PSYCHOCHEMOTHERAPY

The Physician's Manual

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FOREWORD

"Psychochemotherapy" was written to provide the practicing physician with a timely, accurate and usable guide to the treatment of certain emotional illnesses. It was considered important to delineate the mental health problem, to review the classfication of mental disease, and to consider the biochemical hypotheses of these disorders before attempting a discussion of the psychochemicals themselves.

An effort has been made to describe the rationale for the use of these agents and to give specific information about their indications and contraindications, effects and side effects, advantages and disadvantages. In order to keep the contents as current as possible, some investigational drugs are mentioned which have not been accepted for marketing at the time of publication. For the convenience of the busy practitioner a compendium of psychotropic drugs, their indications, dosage, side effects and contraindications is included as an appendix.

The rapidly changing field of psychopharmacology requires periodic revision of concept and content. It is hoped that this volume serves a worthwhile purpose as a concise description of today's theories and facts about the drugs that influence behavior.

The authors gratefully acknowledge the work of Elton Gustafson, technical researcher and science writer, in doing much of the painstaking research required in selecting and organizing the literature, and providing the documentation for this monograph.

THE AUTHORS

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CHAPTER I

Mental Illness: Today's No. 1 Medical Problem

"There is a great pleasure in combatting with success a violent bodily disease, but what is this pleasure compared with that of restoring a fellow creature from the anguish and folly of madness and of reviving in him the knowledge of himself, his family, his friends, and his Gods!"

(Benjamin Rush, 1810, Address to the Managers of the Pennsylvania Hospital).

More than a century and a half ago, before the age of medical specialization, Dr. Rush was indeed the prototype of a general practitioner. Distinguished in many ways, not the least as a patriot, Continental Army doctor, signer of the Declaration of Independence, and the first American epidemiologist, his career as a healer was marked by a catholicity of interest, a scientific curiosity about anything and everything that affected the health and welfare of all mankind, including the wretched, abandoned unfortunates condemned to the inhuman existence of the insame asylum. Because of his pioneering contributions to probably the most difficult of medical specialties, he is justly known today as the "Father of American Psychiatry."

A shrewd observer, self-trained in the art of groping for diagnostic signs, he described many forms of mental illness and elaborated a theory of causation, centering it mainly in the blood vessels of the brain, but triggered by severe stress, organic disease, injury, tumors, poisons and sudden shock. He was the first to recognize insanity as an illness deserving medical attention instead of abuse, punishment and imprisonment. Accordingly, he campaigned for humane and understanding treatment of the insane and their separation from other patients. Some of his therapeutic innovations – physical and occupational therapy, mental catharsis ("talking out" the disease), shock ("sudden excitements"), even by electricity – were far in advance of his time.

The modern physician might well ask: *How far have we progressed in 150 years in elucidating the causes of mental disorders, in establishing meaningful diagnostic categories, and in bringing relief to the emotionally*

and mentally ill? In fact, is it yet fully recognized and accepted by either layman or physician that mental illness like physical illness means disease? The heritage of centuries still crudely or subtly permeates the attitude of the "modern" community toward its emotionally disturbed members. Except in the most sophisticated groups mental illness is not "respectable" and its sufferers in varying degrees must bear the added burden of disguised but nonetheless punitive rejection. To be called diabetic is to be recognized as a sufferer from a bodily illness; to be called neurotic is to be depreciated as a person.

Yet, within recent years some noticeable change in attitude has taken place. This is reflected in the gradual abandonment, at least by professionals, of such terms as "insanity," "lunacy," "madness"; the "lunatic asylum" has been replaced by the "mental hospital"; "derangement" is now "psychiatric illness." One way to measure the advance is to recall that only a generation ago the American Journal of Psychiatry was called the American Journal of Insanity!

The altered attitude toward mental illness began with the spread of psychoanalytic thinking in Europe and America. It has been markedly influenced in the last decade by the concept of specific chemotherapy for psychic disturbances. Chemical agents not only have brought new hope for all the mentally ill, but tangible evidence of a new era in the treatment of severely disturbed patients. There is a changed atmosphere in mental institutions. A new calm and quiet pervades the former ghastly "back wards," where the violent were under forcible restraint and the deeply depressed under constant surveillance against attempts at self-destruction. Now there are open wards and unlocked doors, and the disorder, confusion, untidiness and destruction of clothing and bedding by the neglected unfortunates have been largely eliminated. Patients who required tube feeding now take food voluntarily within a few days after the start of medication, they are more able to care for themselves, and their activities can be constructively directed into rehabilitative and useful channels.

If the new drugs can alter the emotional states and behavior of patients formerly doomed to a lifetime of hopelessness, restore calm to the mentally anguished, and reduce, in many cases eliminate, the burdens of families and society, we have indeed crossed the threshold of a new era in medicine, and are nearer to a solution of the problems relating to the diagnosis, prevention and treatment of mental illness.

While chemotherapy has very nearly made older methods obsolete – fever therapy, insulin shock, leukotomy, lobotomy and to some extent electroconvulsive therapy – and ushered in a whole new approach to

mental and emotional disease, at the same time the problem has become greatly magnified: *the extent of mental illness has so increased in our century that it now constitutes the greatest single group of diseases.*

The cold statistics are staggering. Between 1903 and 1952 the public

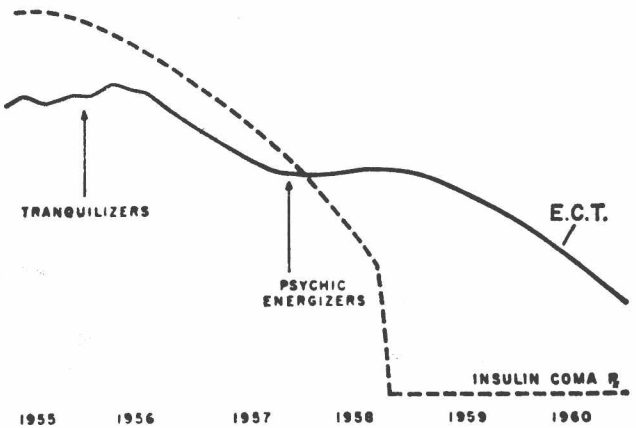

Figure 1. ***Chronological incidence of use of ECT and insulin coma therapy. The falling trend in the use of ECT and insulin coma therapy with the introduction of 1) tranquilizers and 2) psychic energizers. From: Feldman, P. E., Dis. Nerv. Syst. 22 (5) 27, 1961.***

mental hospital population quadrupled (from 133,000 to 532,000) while the country's total population doubled. In 1955, nearly half a million new and returned patients were admitted to mental hospitals and psychiatric units of general hospitals, and more than half of these were admitted for the first time. In 1960, there were well over half a million resident patients in state and county hospitals, at an annual per capita maintenance cost of $1721, and the cost for mental patients in public hospitals in the United States is about 3 million dollars per day.

The figures for public institutions only begin to suggest the enormity of the problem. Since the terms emotional illness and mental illness are semantically relative terms, no one can accurately state how large a segment of our total population falls in these categories. However, some estimates suggest that close to 10 per cent of our population (17 million persons) suffer from some form of mental illness. Half of the patients seen in the every day office practices of physicians suffer from psychiatric illnesses. Ten per cent of public school children are emotionally disturbed and need mental guidance. At least 200,000 children receive treatment each year at mental health clinics. Approximately 5 million children and adults, about 3 per cent of our entire population, are mentally retarded.

Let's put it differently. There are more people in hospitals for mental illness than for poliomyelitis, cancer, heart disease, tuberculosis, *and all other diseases combined.*[1] Of every hundred hospital beds in the United States, 54 are occupied by psychiatric patients, and the majority are in the wage-earning years of their lives. In 1954, one year's loss of earnings for the newly admitted totaled an estimated $160 million.

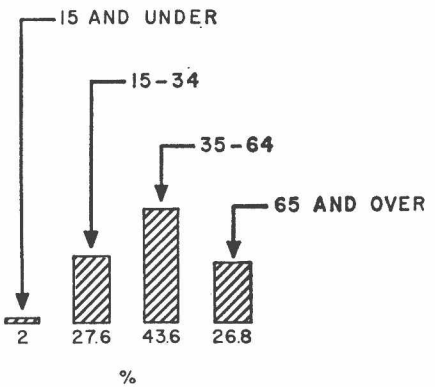

Figure 2. ***New admissions by age to public non-federal mental hospitals. From data published by Biometrics Branch, National Institute Mental Health, Bethesda, Md. 1958.***

As a source of untold human misery and a drain on the resources of society, the toll cannot be measured in dollars. Who knows to what extent mental illness contributes to crime, delinquency, suicide, alcoholism, narcotic addiction, broken homes, and loss in human productiveness?

The demand for care of the mentally ill far exceeds our present ability to provide adequate treatment. In 1955, about two-and-one-half million adults and children were treated for some form of mental disorder in mental hospitals, psychiatric clinics or by psychiatrists in private practice. But the hospital population and those under specialized psychiatric care represent only a small portion of those requiring treatment. For every person receiving such care an estimated 7 others in the United States are suffering in varying degrees from some form of mental illness.

The very magnitude of the problem has enlisted the assistance of enlightened minds from diverse quarters. *While the actual treating of the sick will always fall in the special province of the physician,* the concerted action of many segments of our society is necessary to resolve the predicament of the person with incipient or actual mental illness. Government on all levels is forced to participate; national and community agencies and groups make a vital contribution; public health facilities and the schools are paramount in long-range programs of prevention. And the persistent researches by scientists give promise of fruitful extension of our knowledge of causes and treatment of mental disease.

The rescurces and effective therapeutic tools available to the physician are steadily growing. Since the days of Benjamin Rush many and diverse therapies have been introduced to ameliorate the suffering, if not to cure, the mentally ill patient. Some have had their day of enthusiastic acclaim, but, with more sober appraisal and the passage of time, have been re-evaluated more realistically, and gradually relegated to a position of minor importance or discarded entirely. Other therapeutic advances have proved more resilient. To mention a few: the discoveries of Sigmund Freud, as everyone knows, have fundamentally altered our understanding and basic approach to the psychodynamics of emotional illness. Even his detractors unwittingly use his insights and techniques. The science of interpersonal relationships as elucidated by Harry Stack Sullivan guide the therapeutic efforts of the family physician who may never have heard of him. The imprint on American psychiatry left by Adolph Meyer is no transient mark but deep and lasting. The contributions of these giants of psychiatric thinking have stood the test of time.

Few may recall that Meduna introduced convulsive therapy with the intramuscular injection of camphor in oil and subsequently with a synthetic camphor preparation called metrazol. Pharmacologic convulsive therapy did not survive, but its successor, electroconvulsive therapy, as introduced by Cerletti and Bini, has served for over two decades of wide and intensive use as almost a specific for deep psychotic depression. Analytic investigation and therapy have accounted for great gains, particularly in the psychoneuroses with their attendant symptoms of anxiety, depression, phobias and obsessional rumination.

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Patients with emotional and mental illness are seen by all physicians in every branch of medicine. But almost always the general practitioner is the first physician to see the person who is distressed by an uncomfortable mood, apprehension, discouragement or by a symptom suggestive of a structural, pathological change. His complaint may simulate every known organic symptom, and involve any system. Fatigue, headache, insomnia, muscular pain, nausea, vomiting, diarrhea, constipation, precordial pain, cardiac ectopic beats, tachycardia, certain types of arterial hypertension, urinary frequency, dysuria, various dermatological conditions, and allergic manifestations are as typical of a disturbed psyche as of a disturbed soma.

Less often the patient may be persuaded to consult a physician when he has no somatic complaint but his feelings of self-doubt, insecurity, fear of being hurt, suspiciousness, avoidance of people, long flights into fantasy, or constant hostility have made home and family life unbearable.

What is the meaning of the symptom for which no structural, pathological change is found by careful physical and laboratory examination? By ruling out the serious organic disease, the physician has taken only the first step. He now knows that the manifest symptom disguises or symbolizes an existing or latent illness. He can never assume that NOTHING is wrong. Having excluded organicity he must now proceed to explore other possibilities. The patient with unconsciously disguised symptoms requires all of the knowledge the physician can bring to the case, the keenest diagnostic skill, insight and understanding of the forces that play on his patient's feelings, ingenuity in steering him away from the downhill path to a ruinous psychoneurosis.

The first visit may be crucial in determining whether the patient will be on his way to recovery or regression. It is a truism that the fate of the injured person depends on who administers first aid. Just so, the prognosis of a psychoneurotic complaint may depend upon the kind of "first aid" the first-line physician is able to give. During the initial visit or visits he must determine whether the patient should be treated by a psychiatrist. Is suicide imminent? In that case, an evaluation by a specialist may prove urgent and the physician must decide and prepare the patient for this without transmitting a feeling of rejection.

In making these first correct decisions he can do much for the patient and the family. In the majority of cases he can depend on his own resources, including the skillful use of drugs, to see the patient through to recovery, to prevent exacerbation, or at least to pave the way for further therapy.

Chemotherapy for the patient who presents clinical evidence of emotional disturbance is widely employed by both psychiatrist and general practitioner. Experience has shown that anxiety can be reduced by many drugs, but the chemotherapeutic approach to the depressive reaction has until recently been less effective.

The management of psychotic patients in psychiatric hospitals and to a lesser extent among psychotic outpatients has been facilitated by the use of psychotropic drugs. To be sure, specialists have cautioned against wishful thinking that the latest therapy may be the panacea. Thus, Brill[2] pointed out in a recent symposium that an initial burst of therapeutic claims for some new modality, seemingly adequately supported by scientifically controlled studies, may, as experience accumulates, be gradually followed by contradictory evidence and critical revision.

On the record, psychopharmacology already has done more for the alleviation of mental illness than any other single method of therapy in

nearly a century: despite the upward trend of admissions to hospitals, there is a continued increase in the number of patients discharged. In 1956 the increase over the previous year was 11.8 per cent, 8.9 per cent in 1957, and 7.7 per cent in 1958. The large drop between 1959 and 1960 — 6,614 patients — the greatest annual reduction since 1956 represents an acceleration of the sustained annual reduction, associated in part with the use of psychotropic drugs. In 1960, 40 states reported decreases compared with 30 states in 1959. Current methods can assure improvement and often complete recovery for 7 out of 10 patients entering mental hospitals each year.

It should be pointed out that another recent movement in mental health has complemented and extended the gains offered mental hospitals and their patients by psychochemicals. The concept of the "thera-

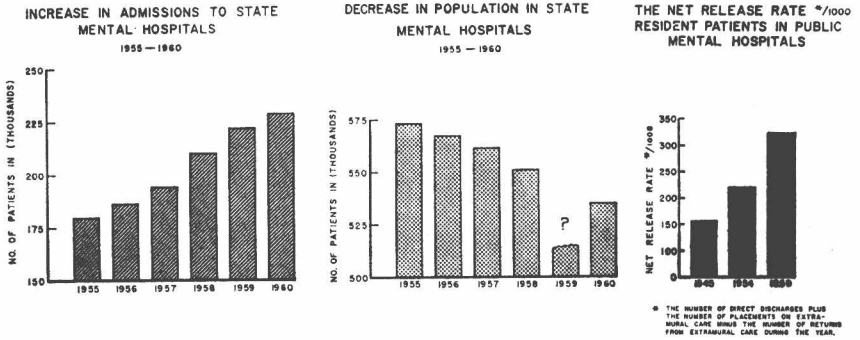

Figure 3. ***From data published in 1) Mental Health Statistics, Current Reports, Jan. 1960, National Institute of Mental Health, Bethesda, Md.; 2) Biometrics Branch; 3) Statistical Abstracts of the United States, 81st Annual Edition, Prepared by E. D. Goldfield, U. S. Department of Commerce, Washington, D.C., 1960.***

peutic community" has spread, locked wards have been opened, and the notion that the psychotic is a person has accelerated his improvement. Without the calming and energizing drugs, the open-door policy in many hospitals might have failed.

The mental "wonder" drugs give promise of being as widely useful for disorders of the mind as sulfonamides and antibiotics have been in the control of infection, perhaps even more for the general practitioner than for the specialist. But no boon is without its hazards.

As with all new tools, full knowledge of how they work, and where and when to use them is essential. Improper use of potent chemicals has its dangers. Added to the profusion of chemical agents introduced within the short space of a decade, and the complexity of their pharmacologic action, there are the problems of largely unknown etiologies of nervous

and mental disorders and the confusing disagreements among psychiatrists concerning their diagnoses and classification.

Where the nineteenth century practitioner was frustrated by the dearth of symptomatic remedies, the physician of today is understandably confounded by what at first glance appears to be a plethora. It is in the attempt to chart a course through this bewildering sea of material, to clarify in some measure the what, how, when and where of the mental drugs, that the following material is presented. *The purpose of this monograph is to present an objective review of one facet of modern psychiatric therapy, namely psychopharmacology.*

It is outside the scope of these pages to attempt to consider other forms of therapy and approaches to the basic problem of psychopathology and psychodynamics of emotional and mental disease. Both the psychiatrist and the non-specialist have much to gain if the addition of psychochemotherapy to the treatment of mental disease proves to be of important and lasting value. The greatest usefulness of psychotropic drugs, however, can be achieved only if clinicians exercise restraint and judgment in their selection, based on study of the indications, limitations, and evaluation of the experience with the "psychiatric wonder drugs."

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CHAPTER II

Classification and Diagnosis of Mental Illness

CURRENT CRITERIA AND THEIR LIMITATIONS

IT IS ACKNOWLEDGED that psychiatry has lagged far behind other fields of medical knowledge. According to two British authorities,[1] "The reason is partly to be found, and partly finds expression, in the lack of a satisfactory method of classification." Although many methods have been proposed, none has received universal acceptance: e.g., the Royal Medical Psychological Association follows one system, the American Psychiatric Association another. This disagreement among psychiatrists themselves as to diagnosis, classification and nomenclature is confusion compounded for the general practitioner.

The bases for dividing and subdividing mental disorders have been etiologic, physiologic, psychologic and symptomatologic, and frequently several have been used simultaneously in the same classification. Each one has its drawbacks and disadvantages.

Classification according to etiology presents an obvious problem: one cause may produce vastly different clinical pictures in different persons, and conversely, a given clinical syndrome may have a multiplicity of causes, not all of which are known. A physiologic classification is impractical at the present stage of inadequate knowledge of mental processes, both normal and pathologic. A serious disadvantage of psychologic classifications – variants of a division into the so-called "intellectual" and "affective" categories – is that they have little usefulness in psychopathology.

On the other hand, a system based on symptomatology, of which Kraepelin was the chief exponent, has several advantages, not the least being its use by clinical psychiatry. And after all, the symptoms bring the patient to the physician and guide the doctor in making his diagnosis and following the course of the disorder during treatment.

The classification adopted by the American Psychiatric Association, involves both symptomatology and etiology. Revised several times during approximately the past thirty years, it is under continuous scrutiny for

any changes that may be necessary because of new knowledge and additional data. In the introduction to the most recently revised nomenclature[2] (1952) the aim is stated: "to provide a classification system consistent with the concepts of modern psychiatry and neurology. It recognizes the present day descriptive nature of all psychiatric diagnoses, and attempts to make possible the gathering of data for future clarification of ideas concerning etiology, pathology, prognosis, and treatment in mental disorders."

Within the limitations of any classification of complex biological phenomena which cannot be strictly compartmentalized, it is a reasonably useful system. In abbreviated form, it is the nomenclature and classification followed here.

CLINICAL CLASSIFICATION

Mental disorders are divided into two major groups:

1) those in which disturbed mental function results from or is precipitated by a primary impairment (gross or diffuse) of brain tissue;

2) those which result from some difficulty in adaptation by the patient.

The first group comprises the cases commonly referred to as *organic* brain disorders, characterized by a basic syndrome involving impairment of orientation, memory, judgment, intellectual functions (comprehension, learning, etc.), and a lability and shallowness of affect or emotion. It is subdivided into "acute" and "chronic," with consequent differences in prognosis, general course and treatment of the illness.

The patient may recover from an acute brain syndrome such as the "acute delirium" of alcoholic intoxication. The same etiology may cause either temporary or permanent brain damage. At the beginning the condition is acute (apparently reversible), but if it results in permanent damage and a persistent organic brain syndrome, the diagnosis will then become "chronic."

Both the acute and chronic disorders are subclassified according to the specific cause of the impairment of brain tissue function, e.g. acute brain syndrome due to drug or poison, chronic brain syndrome associated with intoxication.

The second group includes the disorders of *psychogenic* origin without clearly defined physical cause or structural change in the brain. The characteristics are varying degrees of personality disintegration, failure to

correctly evaluate external reality, to relate effectively to other people or to their own work.

This group is further divided into psychoses, psychophysiologic visceral disorders, psychoneuroses and personality disorders. Here "disorder" designates a group of related psychiatric syndromes; more specific psychiatric conditions are termed "reactions."

A third category is mental deficiency. Strictly classified, all cases in this category could be included in one or the other major group, depending upon etiology, but for convenience they are considered separately. Like "insanity," "mental deficiency" is a legal designation and not meaningful clinically, either from the point of view of cause or treatment. The terms "idiot," "imbecile" and "moron," as descriptive indications of degree of potential mental resource, are helpful in the prognosis of educability. However, since the differentiation is based solely on psychologic testing, e.g., intelligence quotient, itself an unreliable criterion, because it varies with the physical and emotional condition of the individual, exposure to training and other environmental factors, it has limited usefulness.

In the A.P.A. classification mental deficiency includes cases of defective intelligence existing since birth, without demonstrated organic brain disease or known prenatal cause. (In the older terminology, such cases were known as familial or "idiopathic.") The degree of intelligence defect is characterized, according to I.Q., as "mild" (a score of 70 to 85, associated with vocational impairment), "moderate" (50 to 70, indicating functional impairment calling for special training and guidance), and "severe" (below 50, functional impairment demanding custodial protective care). The complete diagnosis also takes into account such other determinants as effectiveness in school, vocational activities and interpersonal relationships, and in addition to the intellectual defect, any psychotic, neurotic or behavioral components that may be present.

I. *Organic Brain Disorders*

Impairment of brain tissue function, manifested by retardation, regression, disordered sensorium, hallucinations, delusions, erratic behavior and convulsive seizures, may be the result of prenatal influences, birth trauma, infection, drug or poison intoxication, cerebral arteriosclerosis or other circulatory disturbance, abnormal metabolism or faulty nutrition, intracraneal neoplasm and diseases such as multiple sclerosis, Pick's or Huntington's disease and cerebral palsy.

These disorders are subclassified according to the cause of brain damage.

1. Prenatal (Constitutional) Influences

The chronic brain syndromes associated with congenital cranial anomalies or developmental defects: microencephaly, microgyria, heteropia, and the results of premature synostosis, internal hydrocephalus, cerebral palsy and mongolism.

2. Infection

Acute and chronic brain syndromes due primarily to intracranial infection, e.g., encephalitis, meningitis, brain abscess, syphilis, tuberculosis and rubella.

3. Toxins

The reversible and chronic brain syndromes caused by agents employed in medical practice — bromides, barbiturates, opiates and hormones — as well as others not used therapeutically: lead, arsenic, mercury, carbon monoxide, a variety of drugs and alcohol.

Alcoholic intoxication may lead to all degrees of permanent brain damage. These manifest themselves in the syndrome formerly designated as Korsakoff's psychosis, characterized by memory impairment, disorientation, confabulation and easy suggestibility. Many chronic alcoholics ultimately show evidence of personality deterioration, defective concentration, unwarranted euphoria, impulsiveness, defective judgment, unreliability and a tendency to place blame of personal failure on others.

Irradiational brain trauma involving mental disorientation may also be included in this group of causes.

4. Circulatory disturbances

Circulatory disturbances: progressive, mental disorders occurring in cerebral arteriosclerosis, cerebral embolism, cerebral hemorrhages, arterial hypertension and other cardiovascular disease.

5. Metabolism and nutrition

Senile and presenile brain syndromes; familial amaurosis, glandular disorders and conditions associated with avitaminosis.

Pellagra, rare in the United States today, once accounted for at least 10 per cent of institutionalized mental patients in the south. The syndrome is characterized by depression and apprehension, confusion, hallucinations, delirium and often complete deterioration.

A deficiency disease superficially resembling pellagra, with which it is often confused, is kwashiorkor, the result of an acute protein lack in the diet.