CHAPTER I.
INTRODUCTION.
A brief historical note on the contributions of other physical sciences to the development of psychological Medicine and its present status.
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Since the dawn of history, man has been puzzled
by sudden ravages made by disease and has tried in several
ways to find remedies against different ailments and dis-
eases. Such remedies have passed through various vic-
situdes from the earliest stages of superstition, magical
ideation and repulsive methods of treatment to the use of
drugs mostly obtained from plants and animal sources and
gradually to the modern era of rational chemotherapy.

It seems justifiable to mention that medicine
today has progressed far beyond its conception as an art
of healing and has become a vast field of scientific know-
ledge because of a combination of research in all other
branches of science. The isolation of pathogenic orga-
nisms, the discovery of antibiotics and other drugs, the
advance in anaesthesia and surgical techniques, are only
some of the bewildering series of successes which have
yielded to research in the modern era. However, it must be admitted that, progress in psychological medicine has not kept pace with that of somatic medicine. Scientific explanation of etiology of mental illness still remains obscure and treatment is mainly based on empiricism. During last few decades, the results of several research works in the experimental and clinical fields have made considerable advances towards the unravelling of the mysteries of the human mind. It seems appropriate to make a survey here of some of the achievements in the various related fields of science so as to evaluate their contributions to psychological medicine as a whole.

It is axiomatic that the most complex structures are based on simple principles and components (Dunne - 1956), which can only be discovered by dissection and analysis of the various connections and associations within its simple components and that all advanced study must be based on a knowledge of fundamental anatomy of such complex structures. While this axiom resulted in the extra-ordinary progress of mathematical, physical and other sciences, as exemplified by the amazing discoveries in chemistry, physics and biology, its application to nervous and mental activity is comparatively recent (Dunne - 1956).
The first analytical approach was made by Freud. This approach, however, was based on subjective analysis and, therefore, was open to the suggestions and criticisms that it was lacking in the exactness on which true science is based.

More than three hundred years ago, Descartes first propounded that nervous and mental activity depended on mechanisms which had an anatomy and physiology. Nervous and mental activity was considered as a response to external or internal stimuli. The responses to stimuli were automatic, whether as a result of inherent or acquired influence. Thus the concept of 'reflex' was born. But its application to higher forms of mental activity did not receive scientific consideration until the advent of Thorndike's classical work (1898), on the result of experimental research based on the behavior of animals under special circumstances.

Experimentations on similar line was carried out at the same time by Pavlov, whose publications have revolutionized the concept of the mechanism of mental and nervous activity. He showed that reflexes are the means on which behavior depends and the discovery of the manner in which reflexes can be conditioned, opened a new path.
towards the understanding of psychological processes.

The principle underlying the conditioning of reflexes would seem to be the basis of Hans Selye's (1956) concept that mental stress is responsible for the production of psychic or psycho-somatic symptoms, and stress is always associated with the production of A.C.T.H. and adreno-corticoids. His exposition of the 'General Adaptation Syndrome' (Specific and non-specific) and diseases of adaptation marks a high light in this branch of science. His concepts of stress as a disease producing agent and its manner of production of a disease is an example of the application of careful study of mechanism as an essential part of the 'holistic approach' (Dunne - 1956).

While the principle and anatomy of the reflex, with its connections and associations within the brain itself and to and from the various organs of the body had been outlined, the energizing basis of its structure remained obscure and knowledge of the source of energy on which cerebral activity was based was very vague. The discovery of Hans Berger (1929), that the brain was the seat of electrical activity marked a phenomenal step towards the knowledge of brain physiology. The tie-up between stress, emotional or otherwise, the increased production of adreno-corticoids,
with the consequent disturbance of potassium metabolism, and the disturbances in the electrical activity of the brain, would seem to be an important chain of events in the production of symptoms.

Physiological discoveries regarding the method of functioning of the brain have encouraged further profitable studies of the mechanisms of the nervous system. These advancements of science have led to a comparison between the mechanisms of man-made machines and the mechanisms of the brain. The analogy has stimulated the application of a new method of study to the mechanism of the brain, the science of Cybernetics. The works of Wiener, Ashby, Grey Walter, Mc Culloch and others are convincing masterpieces of logical, mathematical and scientific deductions in this regard. They have shown that there is a basic principle, the feed-back, which is common to all mechanisms, no matter how complex. A feed-back may be defined (Dunne - 1956) as the return to the central, controlling source of activities, by various channels, of information from all the other parts of the mechanism. It depends on channels through which this information may travel from one part to another, and, therefore, on the integrity of these channels. Anything which affects the
integrity of these channels disturbs the co-ordination and results in defective functioning of the mechanism.

On the basis of his physiological and histological researches, Lorente de No enunciated - "The Law of reciprocity of connections," a physiological axiom which embodies the principle of feed-back in the functioning of the brain. It would seem reasonable, as Dunne (1956) mentioned, to conclude that the principle of the feed-back of the cybernetics and the reflex of the physiologist are one and the same. The simplest reflex arc is at the physiological level. In this there is a receptor, an afferent line of communication to a cell, a line of communication associating with another cell and an efferent line of communication to an effector organ. The response is immediate and automatic.

At the higher level, the same principle exists, but the communication between cells is very much more complex, depending not only on associated nerve pathways, but also on direct influences from cell to cell by means of chemical and electrical interchanges, and on the influences of distant metabolic and glandular products, the result of nervous activity (Dunne - 1956). The final response to stimuli thus, on the higher plane, may be regarded
as the end solution of a problem presented by the stimulus.

Behavioral science firmly rests on the assumption that behavior does not occur by chance, but, rather, is a response to stimulation. This assumption of stimulus - response relationships while explaining behavior leaves the impression, as Heistad (1957 - 58) pointed out that, perhaps electrons, molecules and various nuclei in the nervous system get together for a "conference" to decide when, where, how and why behavior is to be altered. This emphasizes the fact that somatic treatment procedures do not magically replace the lawful stimulus - response relationships which are known to affect behavior, these rather suggest the possibility of certain mechanisms by which various somatic treatments, with the application of stimulus - response relationships, may alter behavior. Although, stimulus - response relationships are not very frequently mentioned in the discussion of behavioral changes resulting from various somatic treatments, this has brought forward a 'bio-psychological' approach to somatic treatments in psychiatry.

From the various approaches to the scientific explanation of mental functioning it seems apparent that a stage has been reached in which different scientific discoveries form a compatible relationship with one another
and conform to the requirements of scientific concepts. Obviously, in the rational use of drugs for the treatment of mental diseases, it is essential to have a complete understanding of the effects of these drugs on total behavior. This includes both bio-chemical and anatomical nerve structures as well as their over-all pharmacologic effects in the total organism which in turn influences the various psychological functions and thus produces a global change in behavior. Drugs have been the most important tools for investigating such processes working inside the organism. If ultimate aim of psychopharmacology is to be reached, that is to devise a rational therapy, the elucidation of the pathology must be made (Saunders - 1961).

Hence, attempt may be made to use the presently available psychopharmacologic agents to provide the changes at the cellular molecular level necessary for the elucidation of both normal and pathological mental processes.

Over the last few decades, novel classes of active substances have been discovered in the field of pharmacological research following the introduction of various organic therapies (e.g., "Malaria therapy," by Wagner-Janvegg; "Insulin coma treatment," by Von Meduna; "Electric Shock" by Cerletti and Bini and Psychosurgery -
by Moniz) during the period 1917 - 1937, which brought with them new possibilities of exerting a pharmacological influence on different psychic functions.

The American pharmacologist David I. Macht coined the term psychopharmacology in the year 1920, and the term was first used in psychiatry by Thoner in "The psychopharmacology of Sodium Amytal," published in the journal of nervous and Mental diseases, February 1935.

The beginning of modern psychopharmacology coincided roughly with the discovery of two drugs which are of special interest in the field of psychiatry. The first of these, Lysergic acid diethylamide (Short form - LSD or LSD-25), was found by accident in 1943 to have extraordinary effects on thinking, perception and emotional responses. The psychological state induced by this drug proved very akin to that found in schizophrenia (Claridge - 1970). The second of these, Chlorpromazine which had its previous application mainly in general medicine and surgery, was later found useful in this field in the year 1952 (Kalinowski - 1969). Almost at the same time a similar effect was claimed for an alkaloid of the Rauwolfia root, which had been used in India for a long time for other physical illnesses. As the introduction of the major tranquilizer
gave an impetus to an over increasing activity in pharma-
cothertapeutic research, Rauwolfia root lost importance in
psychiatry, the number of phenothiazines increased, and
also other groups of drugs like Butyrophenones were added.

Shortly after the advent of the neuroleptic
drugs or "tranquilizers" other observers noticed the eupho-
rizing effect of some drugs used in tuberculosis. This
led to attempts to try these drugs in depression which so
far had been almost the exclusive domain of convulsive the-
rapy. Again, it was not a new bio-chemical discovery that
led to the introduction of the first anti-depressant drug,
iproniazid. Only subsequently the Monoamine Oxidase In-
hibiting properties iproniazid and several similar drugs
was found responsible for the anti-depressant effect.
This theory neither led to the discovery of this group of
drugs nor it is supported by the advent of newer tricyclic
anti-depressants like imipramine, amitryptiline and rela-
ted drugs which are not monoamine oxidase inhibitors
(Kalinowski, L.R. - 1969). The discovery of important
anti-depressant imipramine highlights the continued import-
ance of keen clinical observation in psychiatry.

Lithium Carbonate though known to medicine since
1949 (Cade - 1949; Fiere - 1970-71), had to wait for
another decade or so (Caffey et al. - 1970-71) before its remarkable properties were found of immense value in clinical psychiatry.

At present, research works and treatment using Ayurvedic medicine (Indian medicine) are progressing in India in the field of psychiatry. The origin of these Ayurvedic drugs can be traced several thousand years ago when a drug named "Soma" (the meaning of which according to the old Sanskrit manuscripts was "made one feel like a God") was of great importance in India. As already mentioned earlier, Sarpagandha (Rauwolfia) was one of the earliest drugs used in the treatment of mental illness and more recently drugs like Tagara, Jyotishmati etc. have been used in clinical psychiatry.

During the last few years basic research in psychiatry has been strongly intensified giving impetus to the discovery of many new drugs having psychotrophic properties and thus represents great hope in arriving at a better understanding of mental disorders as well as to find treatments that are based on better rationale, along with the advances which are occurring in the basic sciences, necessary for the understanding of the actions of drugs. Thus, need for an interdisciplinary approach in drug
research in psychiatry has been felt and the gradual
development and use of techniques from different branches
of science, namely, Psychology, Neurophysiology, Bio-
chemistry and so on made possible a more systematic study
of the effects of drugs on the brain and behavior.