

**Textbooks on Clinical Medicine
for International Students**



PSYCHIATRY

Chief Editor
Gao Chengge

**XI'AN JIAOTONG
UNIVERSITY**

Dean's Office of Xi'an Jiaotong University
November 2004

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Foreword

Since our university first admitted international students in 1995, we have fostered many qualified medical workers for the neighboring countries. At the same time, we have developed an outstanding teaching team, who take the lead in teaching foreign students medicine all in English at home.

Although we are among the first to accept international students and have formed our own particular educational system, we have noticed that we should make improvements in the teaching materials. For many years, we have been using original edition of foreign textbooks combined with individual teaching materials of the lecturers. We have long thought of compiling a complete set of textbooks of our own.

To our pleasure, in the celebration of the tenth year of commencing medical education for international students, with the painstaking efforts of the Dean's Office, and active participation of our staff, the English textbooks on clinical medicine for international students in our university are finally printed.

There are 15 textbooks in the set, all of which are compiled according to the characteristics of clinical education and the demand of develop of the subjects, and by teachers who are engaged in the clinical education of international students. The textbooks are students – centered, and the materials accord with the requirements for the medical students.

This set of textbooks is especially for the use of medical international students in our university. It can also be used by the students of the long – schooling and five – year schooling.

In the process of compiling the textbooks, we have been encouraged and supported by the president of the First Hospital of Xi'an Jiaotong University, Li Xu, and the vice president, He Dalin; the section chief and vice section chief of the Office of International Communication, Feng Zhenping, and Song Yuxia; and the teachers in the Teaching Department of the First Hospital. We'd like to take this chance to express our sincere gratitude for those who take part in the great task.

It's the first time we did such work. We are most appreciative of your advice.

A handwritten signature in black ink, appearing to read 'Ma Zhaoming', with a stylized, cursive script.

Ma Zhaoming

November 2004

Preface

This book is written as an introductory textbook for clinical medical students (Chinese students and foreign students) and trainee psychiatrists. We hope that the book will also be useful for purposes of revision and reference to psychiatrists who have completed their training and to general practitioners and other clinicians.

The subject matter of this book is practice of clinical psychiatry. Recent years have seen the increasing development of sub – specialties such as child and adolescent psychiatry, forensic psychiatry, and psychiatry of mental retardation. This book is mainly concerned with general psychiatry, our purpose has been to provide an introduction to each subject, rather than a fully documented account.

This book inclines in 10 parts. The parts 1 – 3 deal mainly with the etiology, classification and diagnosis of mental illnesses and psychiatric signs & syndromes . The parts 4 – 5 mainly discuss mental , delirium, amnesic disorders and substance – related disorders. The parts 6 – 9 mainly discuss anxiety disorders, hysteria, mood disorders and schizophrenia. The part 10 mainly discusses treatment of mental illnesses.

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Part 1 Introduction

Chapter 1 Conception

Psychiatry

Psychiatry is a section of medicine. It is a clinical medicine that studies causes, mechanisms, clinical syndromes or signs, prognosis, diagnosis and treatment of mental illnesses. Psychiatry has many branches, for example, community psychiatry, consultation – liaison psychiatry, geriatric psychiatry, child psychiatry, transcultural psychiatry, judicial psychiatry, Biological psychiatry, clinical psychiatry, etc.

Mental illness or mental disease

Mental Illnesses or Mental Diseases express the disorders in cognition, affection, will, behavior, etc. The disorders are caused by many factors and the social function of patients who suffer from mental illnesses is weakened. Mental Illnesses incline psychosis, mood disorders, anxiety disorders, mental retardation, personality disorders, etc.

Mental health

Mental Health involves in the prevention and treatment of mental illnesses and mental hygiene in normal persons. Its aims are preventing and reducing mental disorders.

Chapter 2 Neurochemistry in psychiatry

The focus of this section will be on the neurotransmitter systems in the central nervous

system that are most relevant to psychiatry. Some of the technological advances that have contributed to a better understanding of psychiatric illnesses will be discussed.

Dopamine

Dopamine, together with its close relative norepinephrine, mediates motivation, arousal, and the reward – reinforcement system. Alterations in dopamine neurotransmission contribute to the pathogenesis of schizophrenia and Parkinson's disease. Many drugs of abuse appear to increase amount of dopamine in the synapse; some investigators have proposed dopamine as a final common pathway in addictions and novelty – seeking behavior.

Dopamine and psychiatric illnesses: The dopamine hypothesis of schizophrenia proposes that patients with this illness have excessive activities in the dopamine system, particularly the D2 receptors in the mesolimbic or mesocortical pathways. The major supports for this hypothesis are that the clinical potency of most antipsychotics correlates strongly with their ability to block D2 receptors and that many drugs such as amphetamine and cocaine that can cause psychotic behaviors are known to increase the amount of dopamine in the synaptic cleft. Some schizophrenic patients appear to have low monoamine oxidase activity, which will reduce the rate of degradation of dopamine and thus increase its amount in the synapses. Post-mortem examinations of the brains of patients with schizophrenia have revealed an increased number of D2 – like binding sites; however, this may be partially attributed to the effects of neuroleptic medications.

Dopamine also plays a role in mood disorders, although to a lesser extent than norepinephrine. The level of dopamine has been found by some investigators to be low in some depressed patients and high in some manic patients.

Norepinephrine

Norepinephrine (also known as noradrenaline) plays a major role in regulation of mood, anxiety, and vigilance or arousal. In physiology it is often discussed together with its close relative epinephrine (also known as adrenaline) which is important in systemically autonomic arousal but appears to play a relatively minor role in the central nervous system.

Norepinephrine and psychiatric illnesses: The first monoamine hypothesis of affective illness stated that underactivity of norepinephrine or serotonin might cause depression and that increased activity in these pathways could result in mania. This hypothesis first arose when

researchers noted that reserpine, which depletes and inhibits storage of catecholamines and serotonin, caused depression. They then noted that effective antidepressant drugs increased the amount of catecholamines and serotonin in the synapse either their presynaptic reuptake or by blocking their presynaptic reuptake or by blocking their degradation. This hypothesis has been revised to account for chronic changes in receptor activity and sensitivity in antidepressant therapy. Studies of patients after 1 – 3 weeks of antidepressant drug treatment have shown increased α_1 – re – receptor sensitivity, increased norepinephrine release and decreased postsynaptic β – and presynaptic α_2 – receptor activity and sensitivity. Current models of mood disorder highlight the importance of disequilibrium in the noradrenergic system, rather than a simple overall increase or decrease in noradrenergic activity.

Norepinephrine is also involved in panic disorder. Yohimbine, a selective α_2 – receptor antagonist, reproduces panic symptoms immediately in susceptible individuals. Researches in schizophrenia have focused on the role of dopamine but overactivity of norepinephrine may play a role as well.

Serotonin

Serotonin plays a key role in mood, the perception of pain and basic activities such as feeding, the sleep – wake cycle, motor activity, sexual behavior and temperature regulation. Serotonin is involved in presynaptic regulation of release of other transmitters and affects many endocrine functions including prolactin, cortisol, growth hormone and possibly β – endorphin release.

Serotonin and psychiatric illnesses: Serotonin is involved in regulation of mood, anxiety and aggression. The actual situation is more complex as serotonin has broad regulatory functions and low levels can destabilize many neurotransmitter systems.

Some researchers have also postulated a role for the serotonin system in schizophrenia. Major support for this hypothesis comes from the study of the potent hallucinogenic drug LSD, which has a very high affinity for 5 – HT_{2c} receptors. In addition, many of the atypical antipsychotics are potent blockers of serotonin receptors, particularly the 5 – HT_{2a} and 5 – HT_{2c} subtypes.

Acetylcholine

In normal central nervous system, the cholinergic neurons are thought to modulate arous-

al, learning, memory, rapid eye movement sleep, pain perception and thirst. It is the main neurotransmitter for the parasympathetic system. Perhaps the most significant role of the cholinergic system in disease occurs in Alzheimer's dementia.

Acetylcholine and psychiatric illnesses: Acetylcholine plays an important role in learning and memory and derangements in the cholinergic system are associated with Alzheimer's dementia. A specific destruction of the cholinergic neurons of the nucleus basalis of Meynert has been observed in at least a subgroup of patients with this disorder. Dementia in general is associated with a decrease in the concentration of acetylcholine in the temporal neocortex, hippocampus and amygdala. Attempts of choline precursors, such as lecithin, in the diet have been disappointing but clinical researches on cholinergic agonists are continuing.

Dopamine and acetylcholine share a dynamic balance in the nigrostriatal pathway involved in the initiation and coordination of muscle movement. Parkinson's disease, characterized by inhibited voluntary movement, is associated with a relative deficiency of dopamine and an excess of acetylcholine, whereas Huntington's chorea and Tourette's syndrome, characterized by increased abnormal involuntary movements, are associated with a relative excess of dopamine and a deficiency of acetylcholine in this pathway. A recent research also implicates a genetic polymorphism in a nicotinic receptor subunit in a subset of schizophrenic patients.

Acetylcholine and psychiatric medications: Many commonly used psychiatric medications are anticholinergic and can cause a number of adversely side effects due to their blockade of the parasympathetic system. Many psychotropic drugs, including tricyclic antidepressants, monoamine oxidase inhibitors and neuroleptics, have anticholinergic effects such as blurred vision, dry mouth, sinus tachycardia, constipation and urinary retention. Because of antipsychotic medications block effects in patients, these side effects can be treated with anticholinergic agents.

γ - Aminobutyric Acid

γ - Aminobutyric Acid (GABA) is the most common inhibitory amino acid neurotransmitter, presenting in perhaps 60% of the synapses in human central nervous system. In normal brain, GABA systems are crucial to the moment - to - moment interactions of neurons, the braking system of brain, in a sense. The GABA systems are important in anxiety, seizures and in the actions of benzodiazepines, barbiturates and alcohol.

GABA and psychiatric illnesses: GABA is the most abundant inhibitory neurotransmit-

ter in brain and coexists in neurons with a wide range of neurotransmitters including serotonin, dopamine, acetylcholine, glutamate, glycine, histamine and peptides such as endorphins. GABA is postulated to have a direct role in anxiety disorders and alcoholism. Because of its wide – ranging regulatory role, GABA has also been implicated in the pathophysiology of schizophrenia, Huntington's disease, Parkinson's disease, epilepsy, tardive dyskinesia and senile dementia. GABA is not likely to provide a "single – bullet" explanation for these disorders but it is involved through its extensive interactions with other neurotransmitters.

Chapter 3 Aetiology of Mental Disorder

The causes of psychiatry are complex. In psychiatry, the study of causation is complicated by two problems. Both of these problems are met in other branches of medicine, but to a less degree.

The first problem is that causes are often remote in time from the effects they produce. For example it is widely believed that childhood experiences partly determine the occurrence of neuroses in adult life. It is difficult to test this idea because the necessary information can only be gathered either by studying children and tracing them many years later, which is difficult; or by asking adults about their childhood experiences, which is unreliable.

The second problem is that a single cause may lead to several effects. For example deprivation of parental affection in childhood has been reported to predispose to antisocial behavior, suicide, depressive illness and several other disorders. Conversely, a single effect may arise from several different causes.

The latter can be illustrated either by different causes in different individuals or by multiple causes in a single individual. For example, mental handicap (single effect) may occur in several children but the cause may be a different genetic abnormality in each child. On the other hand depressive illness (single effect) may occur in one individual through a combination of causes such as genetic factors, adverse childhood experiences, and stressful events in adult life.

The classification of causes

A single psychiatric disorder, as just explained, may result from several causes. For this

reason, a scheme for classifying causes is required. An useful approach is to divide causes chronologically into predisposing, precipitating and perpetuating.

Predisposing factors

These are factors, and many of them are operated from early life, that determine a person's vulnerability to causes acting closely to the time of the illness. many of them operating from early life, They include genetic endowment and the environment in utero, as well as physical, psychological and social factors in infancy and early childhood. The term constitution is often used to describe the mental and physical make – up of a person at any point in life. This make – up changes as life goes on, under the influence of further physical, psychological and social influences. Some writers restrict the term constitution to the make – up at the beginning of life. Whilst others also include characteristics acquired later (this second usage is adopted in this book). The concept of constitution includes the idea that a person may have a predisposition to develop a disorder (such as schizophrenia) even though the latter never manifests it. From the standpoint of psychiatric aetiology, one of the important parts of the constitution is the personality.

When the aetiology of an individual case is formulated, the personality is always an essential element. For this reason the clinicians should be prepared to spend considerable time in talking to the patient and to people who know him, in order to build up a clear picture of his personality. This assessment usually helps to explain why the patient responded to certain stressful events and why he reacted in a particular way. The obvious importance of personality in the individual patient contrasts with the small amount of relevant scientific information so far available. In the evaluation of personality, therefore, it is particularly important to acquire sound clinical skills through supervised practice.

Precipitating factors

These are events that occur shortly before the onset of a disorder and appear to have induced it. They may be physical, psychological or social. Whether they produce a disorder at all and what kind of disorder they produce, depend partly on constitutional factors in the patient (as mentioned above). Physical precipitating factors include, for example, cerebral tumors or drugs. Psychological and social precipitants include personal misfortunes such as the loss of a job and changes in the routine of life such as moving home. Sometimes the same factor can act in more than one way for example a head injury can induce psychological disorder.

der either through physical changes in the brain or through its stressful implications to the patient.

Perpetuating factors

These factors prolong the course of a disorder after it has been provoked. When planning treatment, it is particularly important to give attention to these factors. The original precipitating factors may have ceased to act by the time the patient is seen, and the predisposing factors may be well treatable. For example, in their early stages many psychiatric disorders lead to secondary demoralization and withdrawal from social activities, which in turn help to prolong the original disorder. It is often appropriate to treat these secondary factors whether or not any specific measure is carried out.

Biological, psychological, social factors and psychiatric illnesses

Engel suggested interrelatedness among biological, psychological and social factors. Biological factors included anatomic and molecular factors and those factors related to gender, age, ethnicity and genetics. Psychological factors were related to the individual's personality. According to Engel's theory, social factors included family, society, culture and environment and other authors would include religious and spiritual as well as economic factors in this group.

Genetic factors

A scientific revolution has occurred in the field of genetics with the advent of molecular biological techniques. Using these techniques, researchers have located genes, in specific regions of chromosomes, for many neuropsychiatric diseases. After strong evidence for inheritance of a disorder has been found through family, twin and adoption studies, the tools of molecular biology can be used to locate the relevant gene(s) and designate the precise abnormality.

Three types of population genetic studies – family, twin and adoption studies – are conducted to ascertain whether a particular human phenomenon is genetically influenced.

Family studies

Family studies can answer three critical questions concerning the inheritance of a human phenomenon: First, is the phenomenon found more frequent in the blood of relatives of affected individuals compared to relatives of control subjects? That is, are relatives of affected subject at increased risk for the disorder compared to relatives of control subjects? Second,

are other phenomena (possibly genetically related) what also found more frequent in relatives of affected individuals? That is, may other disorders share a common genetic vulnerability with the phenomenon in question? Third, can a specific mode of inheritance be discerned?

Affective disorders: Family studies of affective disorders have continually demonstrated aggregation of illness in relatives. In a study at the National Institute of Mental Health, 25% of relatives of bipolar probands were found to have bipolar disorder or unipolar illness (depression) themselves, compared to 20% of relatives of unipolar probands and 7% of relatives of control subjects. In the same study, 40% of the relatives of schizoaffective probands - demonstrated affective illness at some point in their lives. These data demonstrate increased risk in relatives of patients and they also show that the various forms of affective illness appear to be related in a hierarchical way. Relatives of schizoaffective probands may have schizoaffective illness themselves but are more likely to have bipolar or unipolar illness. Relatives of bipolar probands have either bipolar or (more likely) unipolar illness.

Schizophrenia: Pooled family study data from Europe show an age - corrected morbid risk for schizophrenia of 5.6% in parents, 10.1% in siblings and 12.8% in children. It is thought that the lower rate in parents is related to a relative decrease in fertility among schizophrenic patients. Because general population figures for morbid risk for schizophrenia are around 1% , all classes of first - degree relatives have a clear increase in prevalence. The risk for offspring of two schizophrenic parents is difficult to estimate because of the small number of cases but probably runs between 35% and 45% (in the pooled data it is 46.3%). Among second - degree relatives (eg, uncles, aunts, nephews, nieces, grandchildren), half - siblings and cousins, the risk ranges from 2% to 4% .

Close relatives of schizophrenic patients are at about a 5 - to 10 - fold excess risk for the illness and the risk diminishes in more distant relatives. An additional group of first - degree relatives appear to develop related or so - called spectrum disorders; however, the majority of close relatives of schizophrenic patients are psychiatrically normal.

Twin studies

Twin studies are based on the fact that monozygotic (MZ) or identical twins represent a natural experiment in which two individuals have the exact same genes. This is in contrast to dizygotic (DZ) or fraternal twins who share 50% of their genes and are no more genetically similar than any pair of siblings. A phenomenon that is under genetic control should be more concordant (i. e. similar) in MZ twins than in DZ twins. By comparing the concordance rate

(how often the second member of a twin pair demonstrates the phenomenon in question when the first member has it) for MZ and DZ twin pairs, investigators can obtain evidence for the genetic determination of a phenomenon. Concordance may be reported as pairwise (each pair of twin is counted once) or probandwise (each affected subject is considered together with his or her co – twin). If twin pairs are identified through affected subjects the probandwise method may be more correct.

Affective disorders: Twin studies show consistent evidence for heritability. On average, MZ twin pairs show concordance 65% of the time and DZ twin pairs show concordance 14% of the time.

Schizophrenia: Twin studies of schizophrenia are summarized and several points may be made with reference to these data. This is consistent with a spectrum concept (i. e. some individuals with the genetic loading for schizophrenia. This is consistent somewhat different condition). Third, the amount of discordance is considerable and even with a broad definition of illness, the total discordance in the twins is 51%.

Adoption studies

Adoption studies represent the strongest test of inheritance of a disorder within the field of population genetics. In the most straightforward type of adoption study, a group of affected subjects who have been adopted are identified. Similarly, a control group of unaffected and adopted subjects are identified. The risk for the disorder is then evaluated in four groups of relatives: the adoptive and the biological adoptive relatives of control adoptees. If the disorder is heritable, one should find an increased risk among the biological relatives of affected subjects compared to the other three groups of relatives. One can also compare risk for illness in adopted – away children of ill parents to risk for illness in adopted – away children of well parents.

Affective disorders: Several adoption studies have focused on affective illness. The results have been generally consistent with genetic hypotheses. In one study, the risk for affective disorder in biological relatives of bipolar probands was 31% as opposed to 2% in relatives of control probands. The risk in biological relatives of adopted bipolar probands was similar to the risk in relatives of bipolar probands who were not adopted away (26%). Adoptive relatives did not show increased risk. Adoption studies that used a broader class of affective probands showed evidence for genetic factors but also possible environmental influences. In some of these studies, adoptive relatives of affective probands had a greater tendency to devel-

op affective illness themselves compared to adoptive relatives of control subjects. These data suggest that genetic factors are more prominent in bipolar illness than in other forms of affective illness.

Schizophrenia: A series of large, systematic studies were based on adoption and psychiatric hospitalization registries in Denmark. In later studies in the series, adoptees were separated from their biological parents at an early age and adopted by nonrelatives. More schizophrenia and schizophrenia spectrum disorders were present in biological relatives of schizophrenic adoptees than in biological relatives of psychiatrically normal adoptees and the prevalences of psychiatric illnesses in adoptive relatives of the two groups were small and comparable.

The frequency of schizophrenia spectrum disorders is higher in adopted – away offspring of schizophrenic parents than in adopted – away offspring of normal parents. These studies have been criticized for the methods used to select subjects, the validity of the diagnoses and the validity of comparisons. However, further independent analysis of the data has confirmed the essential results: biological relatives of schizophrenic patients who have not shared the same environment have a significantly higher prevalence of schizophrenia and schizophrenic spectrum disorders than biological relatives of comparable control groups do.

Up to 30% of first – degree relatives of schizophrenic patients have associated disorders. The particular diagnostics that seem to be implicated are schizotypal personality disorder, paranoid personality disorder and schizoid personality disorder. Older studies used the term borderline schizophrenia to include some individuals who had these personality disorders. Other researchers have argued for a separate entity characterized by paranoid delusions only (e. g. simple delusional disorder) with inheritance independent of schizophrenia and affective disorder.

High – risk studies

Biochemical studies of individuals with psychiatric diseases are always confounded by disease effects. For example, are biochemical differences between affected individuals and control subjects related to the cause of the disorder, or are they related to the effects of the disorder (or its treatment)? When investigating possible biochemical differences for a genetic disease, researchers can address this difficult issue by studying a group of individuals (usually adolescents or young adults) who are at a high risk to develop the disorder under study (usually because they have parents or other relatives with the disorder). The high risk group

may then be followed over time to assess whether the biochemical abnormalities observed are predictive diseases.

Psychological and social factors

Stress

Discussions about stress are often confusing because the term is used in two ways. First, it is applied to events or situations that may have an adverse effect on someone, for example working for an examination. Second, it is applied to the adverse effects that are induced, which may be psychological or physiological changes. In considering aetiology it is advisable to separate these components.

The first set of factors can usefully be called stressors. They include a large number of physical, psychological and social factors in the environment that have potential to produce adverse effects. The term is sometimes extended to include events that are not experienced as adverse at the time though they may still have adverse long-term effects. For example intense competition may produce an immediate feeling of pleasant tension though it might lead to unfavourable long-term effects in some cases.

Psychosocial and environmental problems that may cause mental disorders may be a negative life event, an environmental difficulty or deficiency, a familial or other interpersonal stress, an inadequacy of social support or personal resources or other problem relating to the context in which a person's difficulties have developed. So-called positive stressors, such as job promotion, should be listed only if they constitute or lead to a problem when a person has difficulty adapting to the new situation. In addition to playing a role in the initiation or exacerbation of a mental disorder, psychosocial problems may also develop as a consequence of a person's psychopathology or may constitute problems that should be considered in overall management plan.

Age

Persons in different age groups are at risk for different illnesses and health problems. Congenital abnormalities and premature birth contribute to most deaths of infants during birth and contribute to most deaths of infants during their first year. Many of these are related to maternal risk factors during pregnancy such as poor nutrition, smoking, the use of alcohol and other drugs, pregnancy over age 38 and lack of prenatal care. Young persons die mostly from accidents (primarily automobile accidents) and suicides. People over age of 65 suffer predominantly from chronic illnesses such as arthritis, hypertension and heart disease. Rates