symptoms have persisted (four if the mood is only irritable) and have been present to a significant degree:
- (1) increase in activity (either socially, at work, or sexually) or physical restlessness.
  - (2) more talkative than usual or pressure to keep talking
  - (3) flight of ideas or subjective experience that thoughts are racing
  - (4) inflated self-esteem (grandiosity, which may be delusional)
  - (5) decreased need for sleep
  - (6) distractibility, i.e., attention is too easily drawn to unimportant or irrelevant external stimuli
  - (7) excessive involvement in activities that have a high potential for painful consequences which is not recognized, e.g. buying sprees, sexual indiscretions, foolish business investments, reckless driving.
- C. Neither of the following dominates the clinical picture when an affective syndrome is absent (i.e., symptoms in criteria A and B above):
- (1) preoccupation with a mood-incongruent delusion or hallucination (see definition below)
  - (2) bizarre behavior
- D. Not superimposed on either Schizophrenia, Schizophreniform Disorder, or a Paranoid Disorder.
- E. Not due to any Organic Mental Disorder, such as Substance Intoxication.
- (Note: A hypomanic episode is a pathological disturbance similar to, but not as severe as, a manic episode.)

#### Diagnostic criteria for major depressive episode

- A. Dysphoric mood or loss of interest or pleasure in all or almost all usual activities and pastimes. The dysphoric mood is characterized by symptoms such as the following: depressed, sad, blue, hopeless, low, down in the dumps, irritable. The mood disturbance must be prominent and relatively persistent, but not necessarily the most dominant symptom, and does not include momentary shifts from one dysphoric mood to another dysphoric mood, e.g., anxiety to depression to anger, such as are seen in states of acute psychotic turmoil. (For children under six, dysphoric mood may have to be inferred from a persistently sad facial expression.)

Table I (continued)

- 
- B. At least four of the following symptoms have each been present nearly every day for a period of at least two weeks (in children under six, at least three of the first four).
- (1) poor appetite or significant weight loss (when not dieting) or increased appetite or significant weight gain (in children under six, consider failure to make expected weight gains)
  - (2) insomnia or hypersomnia
  - (3) psychomotor agitation or retardation (but not merely subjective feelings of restlessness or being slowed down) (in children under six, hypoactivity)
  - (4) loss of interest or pleasure in usual activities, or decrease in sexual drive not limited to a period when delusional or hallucinating (in children under six, signs of apathy)
  - (5) loss of energy; fatigue
  - (6) feelings of worthlessness, self-reproach, or excessive or inappropriate guilt (either may be delusional)
  - (7) complaints or evidence of diminished ability to think or concentrate, such as lowered thinking, or indecisiveness not associated with marked loosening of associations or incoherence
  - (8) recurrent thoughts of death, suicidal ideation, wishes to be dead, or suicide attempt.
- C. Neither of the following dominate the clinical picture when an affective syndrome is absent (i.e., symptoms in criteria A and B above):
- (1) preoccupation with a mood-incongruent delusion or hallucination (see definition below)
  - (2) bizarre behavior
- D. Not superimposed on either Schizophrenia, Schizophreniform Disorder, or a Paranoid Disorder.
- E. Not due to any Organic Mental Disorder or Uncomplicated Bereavement.

#### 296.6 Diagnostic criteria for Bipolar Disorder, Mixed

- A. Current (or most recent) episode involves the full symptomatic picture of both manic and major depressive episodes intermixed or rapidly alternating every few days.
- B. Depressive symptoms are prominent and last at least a full day.

#### 296.4 Diagnostic criteria for Bipolar Disorder, Manic

Currently (or most recently) in a manic episode (if there has been a previous manic episode, the current episode need not meet the full criteria for a manic episode.)



Table I (continued)

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 296.5 Diagnostic criteria for Bipolar Disorder, Depressed

- A. Has had one or more manic episodes
- B. Currently (or most recently) in a major depressive episode (if there has been a previous major depressive episode, the current episode of depression need not meet the full criteria for a major depressive episode.)

## 296.2 Diagnostic criteria for Major Depression

- A. One (296.2) or more (296.3) major depressive episodes
- B. Has never had a manic episode.

## 301.13 Diagnostic criteria for Cyclothymic Disorder

- A. During the past two years, numerous periods during which some symptoms characteristic of both the depressive and the manic syndromes were present, but were not of sufficient severity and duration to meet the criteria for a major depressive or manic episode.
- B. The depressive periods and hypomanic periods may be separated by periods of normal mood lasting as long as months at a time, they may be intermixed, or they may alternate.
- C. During depressive periods there is depressed mood or loss of interest or pleasure in all or almost all, usual activities and pasttimes, and at least three of the following:
 

<ul style="list-style-type: none"> <li>(1) insomnia or hypersomnia</li> <li>(2) low energy or chronic fatigue</li> <li>(3) feelings of inadequacy</li> <li>(4) decreased effectiveness or productivity at school, work, or home</li> <li>(5) decreased attention, concentration, or ability to think clearly</li> <li>(6) social withdrawal</li> <li>(7) loss of interest in or enjoyment of sex</li> </ul>	During <u>hypomanic</u> periods there is an elevated, expansive, or irritable mood and at least three of the following: <ul style="list-style-type: none"> <li>(1) decreased need for sleep</li> <li>(2) more energy than usual</li> <li>(3) inflated self-esteem</li> <li>(4) increased productivity, often associated with unusual and self-imposed working hours</li> <li>(5) sharpened and unusually creative thinking</li> <li>(6) uninhibited people-seeking (extreme gregariousness)</li> <li>(7) hypersexuality without recognition of possibility of painful consequences</li> </ul>
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Table I (continued)

(8) restriction of involvement in pleasurable activities; guilt over past activities	(8) excessive involvement in pleasurable activities with lack of concern for the high potential for painful consequences, e.g., buying sprees, foolish business investments, reckless driving
(9) feeling slowed down	(9) physical restlessness
(10) less talkative than usual	(10) more talkative than usual
(11) pessimistic attitude toward the future, or brooding about past events	(11) overoptimism or exaggeration of past achievements
(12) tearfulness or crying	(12) inappropriate laughing, joking, punning

D. Absence of psychotic features such as delusions, hallucinations, incoherence, or loosening of associations.

E. Not due to any other mental disorder, such as partial remission of Bipolar Disorder. However, Cyclothymic Disorder may precede Bipolar Disorder.

#### 296.70 Atypical Bipolar Disorder

This is a residual category for individuals with manic features that cannot be classified as Bipolar Disorder or as Cyclothymic Disorder. For example, an individual who previously had a major depressive episode and now has an episode of illness with some manic features (hypomanic episode), but not of sufficient severity and duration to meet the criteria for a manic episode. Such cases have been referred to as "Bipolar II."

#### 300.40 Diagnostic criteria for Dysthymic Disorder

- A. During the past two years (or one year for children and adolescents) the individual has been bothered most or all of the time by symptoms characteristic of the depressive syndrome but that are not of sufficient severity and duration to meet the criteria for a major depressive episode.
- B. The manifestations of the depressive syndrome may be relatively persistent or separated by periods of normal mood lasting a few days to a few weeks, but no more than a few months at a time.
- C. During the depressive periods there is either prominent depressed mood (e.g., sad, blue, down in the dumps, low) or marked loss of interest or pleasure in all, or almost all, usual activities and pastimes.

Table I. (continued)

- 
- D. During the depressive periods at least three of the following symptoms are present:
- (1) insomnia or hypersomnia
  - (2) low energy level or chronic tiredness
  - (3) feelings of inadequacy, loss of self-esteem, or self-appreciation
  - (4) decreased effectiveness or productivity at school, work, or home
  - (5) decreased attention, concentration, or ability to think clearly
  - (6) social withdrawal
  - (7) loss of interest in or enjoyment of pleasurable activities
  - (8) irritability or excessive anger (in children, expressed toward parents or caretakers)
  - (9) inability to respond with apparent pleasure to praise or rewards
  - (10) less active or talkative than usual, or feels slowed down or restless
  - (11) pessimistic attitude toward the future, brooding about past events, or feeling sorry for self
  - (12) tearfulness or crying
  - (13) recurrent thoughts of death or suicide
- E. Absence of psychotic features, such as delusions, hallucinations, or incoherence, or loosening of associations.
- F. If the disturbance is superimposed on a preexisting mental disorder, such as Obsessive Compulsive Disorder or Alcohol Dependence, the depressed mood, by virtue of its intensity or effect on functioning, can be clearly distinguished from the individual's usual mood.

#### 296.82 Atypical Depression

This is a residual category for individuals with depressive symptoms who cannot be diagnosed as having a Major or Other Specific Affective Disorder or Adjustment Disorder. Examples include the following:

- (1) A distinct and sustained episode of the full depressive syndrome in an individual with Schizophrenia, Residual Type, that develops without an activation of the psychotic symptoms.
- (2) A disorder that fulfills the criteria for Dysthymic Disorder; however, there have been intermittent periods of normal mood lasting more than a few months.
- (3) A brief episode of depression that does not meet the criteria for a Major Affective Disorder and that is apparently not reactive to psychosocial stress, so that it cannot be classified as an Adjustment Disorder.

Table II

<b>PERSONALITY DISORDERS</b>	
301.00	Paranoid
301.20	Schizoid
301.22	Schizotypal
301.50	Histrionic
301.81	Narcissistic
301.70	Antisocial
301.83	Borderline
301.82	Avoidant
301.60	Dependent
301.40	Compulsive
301.84	Passive-Aggressive
301.89	Atypical, mixed or other personality disorder

Axis II diagnoses of DSM-III: Personality disorders.

Table III

<b>Code</b>	<b>Term</b>	<b>Adult examples</b>	<b>Child or adolescent examples</b>
1	None	No apparent psychosocial stressor	No apparent psychosocial stressor
2	Minimal	Minor violation of the law; small bank loan	Vacation with family
3	Mild	Argument with neighbor; change in work hours	Change in schoolteacher; new school year
4	Moderate	New career; death of close friend; pregnancy	Chronic parental fighting; change to new school; illness of close relative; birth of sibling
5	Severe	Serious illness in self or family; major financial loss; marital separation; birth of child	Death of peer; divorce of parents; arrest; hospitalization; persistent and harsh parental discipline
6	Extreme	Death of close relative; divorce	Death of parent or sibling; repeated physical or sexual abuse
7	Catastrophic	Concentration camp experience; devastating natural disaster	Multiple family deaths
0	Unspecified	No information, or not applicable	No information, or not applicable

Axis IV diagnoses of DSM-III: Severity of psychosocial stressors.

Table IV

Levels	Adult examples	Child or adolescent examples
<b>1 SUPERIOR</b> —Unusually effective functioning in social relations, occupational functioning, and use of leisure time.	Single parent living in deteriorating neighborhood takes excellent care of children and home, has warm relations with friends, and finds time for pursuit of hobby.	A 12-year-old girl gets superior grades in school, is extremely popular among her peers, and excels in many sports. She does all of this with apparent ease and comfort.
<b>2 VERY GOOD</b> —Better than average functioning in social relations, occupational functioning, and use of leisure time.	A 65-year-old retired widower does some volunteer work, often sees old friends, and pursues hobbies.	An adolescent boy gets excellent grades, works part-time, has several close friends, and plays banjo in a jazz band. He admits to some distress in "keeping up with everything."
<b>3 GOOD</b> —No more than slight impairment in either social or occupational functioning.	A woman with many friends functions extremely well at a difficult job, but says "the strain is too much."	An 8-year-old boy does well in school, has several friends, but bullies younger children.
<b>4 FAIR</b> —Moderate impairment in either social relations or occupational functioning, or some impairment in both.	A lawyer has trouble carrying through assignments; has several acquaintances, but hardly any close friends.	A 10-year-old girl does poorly in school, but has adequate peer and family relations.
<b>5 POOR</b> —Marked impairment in either social relations or occupational functioning, or moderate impairment in both.	A man with one or two friends has trouble keeping a job for more than a few weeks.	A 14-year-old boy almost fails in school and has trouble getting along with his peers.
<b>6 VERY POOR</b> —Marked impairment in both social relations and occupational functioning.	A woman is unable to do any of her housework and has violent outbursts toward family and neighbors.	A 6-year-old girl needs special help in all subjects and has virtually no peer relationships.
<b>7 GROSSLY IMPAIRED</b> —Gross impairment in virtually all areas of functioning.	An elderly man needs supervision to maintain minimal personal hygiene and is usually incoherent.	A 4-year-old boy needs constant restraint to avoid hurting himself and is almost totally lacking in skills.
<b>0 UNSPECIFIED</b>	No information.	No information.

Axis V diagnoses of DSM-III: Highest level of adaptive functioning past year.

APPENDIX V

RESEARCH DIAGNOSTIC CRITERIA

The development and various research diagnostic criteria were presented and discussed by Berner, Gabriel, Katschnig, Kieffer, Koehler, Lenz and Simhandl in a book entitled Diagnostic Criteria for Schizophrenic and Affective Disorders, which was published by the World Psychiatric Association in 1983 and distributed by the American Psychiatric Association. The four research diagnostic criteria presented in Tables I-IV are adapted from this volume.



Table I

---

Schizophrenia

For a diagnosis of schizophrenia, A through C are required.

- A. Both of the following are necessary:
1. Chronic illness with at least six months of symptoms prior to the index evaluation without return to the premorbid level of psychosocial adjustment.
  2. Absence of a period of depressive or manic symptoms sufficient to qualify for affective disorder or probable affective disorder.
- B. The patient must have at least one of the following:
1. Delusions or hallucinations without significant perplexity or disorientation associated with them.
  2. Verbal production that makes communication difficult because of a lack of logical or understandable organization. (In the presence of muteness the diagnostic decision must be deferred.)
- C. At least three of the following manifestations must be present for a diagnosis of "definite," and two for a diagnosis of "probable" schizophrenia.
1. Single
  2. Poor premorbid social adjustment or work history
  3. Family history of schizophrenia
  4. Absence of alcoholism or drug abuse within one year of onset
  5. Onset of illness prior to age 40.

Primary Affective Disorders

For a diagnosis of depression, A through C are required.

- A. Dysphoric mood characterized by symptoms such as the following: depressed, sad, blue, despondent, hopeless, "down in the dumps," irritable, fearful, worried, or discouraged.
- B. At least five of the following criteria are required for "definite" depression; four are required for "probable" depression.

Table I. (continued)

- 
1. Poor appetite or weight loss (positive if 2 lb a week or 10 lb or more a year when not dieting).
  2. Sleep difficulty (include insomnia or hypersomnia).
  3. Loss of energy, e.g., fatigability, tiredness.
  4. Agitation or retardation.
  5. Loss of interest in usual activities, or decrease in sexual drive.
  6. Feelings of self-reproach or guilt (either may be delusional).
  7. Complaints of or actually diminished ability to think or concentrate, such as slow thinking or mixed-up thoughts.
  8. Recurrent thoughts of death or suicide, including thoughts of wishing to be dead.
- C. A psychiatric illness lasting at least one month with no preexisting psychiatric conditions such as schizophrenia, anxiety neurosis, phobic neurosis, obsessive-compulsive neurosis, hysteria, alcoholism, drug dependency, antisocial personality, homosexuality and other sexual deviations, mental retardation, or organic brain syndrome. (Patients with life-threatening or incapacitating medical illness preceding and paralleling the depression do not receive the diagnosis of primary depression.)
- D. There are patients who fulfill the above criteria, but who also have a massive or peculiar alteration of perception and thinking as a major manifestation of their illness. These patients are currently classified as having a schizoaffective psychosis (Feighner 1979, 1981).

For a diagnosis of mania, A through C are required.

- A. Euphoria or irritability
- B. At least three of the following symptom categories must also be present.
  1. Hyperactivity (includes motor, social, and sexual activity)
  2. Push of speech (pressure to keep talking)
  3. Flight of ideas (racing thoughts)
  4. Grandiosity (may be delusional)
  5. Decreased sleep
  6. Distractibility
- C. A psychiatric illness lasting at least two weeks with no preexisting psychiatric conditions such as schizophrenia, anxiety neurosis, phobic neurosis, obsessive-compulsive neurosis, hysteria, alcoholism, drug dependency, antisocial personality, homosexuality and other sexual deviations, mental retardation, or organic brain syndrome.

Table VI (continued)

- 
- D. There are patients who fulfill the above criteria, but who also have a massive or peculiar alteration of perception and thinking as a major manifestation of their illness. These patients are currently classified as having a schizoaffective psychosis (Feighner 1979, 1981).

Secondary Affective Disorders

Secondary depression, "definite" or "probable," is defined in the same way as primary depression, except that it occurs with one of the following:

1. A preexisting non-affective psychiatric illness which may or may not still be present.
2. A life-threatening or incapacitating medical illness which precedes and parallels the symptoms of depression.

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St. Louis criteria (Feighner et al., 1972) for schizophrenia and affective disorders. (Adapted from Feighner JP, Robins E, Guze SB, Woodruff RA, Winokur G and Munoz R: Diagnostic criteria for use in psychiatric research. Arch. Gen. Psychiat. 26: 57-63, 1972.

Table II

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Schizophrenic Disorders

A through C are required.

- A. During an active phase of the illness (may or may not now be present) at least two of the following are required for definite and one for probable:
1. Thought broadcasting, insertion, or withdrawal.
  2. Delusions of being controlled (or influenced), other bizarre delusions, or multiple delusions.
  3. Somatic, grandiose, religious, nihilistic, or other delusions without persecutory or jealous content lasting at least one week.
  4. Delusions of any type if accompanied by hallucinations of any type for at least one week.
  5. Auditory hallucinations in which either a voice keeps up a running commentary on the subject's behaviors or thoughts as they occur, or two or more voices converse with each other.
  6. Non-affective verbal hallucinations spoken to the subject.
  7. Hallucinations of any type throughout the day for several days or intermittently for at least one month.
  8. Definite instances of marked formal thought disorder accompanied by either blunted or inappropriate affect, delusions or hallucinations of any type, or grossly disorganized behavior.
- B. Signs of illness have lasted at least two weeks from the onset of a noticeable change in the subject's usual condition (current signs of the illness may not now meet criterion A and may be residual symptoms only, such as extreme social withdrawal, blunted or inappropriate affect, mild formal thought disorder, or unusual thoughts or perceptual experiences).
- C. At no time during the active period (delusions, hallucinations, marked formal thought disorder, bizarre behavior, etc.) of illness being considered did the subject meet the full criteria for either probable or definite manic or depressive syndrome to such a degree that it was a prominent part of the illness.

Manic Disorder

A through E are required for the episode of illness being considered.

- A. One or more distinct periods with a predominantly elevated, expansive, or irritable mood. The elevated, expansive, or irritable mood must be a prominent part of the illness and relatively persistent although it may alternate with depressive mood. Do not include if apparently due to alcohol or drug use.

Table II (continued)

- 
- B. If mood is elevated or expansive, at least three of the following symptom categories must be definitely present to a significant degree, four if mood is only irritable. (For past episodes, because of memory difficulty, one less symptom is required.) Do not include if apparently due to alcohol or drug use.
1. More active than usual, either socially, at work, at home, sexually, or physically restless.
  2. More talkative than usual or feels a pressure to keep talking.
  3. Flight of ideas or subjective experience that thoughts are racing.
  4. Inflated self-esteem (grandiosity, which may be delusional).
  5. Decreased need for sleep.
  6. Distractibility, i.e., attention is too easily drawn to unimportant or irrelevant external stimuli.
  7. Excessive involvement in activities without recognizing the high potential for painful consequences, e.g., buying sprees, sexual indiscretions, foolish business investments, reckless driving.
- C. Overall disturbance is so severe that at least one of the following is present:
1. Meaningful conversation is impossible.
  2. Serious impairment socially, with family, at home, at school, or at work.
  3. In the absence of (1) or (2), hospitalization.
- D. Duration of manic features at least one week beginning with the first noticeable change in the subject's usual condition (or any duration if hospitalized). It became "manic" after hospitalization, the rater should differentiate between manic and hypomanic periods on the basis of apparent severity.
- E. None of the following which suggest Schizophrenia is present. (Do not include if apparently due to alcohol or drug use.)
1. Delusions of being controlled (or influenced), or thought broadcasting, insertion, or withdrawal.
  2. Non-affective hallucinations of any type throughout the day for several days or intermittently throughout a one week period.
  3. Auditory hallucinations in which either a voice keeps up a running commentary on the subject's behaviors or thoughts as they occur, or two or more voices converse with each other.
  4. At some time during the period of illness had more than one week when exhibited no prominent depressive or manic symptoms but had delusions or hallucinations.

Table II (continued)

- 
5. At some time during the period of illness had more than one week when exhibited no prominent manic symptoms but had several instances of marked formal thought disorder, accompanied by either blunted or inappropriate affect, delusions or hallucinations of any type, or grossly disorganized behavior.

#### Hypomanic Disorder

A through D are required.

- A. Has had a distinct period with predominantly elevated, expansive, or irritable mood. The elevated, expansive, or irritable mood must be relatively persistent or occur frequently. It may alternate with depressive mood. Do not include if mood change is apparently due to alcohol or drug use.
- B. If the mood is elevated or expansive, at least two of the symptoms noted in Manic Disorder B must be present, three symptoms if mood is only irritable.
- C. Duration of mood disturbance at least two days. Definite if elevated, expansive, or irritable mood lasted for one week, probable if two to six days.
- D. The episode being considered does not meet the criteria for Schizophrenia, Schizoaffective Disorder, or Manic Disorder.

#### Major Depressive Disorder

A through F are required for the episode of illness being considered.

- A. One or more distinct periods with dysphoric mood or pervasive loss of interest or pleasure. The disturbance is characterized by symptoms such as the following: depressed, sad, blue, hopeless, low, down in the dumps, "don't care anymore," or irritable. The disturbance must be prominent and relatively persistent but not necessarily the most dominant symptom. It does not include momentary shifts from one dysphoric mood to another dysphoric mood, e.g., anxiety to depression to anger, such as are seen in states of acute psychotic turmoil.
- B. At least five of the following symptoms are required to have appeared as part of the episode for definite and four for probable (for past episodes, because of memory difficulty, one less symptom is required).
  - 1. Poor appetite or weight loss or increased appetite or weight gain (change of 1 lb. a week over several weeks or ten lbs. a year when not dieting).
  - 2. Sleep difficulty or sleeping too much.
  - 3. Loss of energy, fatigability, or tiredness.

Table II (continued)

- 
4. Psychomotor agitation or retardation (but not mere subjective feeling of restlessness or being slowed down).
  5. Loss of interest or pleasure in usual activities, including social contact or sex (do not include if limited to a period when delusional or hallucinating). (The loss may or may not be pervasive.)
  6. Feelings of self-reproach or excessive or inappropriate guilt (either may be delusional).
  7. Complaints or evidence of diminished ability to think or concentrate, such as slowed thinking, or indecisiveness (do not include if associated with marked formal thought disorder).
  8. Recurrent thoughts of death or suicide, or any suicidal behavior.
- C. Duration of dysphoric features at least one week beginning with the first noticeable change in the subject's usual condition (definite if lasted more than two weeks, probable if one to two weeks).
- D. Sought or was referred to help from someone during the dysphoric period, took medication, or had impairment in functioning with family, at home, at school, at work, or socially.
- E. None of the following which suggest Schizophrenia is present:
1. Delusions of being controlled (or influenced), or of thought broadcasting, insertion, or withdrawal.
  2. Non-affective hallucinations of any type throughout the day for several days or intermittently throughout a one week period.
  3. Auditory hallucinations in which either a voice keeps up a running commentary on the subject's behaviors or thoughts as they occur, or two or more voices converse with each other.
  4. At some time during the period of illness had more than one month when he exhibited no prominent depressive symptoms but had delusions or hallucinations (although typical depressive delusions such as delusions of guilt, sin, poverty, nihilism, or self-depreciation, or hallucinations with similar content are not included).
  5. Preoccupation with a delusion or hallucination to the relative exclusion of other symptoms or concerns (other than typical depressive delusions of guilt, sin, poverty, nihilism, self-depreciation or hallucinations with similar content).
  6. Definite instances of marked formal thought disorder accompanied by either blunted or inappropriate affect, delusions or hallucinations of any type, or grossly disorganized behavior.
- F. Does not meet the criteria for Schizophrenia, Residual Subtype.
- 

Research diagnostic criteria (Spitzer, Endicott and Robins, 1978) for schizophrenic and affective disorders. (Adapted from Spitzer RL, Endicott, J and Robins E: Research Diagnostic Criteria RDC for a Selected Group of Functional Disorders. 3rd Edition. State Psychiatric Institute, New York, 1978).

Table III

Schizophrenia

The criteria include all of A through D.

- A. At least one of 1 through 3
  - 1. Formal thought disorder (driveling, tangentiality, neologisms, paraphasias, nonsequiturs, private words, stock words)
  - 2. First rank symptoms (at least one)
  - 3. Emotional blunting (a constricted, inappropriate, unrelated affect of decreased intensity, with indifference/unconcern for loved ones, lack of emotional responsivity, and a loss of social graces)
- B. Clear consciousness
- C. No diagnosable affective disorder
- D. No diagnosable coarse brain disease, no past hallucinogenic or psychostimulant drug abuse, and no medical condition known to cause schizophrenic symptoms.

Mania

A diagnosis requires all four of the following criteria:

- A. Hyperactivity
- B. Rapid/pressured speech
- C. Euphoric/expansive/irritable mood, with a broad affect
- D. No diagnosable coarse brain disease, no psychostimulant drug abuse in the past month, and no medical illness known to cause manic symptoms.

Endogenous Depression

The criteria include all three of the following:

- A. Sad, dysphoric, or anxious mood
- B. Three of 1 through 6:
  - 1. early morning waking
  - 2. diurnal mood swing (worse in A.M.)
  - 3. weight loss of more than five pounds in three weeks



Table III (continued)

- 
4. retardation or agitation
  5. suicidal thoughts/behavior
  6. feelings of guilt/hopelessness/worthlessness
- C. No diagnosable coarse brain disease, no use of steroids or reserpine in past month, and no medical illness known to cause depressive symptoms.
- 

Taylor/Abrams criteria (Taylor and Abrams 1978; Taylor, Redfield and Abrams, 1981) for schizophrenia, mania and endogenous depression. (Based on Taylor MA and Abrams R: The prevalence of schizophrenia: A reassessment using modern diagnostic criteria. *Am. J. Psychiat.* 135: 945-948; 1978 and Taylor, MA, Redfield J and Abrams R: Neurophysiological dysfunction in schizophrenia and affective disease. *Biological Psychiatry* 16: 467-478, 1981).

Table IV

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Endogenomorphic-Schizophrenic Axial Syndrome

- A. Incoherence without marked pressure or retardation of thinking or marked autonomous anxiety. At least one of the following symptoms required:
1. Blocking  
Sudden cessation in the train of thought; after a gap the previous thought may (a) or may not (be) be taken up again
  2. Derailment  
Gradual (a) or sudden (b) deviation from the train of thought without gap
  3. Pathologically "muddled speech"  
Fluent speech, for the most part correct syntax, but the elements of different thoughts (which, for the patient, may belong to a common idea) get muddled together
- B. Cryptic neologisms  
(the patient does not explain their private meaning spontaneously)
- C. Affective blunting (without evidence of marked depression, tiredness, or drug effect). It includes flatness of affect, emotional indifference, and apathy. Essentially, the symptom involves a discrimination of emotional response.

Definitive: A and/or B Present

Probably: Only C Present

Endogenomorphic-Depressive Axial Syndrome

A and B obligatory

- A. Appearance of marked changes in affectivity, emotional resonance, or drive following a period of habitual functioning. At least one of the following symptoms is required.
1. Depressive mood (with or without anxiety)
  2. Emotional resonance either lacking or limited to depressive responses
  3. Reduced drive or agitation
- B. Appearance of biorhythmic disturbances. Symptoms 1 and 2 are required.
1. Diurnal variations of one or more of the symptoms under A.
  2. Shortened sleep.

Table IV (continued)

Endogenomorphic-Dysphoric Axial Syndrome

A and B obligatory

- A. Appearance of marked changes in affectivity, emotional resonance, or drive following a period of habitual functioning. At least one of the following symptoms required:
1. Irritable mood (dysphoria)
  2. Emotional resonance limited to hostile responses
  3. Increased readiness to hostile acting out.
- B. Appearance of biorythmic disturbances. Symptoms 1 and 2 are required.
1. Diurnal variations of one or more of the symptoms under A.
  2. Sleep disturbance (At least one of the following symptoms required)
    - a. interrupted sleep
    - b. early awakening

Endogenomorphic-Axial Syndrome of Unstable Mixed States

A and B obligatory

- A. Appearance of rapidly alternating swings in affectivity, emotional resonance, or drive following a period of habitual functioning. At least one of the following symptoms required:
1. Rapidly alternating swings between depressive and/or anxious, euphoric/expansive, or hostile mood.
  2. Rapidly alternating and exaggerated emotional resonance touching various affective states (depressive, anxious, manic, hostile).
  3. Rapid change between inhibition, agitation, increased drive, and occasionally aggression. (The rapid swinging can bring about "concordant" changes in affectivity and drive--for example, manic mood combined with decreased drive--because each element may swing in a different biorythmi).
- B. Appearance of biorythmic disturbances. Symptoms 1 and 2 are required.
1. Diurnal variations of one or more of the symptoms under A.
  2. Sleep disturbances. At least one of the following symptoms required
    - a. interrupted sleep
    - b. early awakening

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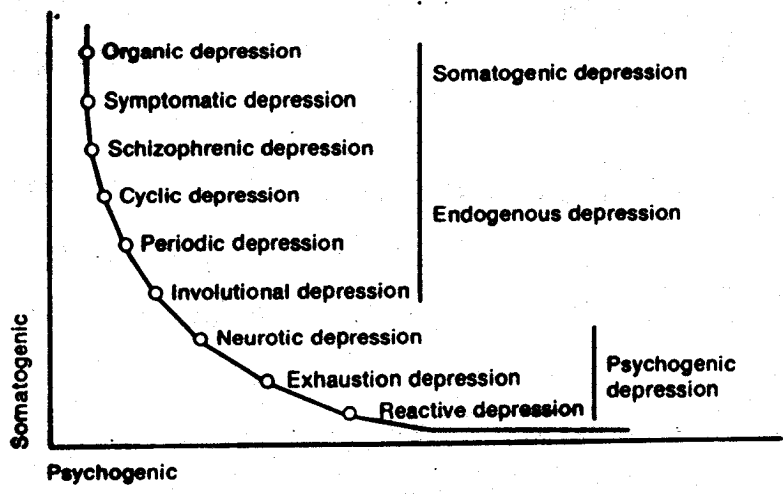
The Vienna Research Criteria (Berner and Katschnig, 1983) for endogenomorphic axial syndromes. (Based on Berner P and Katschnig: Principles of "multi-axial classification in psychiatry as a basis of modern methodology. In Helgason T. ed.: Methods in Evaluation of Psychiatric Treatment. Cambridge University Press, Cambridge, 1983).

APPENDIX VI

CLASSIFICATIONS OF DEPRESSIONS

The development of different systems of classification of depression are presented by Ban in his book entitled Psychopharmacology of Depression, which was published by Karger in 1981. The four classifications presented in Figure 1 and Tables I-III are adapted from this book.

Figure 1



Kielholz's (1972) classification of depressive states. (Based on Kielholz P: Diagnostic aspects in the treatment of depression. In Kielholz P ed.: Depressive Illness. Diagnosis, Assessments, Treatment. Hans Huber, Bern, 1972).

Table I

Authors	Year	Endogenous	Neurotic	Psychotic
Kiloh and Garside	1963	Age over 40	Responsive to environmental change	
		Depression worse in morning	Self-pity	
		Weight loss 7 lbs or more	Initial insomnia	
Kendell	1968		Anxiety	Disturbance of food intake
			Tension	Weight loss
			Brief durations of illness	Delusions of guilt and unworthiness

The separation of endogenous from neurotic depressions by Kiloh and Garside (1963) and of psychotic from neurotic depression by Kendell (1968). (Based on Kiloh LG and Garside RF: The independence of neurotic depression and endogenous depression. *Br. J. Psychiat.* 109: 451-463, 1963 and Kendell RE: *The Classification of Depressive Illness*. Oxford University Press, London, 1968).

Table II

	Primary Depression	Secondary Depression
Obligatory	Absence of preexisting non-affective psychiatric disorder	Presence of preexisting non-affective psychiatric disorder, and/or
	Not associated with medical illness	Associated with medical illness
Facultive	Psychomotor dysfunction	Lifelong depressive coping style
	Vegetative dysfunction	More but less serious suicide attempts
	Dysphoria	Hostility
	Hopelessness	Difficulty
	Worthlessness	Difficulties in falling asleep
	Guilt	Somatization
	Suicidal preoccupation	

Andreasen and Winokur's (1979) symptoms and signs of primary and secondary depressions. (Based on Andreasen NC and Winokur J: Newer experimental methods for classifying depression. A report from the NIMH Collaborative Pilot Study. Arch. Gen. Psychiat. 36: 447-452, 1979).



Table III

Diagnoses	Definition	Characteristics
Pure Depression	Family history of only affective disorder	Late onset (over 40) Equal sex distribution Equal incidence of primary and secondary depression
Depressive Spectrum Disease	Family history of other than affective disorders; e.g., alcoholism antisocial personality	Early onset (before 40) Female prevalence Equal incidence of primary and secondary depression
Nonfamilial or Sporadic Depression	No family history of psychiatric illness	More often primary than secondary

Winokur's (1979) genetic classification of depression. (Based on Winokur G: Unipolar depression. Is it divisible into autonomous subtypes? Arch. Gen. Psychiat. 36: 47-52, 1979).

APPENDIX VII

DIAGNOSTIC CRITERIA OF SCHIZOPHRENIA

Frequently employed criteria for the diagnosis of schizophrenia are presented in Tables I-V in chronological order of their development.

Table I

FUNDAMENTAL OR BASIC SYMPTOMS	PRIMARY SYMPTOMS
1. Disorder (loosening) of associations	Disturbance of associations
2. Disorder (inappropriateness) of affect	Clouded States
3. Ambivalence (simple functioning)	Affective changes
4. Autism (complex function)	Possibly hallucinations
5.	Possibly stereotypy
6.	Physical changes

Bleuler's (1911) fundamental (basic) and primary symptoms of schizophrenia.  
 (Based on Bleuler E: Dementia Praecox oder Gruppe der Schizophrenien.  
 Deuticke, Leipzig, 1911).

Table II

- 
1. The hearing of one's thoughts spoken aloud within one's head (Gedankenlautwerden)
  2. The hearing of voices that comment on what one is doing at the time
  3. Experiences of bodily influence
  4. Thought withdrawal and other forms of thought interference
  5. Thought diffusion (Gedankenansbreitung)
  6. Delusional perception
  7. Everything in the spheres of feeling, drive, and volition which the patient experiences as imposed on him or influenced by others
- 

Schneider's (1957) first rank symptoms of schizophrenia. (Based on Schneider K: Primäre und sekundäre Symptomen bei Schizophrenie, Fortschr. Neurol. Psychiat. 25: 487-490, 1957).

Table III

- 
1.
    - a. Delusions (not specified or other than depressive)
    - b. Hallucinations (auditory)
    - c. Hallucinations (visual)
    - d. Hallucinations (other)
  2. Crazy thinking and/or thought disorder. Any of the following:
    - a. Bizarre thinking
    - b. Autism or grossly unrealistic private thoughts
    - c. Looseness of associations, illogical thinking, overinclusion
    - d. Blocking
    - e. Concreteness
    - f. Derealization
    - g. Depersonalization
  3. Inappropriate affect
  4. Confusion
  5. Paranoid ideation
  6. Catatonic behavior
    - a. Excitement
    - b. Stupor
    - c. Waxy flexibility
    - d. Negativism
    - e. Mutism
    - f. Encholalia
    - g. Stereotyped motor activity
- 

The New Haven Schizophrenia Index developed by Astrachan et al. (1972).

To be considered as part of the schizophrenic group, the patient must score on either item 1 or items 2a, 2b, 2c and must attain a total score of at least four points.

He can achieve a maximum of four points on item 1: two for the presence of delusions, two for hallucinations.

On item 2 he can score two points for any of symptoms a through c, one point for either or both symptoms d through e, and one point each for f and g. He can thus score a maximum of five points on items 2.

Items 3, 4, 5 and 6 each receive one point.

NOTE: Where the fourth point necessary for inclusion in the sample is provided by 2d or 2e, these symptoms are not scored.

(Based on Astrachan BM, Harrow M, Adler D, Brauer L, Schwartz A and Schwartz C: A checklist for the diagnosis of schizophrenia. Br. J. Psychiatry 121: 529-539, 1972).

Table IV

- 
1. Restricted affect
  2. Poor insight
  3. Poor rapport
  4. Incoherent speech
  5. No waking early
  6. No depressed facies
  7. Thoughts aloud/thought broadcasting
  8. Widespread delusions
  9. Bizarre delusions
  10. Nihilistic delusions
  11. No elation
  12. Unreliable information
- 

The Flexible System Criteria for the Diagnosis of Schizophrenia, also referred to as the CSB System (Carpenter, Strauss and Bartko, 1973). The presence of five of the 12 items qualifies for a wider concept of schizophrenia and the presence of six for a narrower concept. (Based on Carpenter WT, Strauss JS and Bartko JJ: Flexible system for the diagnosis of schizophrenia. Report from the WHO International Pilot Study of Schizophrenia. Science 182: 1275-1278, 1973).

Table V

---

A through E are necessary

- A. Age of onset 40 or below
- B. Onset: acute (first episode with a diagnosis of "bouffee delirante") or progressive with or without abnormal premorbid personality and/or abnormal psychosocial adjustment.
- C. Chronicity: active phases are followed by residual phase marked by permanent deficit of variable severity
- D. Characteristic symptoms (at least two of the following four symptom groups):
  - 1. Markedly illogical: unrealistic, bizarre, and/or magical thinking
  - 2. Inappropriate affect: blunted, flat, and/or discordant affect and/or ambivalence
  - 3. Formal thought disorder: loosening of associations, inefficient thinking, incoherent speech
  - 4. Delusional ideas: fragmented and do not develop into delusional system
- E. Not due to an organic psychosis, alcoholism or drug abuse

---

The French Empirical Diagnostic Criteria for Schizophrenia by Pull, Pull and Pichot (1981). (Based on Pull CB, Pull CM and Pichot P: Empirical diagnostic criteria for schizophrenia and related non-affective psychoses in France. Paper presented at the Conference "Concepts of Schizophrenia," 4-6 October 1981, Cologne, FRG. Adapted from Berner G, Gabriel E, Katschnig H, Kieffer W, Koehler K, Lenz G and Simhandl Ch: Diagnostic Criteria for Schizophrenic and Affective Psychoses. World Psychiatric Association, 1983).



APPENDIX VIII

CLASSIFICATIONS OF SCHIZOPHRENIAS

Frequently employed classifications of schizophrenias are presented in Tables I-IV in chronological order of their development.

Table I

- 
1. Cure
  2. Cure with defect
  3. Simple deterioration
  4. Imbecility with confusion of speech
  5. Hallucinatory deterioration
  6. Hallucinatory insanity
  7. Dementia paranoides
  8. Flighty, silly deterioration
  9. Dull, apathetic dementia
- 

Kraepelin's (1919) nine different end-states of schizophrenia. (Based on Kraepelin E: *Dementia Praecox and Paraphrenia*. Translated by R.M. Barclay, Edinburgh, Livingston, 1919).

Table II

- I. Symptomatological criteria - Significant clues for a diagnosis of schizophrenia are (if no sign of organic brain disorder, infectious or intoxication can be demonstrated):
- Changes in personality, which manifest as emotional blunting, loss of initiative, and peculiar behavior. (In hebephrenia, these changes are the main clues for the diagnosis).
  - In catatonia patient's history as well as periods of restlessness and stupor (with negativism, oily facies, catalepsy, special negative symptoms, etc.).
  - In paranoid psychoses essential manifestations are split personality, depersonalization, derealization and/or primary delusions.
  - Chronic hallucinations.
- II. Course criterion - A final decision about diagnosis cannot be made before a followup period of at least five years has shown a chronic course of the disease.

<u>Schizophrenic</u> (Unfavorable prognostic factors)	<u>Schizophreniform</u> (Favorable prognostic factors)
1. An emotionally and intellectually poor premorbid personality	An emotionally and intellectually premorbid personality
2. No demonstrable precipitatory factors	Demonstrable precipitatory factors
3. Insidious onset	Acute onset
4. Symptoms of autism and emotional blunting. Particularly unfavorable prognostic factors are depersonalization and derealization with clear consciousness	Mixed clinical picture, manic-depressive traits, cloudiness, symptoms of organic and psychogenic origin, and lacking of blunted affect
5. An unfavorable environment before and after the outbreak of the disease	A favorable environment before and after the outbreak of the disease

Langfeldt's (1937, 1939) criteria for schizophrenic psychoses with an unfavorable outcome and schizophreniform psychoses with a favorable outcome. (Based on Langfeldt G: The Prognosis in Schizophrenia and the Factors Influencing the Course of the Disease. Munksgaard, Copenhagen, 1937 and Oxford University Press, London, 1937; and Langfeldt G: The Schizophreniform States. Munksgaard, Copenhagen, 1939, Oxford University Press, London, 1939. Adapted from Berner P, Gabriel E, Katschnig H, Kieffer W, Koehler K, Lenz G and Simhandl Ch: Diagnostic Criteria for Schizophrenia and Affective Psychoses, World Psychiatric Association, 1983).

Table III

- 
1. Continuous schizophrenia
    - a. sluggish form (latent, pseudoneurotic, pseudopsychopathic, paranoid)
    - b. malignant juvenile (hebephrenic, malignant catatonic, malignant juvenile paranoid)
    - c. moderately progressive (delusional and hallucinatory schizophrenia with an onset of middle age)
  2. Periodic (recurrent) schizophrenia
    - a. with a prevalence of encephaloid-catatonic episodes
    - b. with a prevalence of circular-affective episodes
    - c. with a mixed and changeable structure of episodes
  3. Shift-like progressive schizophrenia
    - a. with a sluggish pseudoneurotic development and affective cyclothymic episodes
    - b. moderately progressive - with a sluggish pseudopsychopathic development, distinct paranoid disturbance in intervals and affective delusional episodes.
    - c. crude - progressive juvenile forms with pseudopsychopathic, delusional disturbances in intervals and catatonohebephrenic episodes.
- 

Snezhnewski's (1966) classification of schizophrenias. (Based on Nadzharow RA: The clinical aspect of biological investigation of the pathogenesis of schizophrenia. Transactions of Symposium on Biological Research in Schizophrenia, Moscow, 1967. Adapted from Berner P, Gabriel E, Katschnig H, Kieffer W, Koehler K, Lenz G and Simhandl Ch: Diagnostic Criteria for Schizophrenic and Affective Psychoses. World Psychiatric Association, 1983).

Table IV

	Type I Syndrome	Type II Syndrome
1. Symptoms	Positive symptoms delusions hallucinations thought disorder	Negative symptoms affective flattening poverty of speech loss of volition
2. Type of illness	Acute schizophrenia	Chronic schizophrenia
3. Response to neuroleptics	Good	Poor
4. Intellectual impairment	Absent	Sometimes present
5. Outcome	Reversible	Irreversible (?)
6. Pathological process	Increased dopamine receptors	Cell loss and structural changes in the brain

Crow's (1980) Type I and Type II Syndromes; differential characteristics.  
(Based on Crow TJ: Molecular pathology of schizophrenia; more than one disease process? Brit. Med. J. 280: 66-68, 1980).

APPENDIX IX

GUIDES TO LEONHARD'S CLASSIFICATION

Guides to Leonhard's classification of chronic schizophrenias developed by Fish (1964) and Ban (1982) are presented in Tables I (a,b, and c) and II (a,b and c) respectively.



Table Ia

Symptoms and Signs	Phonemic	Hypochondriacal	Expansive	Confabulatory	Fantastic	Incoherent
Phonemes	+	+			+	+
Voices complained of		-				
Content complained of	+					
Voices from own body	+					
Seen speaking to voices at times	+					+
Voices attributed to other persons	+					
Birds and inanimate objects speak					+	
Aversion due to phonemes						+
Speaks to voices continuously						+
<b>Bodily Hallucinations</b>						
Unpleasant but not detailed		-				
Fantastic		-				
Sexual						
Visual hallucinations						
Scenic hallucinations						
Mass hallucinations					+	
<b>Delusions</b>						
Persecutory, related to phonemes	=					
Grandiose			+	+		
Fantastic				+		
Misidentifications				++		
Confabulations					=	
<b>Mood and Affect</b>						
Slight blunting	+					
Slight blunting with depression						
Euphoria			+	+		
Working ability	G	G	F.P	P	P	Nil
Thought disorder	=	=	+	++	++	++

G = good; F = fair; P = poor.

Symptoms and signs of systematic paraphrenias according to Fish (1964). (Adapted from Fish FJ: A guide to the Leonhard classification of chronic schizophrenia. Psychiat. Quart. 38: 438-450, 1964).

Table Ib

Symptoms and Signs	Artistic	Eccentric	Shallow	Silly
Hallucinatory excitements			+	
<b>Mood</b>				
Cheerful or contented			+	+
Depressed and irritable	+	+		
<b>Attitude</b>				
Giggling or smiling				+
Apathetic indifference			+	
Depressed and querulous		+		
Rejecting all contact	+			
<b>General Behavior</b>				
Mannerisms, especially collecting		+		
Restless and interfering				+
Spiteful tricks				+
Working ability	G	F	F-P	P

G - good; F - fair; P - poor.

Symptoms and signs of systematic hebephrenias according to Fish (1964). (Adapted from Fish FJ: A guide to the Leonhard classification of chronic schizophrenia. Psychiat. Quart. 38: 438-450, 1964).

Table Ic

Symptoms and Signs	Parakinetic	Speech-prompt	Prokinetic	Speech-inactive	Manneristic	Negativistic
<b>Disorders of Motor Performance</b>						
Ambitendency						+
Mannerism					+	+
Jerkiness	+					
<b>Abnormal Spontaneous Movements</b>						
Stereotypy			+			
Parakinesia and grimacing	+		+			
Handing and intertwining					+	+
Impulsive actions						
<b>Abnormally Induced Movements</b>						
Echopraxia			+			
Perseveration			+			
Forced grasping			+			
Mitgehen			+			
Mitmachen (cooperation)			+			
Gegenhalten (opposition)					+	
<b>Abnormal Postures</b>						
Manneristic					+	
Generalized rigidity					+	
Twisted						
Haltungsverharren (waxy flexibility)					+	
Psychological pillow					+	
<b>Abnormal Attitudes</b>						
Marked aversion			+			++
Marked aversion				+		+
True negativism						
<b>Speech</b>						
Jerky	+					
Vorbereden						
Murmuring and verbigeration			+			
Whispering to phonemes				+		
Mutism						
Partial answers, ambitendency					+	

Symptoms and signs of systematic catatonias according to Fish (1964). (Adapted from Fish FJ: A guide to the Leonhard classification of chronic schizophrenia. Psychiat. Quart. 38: 438-450, 1964).

Table IIa

No.	General Features (Items)	Affect-laden Paraphrenia	Paraphrenias					Hebephrenias			Catatonias				
		Catatonia Periodic Catatonia	Phonemic Hypochondriacal Expansive Confabulatory Fantastic Incoherent						Autistic Eccentric Shallow Silly		Parakinetic Speech Prompt Proskinetik Speech Inactive Humoristic Negativistic				
1.	Rapid onset	+++													
2.	Insidious onset		+++++					++++			+++++				
3.	Paranoid and/or grandiose delusions		+++++												
4.	Auditory and/or other hallucinations		++		++										
5.	Blunted affect and/or lack of initiative							++++							
6.	Dereistic thinking and/or autistic behavior							++++							
7.	Disorder of movement and/or speech		+								+++++				
8.	Loss of grace of movements		+								+++++				
9.	Intermittent - episodic	+++													
10.	Processual with slow progress		++												
11.	Processual with moderate progress			++				++							
12.	Processual with fast progress					++		++			+++++				
13.	Good working ability	+++	++					+							
14.	Some working ability			+				++							
15.	No working ability					+++			+		+++++				
16.	Mild defect	+++	++					+							
17.	Moderate effect			+				++							
18.	Marked defect					+++			+		+++++				

Ban's (1982) guide to Leonhard's classification of schizophrenias (Form One). (Adapted from Ban TA: Chronic schizophrenias: A guide to Leonhard's classification. Comprehensive Psychiatry 23: 155-170, 1982).

Table Iib

Sub-population	Statements	Subtype
<i>Non-systematic</i>	Paranoid delusions with affective loading and mood swings; disgusted and irritated when delusions discussed and threatening when delusions challenged.	Affect-laden Paraphrenia
	Confusion of speech with well ordered behavior; pressure of speech with grammatical mistakes or inhibition of speech and thinking with neologisms.	Cataphasia
	Episodic hyperkinesia or hypokinesia (akinesia) with loss of natural grace of movements or aimless movements; mixed excitatory and inhibitory symptoms.	Periodic Catatonia
<i>Systematic-Paraphrenia</i>	Verbal hallucinations (voices of people) comment on or talk to patient; replies to hallucinatory voices. Thoughts spoken aloud and/or broadcasting with wooly thinking.	Phonemic
	Bizarre bodily hallucinations with irritable, morose, dissatisfied mood; verbal hallucinations of disconnected phrases. Passivity experience, the feeling that one's thoughts are under external control.	Hypochondriacal
	Expansive delusions with haughty pose; coarsening of thinking.	Expansive
	Vivid and detailed description of alleged experiences (falsification of memory) which may sometimes happen in a trance or dream-like state with perceptual falsifications.	Confabulatory
	Fantastic delusions with mixed (bodily and visual) hallucinations; misidentification of people. Scenic hallucinations with derailment of thinking.	Fantastic
	Incoherence of thinking and confusion of speech with disordered behavior; massive auditory hallucinations and permanent hallucinatory distraction.	Incoherent
<i>Systematic-Hebephrenia</i>	Extreme autism with stiff face and offputting verbal responses; episodic aggressive outbursts.	Autistic
	Hypochondriac and querulous complaintativeness with hoarding and senseless stealing; takes no care of self.	Eccentric
	Extreme Flatness of affect with meager symptomatology; episodic outbursts with hallucinatory excitements.	Shallow
	Inane giggling and smiling with spiteful tricks; can answer simple questions but unable to carry out ordered conversation.	Silly
<i>Systematic-Catatonia</i>	Excessive unnatural-awkward voluntary and jerky involuntary expressive movements with facial grimacing and chopped up speech.	Parakinetic
	Obedient answering, but talking beside the point; empty facial expression	Speech Prompt
	Cooperation in movements; verbigeration of isolated phrases: monotonous mumbling speech.	Proskinetik
	Replies slowly or remains mute; whispering to oneself in reference to inner voices; screams and gesticulates to inner experiences.	Speech Inactive
	Stiff movements and posture with manneristic omissions and stereotype attitudes; waxy flexibility.	Manneristic
	Aversion with ambivalence or opposition; negativistic excitements.	Negativistic

Ban's (1982) guide to Leonhard's classification of schizophrenias (Form Two). (Adapted from Ban TA: Chronic schizophrenias: A guide to Leonhard's classification. *Comprehensive Psychiatry* 23: 155-170, 1982).

Table IIc

No.	Psychopathological Symptom	a	b	c	d	e	f	g	h	i	k	m	n	o	p	q	r	s
1.	Paranoid delusions with affective loading.....+																	
2.	Disgusted and irritated when delusions discussed...+																	
3.	Threatening when delusions challenged.....+																	
4.	Affective swings into anxiety (depression) and ecstasy (elation).....+																	
5.	Confusion of speech with well ordered behavior.....+																	
6.	Pressure of speech with grammatical mistakes.....+																	
7.	Inhibition of speech with neologisms.....+																	
8.	Hyperkinesia with loss of natural grace of movements...+																	
9.	Hypokinesia (or akinesia) with aimless movements.....+																	
10.	Verbal hallucinations (voices of people) comment on or talk to patient.....+																	
11.	Thought spoken aloud and/or broadcasting.....+																	
12.	Wooly thinking.....+																	
13.	Bizarre bodily hallucinations.....+																	
14.	Verbal hallucinations of disconnected phrases.....+																	
15.	Complaints about hallucinatory voices but not of their content.....+																	
16.	Passivity experience, thoughts under external control.....+																	
17.	Expansive delusions.....+																	
18.	Haughty attitude.....+																	
19.	Coarsening of thinking.....+																	
20.	Falsification of memory.....+																	
21.	Dream-like experiences.....+																	
22.	Vivid and detailed description of alleged experiences.....+																	
23.	Fantastic delusions with mixed (auditory, visual and/or bodily) hallucinations.....+																	
24.	Scenic hallucinations.....+																	
25.	Derailment of thinking.....+																	
26.	Confusion of speech with disordered behavior.....+																	
27.	Incoherence of thinking.....+																	
28.	Active autism.....+																	
29.	Stiff face.....+																	
30.	Off-putting verbal responses.....+																	
31.	Hypochondriacal and querulous complaintiveness.....+																	
32.	Senseless stealing and hoarding.....+																	
33.	No care of self.....+																	
34.	Meager symptomatology.....+																	
35.	Hallucinatory excitement.....+																	
36.	Inane giggling and smiling.....+																	
37.	Spiteful tricks.....+																	
38.	Parakinetic movements.....+																	
39.	Facial grimacing.....+																	
40.	Chopped-up speech.....+																	
41.	Obedient answering.....+																	
42.	Talks besides the point.....+																	
43.	Adversion.....+																	
44.	Automatic obedience and/or cooperation in movements.....+																	
45.	Verbigeration of isolated phrases.....+																	
46.	Replies slowly or remains mute.....+																	
47.	Screaming and gesticulation to inner experiences.....+																	
48.	Manneristic omissions with stereotype attitudes.....+																	
49.	Stiff movements and posture.....+																	
50.	Waxy flexibility.....+																	
51.	Aversion.....+																	
52.	Ambitendency.....+																	
53.	Opposition.....+																	

a = affect-laden paraphrenia; b = cataphasia; c = periodic catatonia; d = phonemic paraphrenia; e = hypochondriacal paraphrenia; f = expansive paraphrenia; g = confabulatory paraphrenia; h = fantastic paraphrenia; i = incoherent paraphrenia; j = autistic hebephrenia; k = eccentric hebephrenia; l = shallow hebephrenia; m = silly hebephrenia; n = parakinetic catatonia; o = speech prompt; p = proskinetik catatonia; q = speech inactive catatonia; r = manneristic catatonia; and s = negativistic catatonia.

Ban's (1982) guide to Leonhard's classification of schizophrenias (Form Three). (Adapted from Ban TA: Chronic schizophrenias: A guide to Leonhard's classification. Comprehensive Psychiatry 23: 155-170, 1982).

APPENDIX X

CYCLOID PSYCHOSES: DIFFERENTIAL CHARACTERISTICS

Differential characteristics of cycloid psychoses from other psychoses are presented in Tables I-III.



Table I

	Cycloid	Manic	Depressive	Schizo- phrenic	Schizo- affective
<b>Cycloid features</b>					
Delusions/hallucinations	100	68	44	99	100
Perplexity	88	3	13	16	37
Motility disturbances	48	7	0	10	4
Panxiety	41	8	8	14	27
Ecstasy	10	3	0	0	2
Mood swings	100	62	13	3	8
<b>Conventional features</b>					
Depression alone	0	0	87	22	73
Elation alone	0	37	0	4	19
Thought disorder	70	11	3	26	24
Auditory hallucinations	59	11	13	62	49
Visual hallucinations	26	8	5	16	16
Paranoid delusions	32	26	18	67	57
Delusions of reference	48	15	16	33	47
First rank symptoms	53	8	3	60	40

Differential characteristics of patients with cycloid psychoses from some of the other psychoses. The entries represent the percentage of patients in any group exhibiting the feature. Adapted from Cutting, JC, Clare AW and Mann AH: Cycloid psychosis: an investigation of the diagnostic concept. *Psychological Medicine*, 8: 637-648, 1978).

Table II

Diagnosis	No. of Patients	Full Recovery
Psychoses	233	67%
Cycloids	30	90%
Cycloids with CATEGO dg. of Schizophrenia	24	92%
Non-cycloids with CATEGO dg. of Schizophrenia	102	59%

Outcome for 30 patients with cycloid psychoses in comparison to patients with schizophrenic psychoses. (Based on Brockington IF, Perris C and Meltzer HY: Cycloid psychoses. Diagnosis and heuristic value. The Journal of Nervous and Mental Diseases 170: 651-656, 1982).

Table III

Diagnosis	Recovery from Index Episode	Percentage of Patients with One or More Readmissions	Admission Rate Per Year	Time Spent in Hospital in Months
Cycloids	90%	72%	.28	.86
Depression	87%	24%	.06	.24
Mania	74%	53%	.18	.46
Schizophrenia	51%	68%	.20	2.52

Outcome for 73 patients with cycloid psychosis in comparison to other psychotics. (Based on Cutting JC, Clare AW and Mann AH: Cycloid psychosis: an investigation of the diagnostic concept. *Psychological Medicine* 8: 637-648, 1978; Adapted from Brockington IF, Perris C and Meltzer HY: Cycloid Psychoses. *Diagnosis and heuristic value. The Journal of Nervous and Mental Diseases* 170: 651-656, 1982).

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