THE DEVELOPMENT OF THE BRAIN

AND ITS DISTURBANCE BY HARMFUL FACTORS

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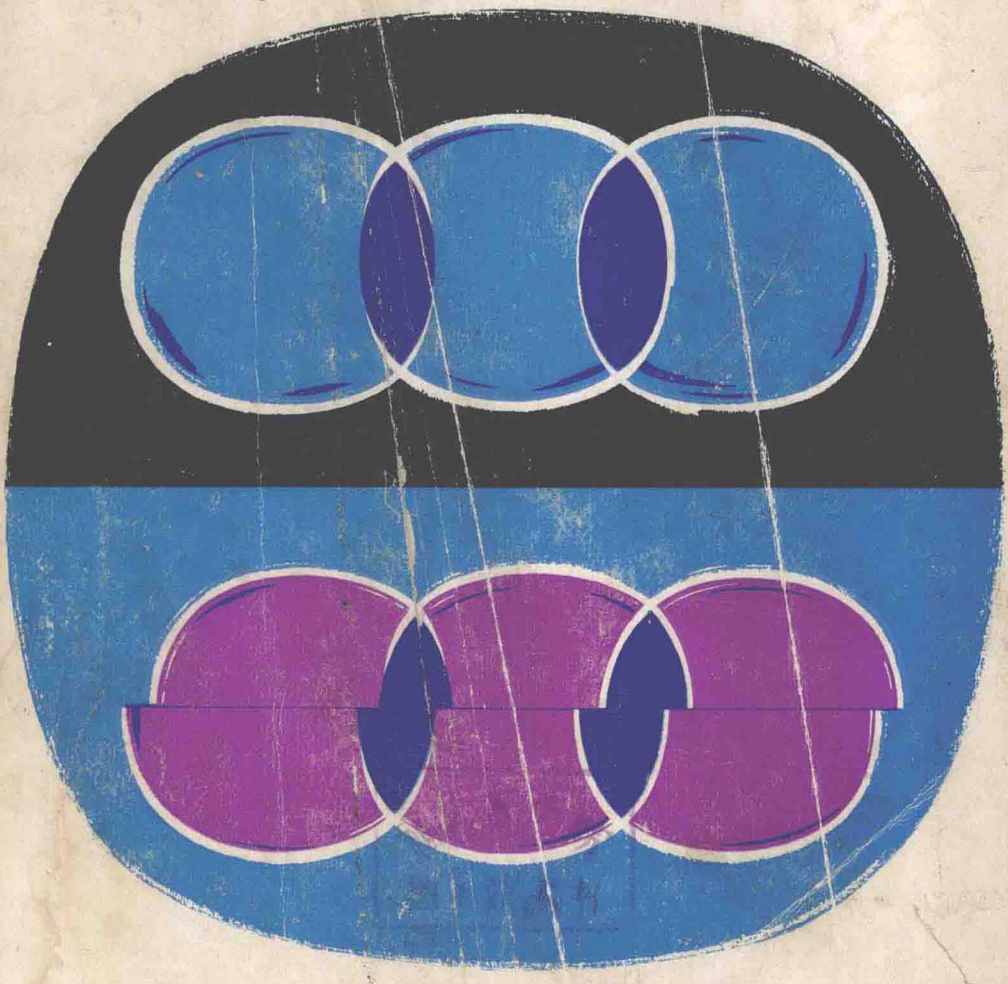

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THE DEVELOPMENT OF THE BRAIN AND ITS DISTURBANCE BY HARMFUL FACTORS

ПРОБЛЕМА РАЗВИТИЯ МОЗГА И ВЛИЯНИЯ НА НЕГО ВРЕДНЫХ ФАКТОРОВ

Б. Н. КЛОСОВСКИЙ

PREFACE TO THE ENGLISH EDITION

VARIOUS factors have stimulated the study of the causes of congenital diseases of the brain, developmental defects of the brain, and retardation of its development. In the first place theoretical investigations, with the aim of elucidating the principles of normal brain development, prompted me to look for the factors interfering with its development. Secondly, in the course of my work as a practising neurosurgeon, I eventually became convinced not only that methods of early diagnosis of brain tumours must be improved and progress made in the diagnosis and operative treatment of latent developmental brain defects, but also that the causes of these pathological conditions must be discovered. I naturally hoped to combine these two aims—theoretical and practical—into a single, common purpose. Such research would help to explain the pathological changes taking place during embryonic life as a result of changes in the conditions of the external and internal environment, and would also suggest preventive measures.

Accordingly, a psychoneurological clinic was opened at the Laboratory for the Study of Brain Development and under its theoretical direction. In addition to the study of various forms of congenital brain disease and their treatment, particular attention is paid to the elucidation of the causes of developmental anomalies of the central nervous system; a careful investigation is made of the mother's health and of the course and outcome of her pregnancy, especially should it terminate in the birth of a maldeveloped child.

At the outset of my research I took into consideration certain factors already known to have an unfavourable effect on embryogenesis. Some of these, for example malnutrition, oxygen insufficiency, infectious diseases, and the influence of radiant energy and of certain drugs or chemical agents, were known to be possible causes of serious disturbances of the development of the embryo and, in particular, of its nervous system. The mode of action of these factors is as yet imperfectly studied, although it might be assumed from certain clinical and experimental investigations that external environmental agents may give rise to metabolic and hormonal changes in the mother as a result of disturbance of, for example, the

endocrine glands of the pregnant woman (the thyroid, pancreas, hypophysis, adrenals and so on), thereby causing unfavourable conditions for the developing foetus.

In the Laboratory and the psychoneurological clinic the principle was adopted that each investigation should be conducted simultaneously by two methods, i.e. clinically and experimentally.

For the solution of the clinical part of the problem, information was collected from various hospitals, clinics, institutes and so on about women with metabolic diseases or various endocrine diseases, and a careful obstetrical history was taken from these women; the mother and her children born before and during the disease were then examined. In each case attention was directed to the general medical, neurological and endocrinological state of health of the mother and child, and to the effect of the treated, partially treated or untreated disease of the pregnant woman on the child's development.

Most of the children with disturbances of brain development born of mothers suffering from these diseases were kept under observation as out-patients, but some were admitted to the psychoneurological clinic for more detailed investigation and treatment. In all cases particular attention was directed to the psychomotor development of the children, to the state of their endocrine glands, and to the development of their skeletal system, internal organs and so on.

Concurrently with this programme of clinical research, these various diseases or disorders of the endocrine glands were produced experimentally in animals before and during pregnancy, after which the foetuses and in particular, their brains were investigated. From a comparison of the results of the clinical and experimental investigations the degree and character of the influence of the various harmful factors on the foetus could be assessed.

The results obtained provide a basis for the present and future development of pre-natal prophylaxis in the Soviet Union. We feel, moreover, that the work undertaken in this field may contribute to the promotion of health of humanity as a whole.

In this monograph only that part of the work is described which was carried out under my personal direction, and at the present time a second volume of the book is being prepared for publication. In this second volume the influence of many other harmful factors on the brain development of the foetus and child will be discussed and, in addition, the results of investigations of the role of the external environment and of heredity in the formation of the organism and its nervous system will be described.

The rational development of pre-natal prophylaxis and the care of the brain are questions of the utmost importance to subsequent generations. I should like to mention that very great importance is also attached to this problem in Great Britain, as is shown by the publication of a journal such as the "Cerebral Palsy Bulletin (Developmental Medicine and Child Neurology)".

In conclusion I wish to express my sincere gratitude to Dr. B. Haigh for translating and editing this monograph, to Dr. L. Crome for reading the manuscript and for his many helpful comments, to Robert Maxwell for publishing it in English, and also to Mrs. Otella Szczepanska.

B. N. KLOSOVSKII

Active Member of the Academy of Medical Sciences of the U.S.S.R.

PREFACE

Now that some of the more pressing problems of infancy and childhood, such as infections and conditions caused by poverty and malnutrition, are coming under control, congenital diseases, especially those of the brain, are beginning to emerge in their true size and importance. Notable advances have been made in recent years, and the scale and tempo of research is increasing. It is a field attracting convergent exploration by workers of such diverse and distant outlook as biochemists, biologists, educationalists, physicists, neurologists, obstetricians, and others.

Little has hitherto been known of Soviet contributions in this field. Some of the earlier Russian work used to be published abroad, chiefly in German periodicals. But this practice ceased some 30 years ago, and foreign readers were since faced not only with the language barrier but also with sheer inaccessibility, since even the largest libraries filed only few Russian publications. Similar difficulty was evidently experienced by some Russian workers, whose work often bears the imprint of relative isolation from "The West". Fortunately, the position is rapidly improving, and it is particularly gratifying that The Pergamon Press has undertaken the English presentation of some Soviet publications, including the present monograph.

This sets forth the views held by Professor Klosovskii and members of his team on some of the significant processes in the development of the brain and factors disturbing this development. The latter include, asphyxia, whooping cough, deficiency or excess of maternal thyroid function, diabetes, effects of quinine, prematurity, trauma, and malnutrition. However, the monograph is by no means comprehensive and some well recognized causes of neural maldevelopment, such as inheritance, maternal rubella, blood group incompatibility and ionizing radiation receive little or no mention. All conclusions are based on clinical and experimental work, most of which confirms or adds emphasis to similarly reached views of workers in other countries. Other inferences are more original and some of these are controversial and likely to stimulate useful discussion.

Professor Boris Nikodimovitch Klosovskii is a member of the Soviet Academy of Medical Science. He is a veteran in the study of the normal

and pathological development of the brain. Already as a student he combined work in the Anatomy Department with his medical training at the Azerbaidzhan University, from which he graduated in 1925. Later he worked under V. M. Bekhterev at the Leningrad Brain Institute, completing his thesis on the nerve fibres in the floor of the third ventricle in 1929. Professor Klosovskii has now some 173 publications to his credit, including 8 monographs. From 1932–1942 he was on the staff of the Moscow Institute of Neurosurgery, directing there a laboratory on brain study and being also in charge of one of the clinical neurosurgical departments. In 1931 he became head of the department dealing with the study of brain development at the Academy of Medical Science Institute of Paediatrics in Moscow. A clinical psychoneurological department was opened in association with Professor Klosovskii's laboratory in 1952. Professor Klosovskii also directs the department of brain pathophysiology at the Moscow Institute of Neurology.

Throughout his career Professor Klosovskii combined clinical work with theoretical studies, and this is also a guiding and obligatory principle for all members of this staff. His department employs over 30 research workers, and is thus one of the largest neuro-paediatric centres in the world. Members of the department are keen on contacts with foreign colleagues; I have been personally fortunate in meeting Professor Klosovskii at a symposium on the phacomatoses held in Paris a few years ago. One of his senior research assistants, Dr. Boris Viktorovich Lebedev, spent some time last year at our hospital during his study tour in England, and visited many other centres in this country.

The value of such personal contacts will be enhanced by more intimate knowledge of each other's work, and it is in this spirit that the present monograph will be welcomed by English readers. Professor Klosovskii and his staff continue their work on the principles underlying the development of the brain and are now engaged on a still wider programme of research which embraces, among other things, such topics as the inheritance and the prevention of brain abnormalities. In this they would no doubt be helped by exchange of views and experience, and some readers may wish to communicate with them directly. The Institute is moving shortly to new premises and the address is: The Institute of Paediatrics of the Academy of Medical Sciences of the U.S.S.R., Lomonosovskii Prospekt 2/40, Moscow V–261, U.S.S.R.

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CHAPTER 1

FUNDAMENTAL FACTS CONCERNING THE STAGES AND PRINCIPLES OF DEVELOPMENT OF THE BRAIN AND ITS RESPONSE TO NOXIOUS AGENTS

ONE of the most important tasks of paediatrics is the safeguarding of the mental and physical health of the child. In the prophylactic field, this task must begin at the very beginning of the existence of the organism, i.e. at the onset of pregnancy, and it must continue through the period of parturition and early life, until the time when the child leaves school. The object of therapeutic measures must not only be to lower the mortality rate, but also to eradicate disease and to prevent its complications, particularly as they affect the central nervous system.

In both the developing organism and the adult, the human brain is an organ which regulates all the processes of the body and ensures its adaptation to the constantly changing conditions of the external environment and, in turn, the adaptation of the external environment to the requirements of the organism. Research in this field must therefore be directed primarily towards the study of the stages and principles of development of the brain, and the elucidation of the factors which may adversely affect its development.

Incomplete or abnormal, pathological development of the brain and degenerative phenomena in the brain of the foetus result from the action of injurious factors. These may arise in consequence of diseases of the mother during pregnancy, or as a result of the taking of abortifacient substances by the pregnant woman, in doses insufficient to expel the foetus. Maldevelopment of the brain, retarded or incorrect development of the brain may also be the result of pathological labour. The most important noxious factor which may affect the brain during labour is asphyxia. The longer the duration of asphyxia, the more serious are its consequences. Asphyxia of the child during labour may be associated with certain other injuries of the brain, taking place when the head negotiates the birth passages, in cases of mismanagement of labour, and so on. The usual

consequence of birth trauma of the brain is haemorrhage, often accompanied by localized or generalized, disseminated areas of destruction of the brain substance.

Defects in the development of the brain may arise in connexion with nutritional disorders of new-born and young infants and with various infectious diseases (whooping cough, measles and so on).

Research into the problem of the influence of injurious factors on brain development must be aimed, not only at the elucidation of all the causes of incomplete or imperfect development of the brain, but also at the search for methods of treatment of diseases of the brain when they occur. A knowledge of the mechanism of action of the noxious factor will facilitate the early diagnosis of such diseases, and this, in turn, will enable treatment to be instituted in early stages of the pathological condition. The solution of this problem is thus intimately bound up with the prophylaxis and treatment of certain injuries of the brain.

The study of incomplete and pathological development of the brain cannot be limited to the investigation only of gross forms, but it must also extend to very slight disturbances of development, which occur especially frequently.

This problem of the influence of injurious factors on brain development cannot be solved without the simultaneous study of the principles and laws governing the structural and functional development of the brain. The successful solution of this problem will be largely determined by a combined approach in these two directions, making use of clinical observations and experiments on animals.

This monograph is the first attempt to analyse the problem as a whole, on the basis of results obtained by a group of workers at the Laboratory of Brain Development and the Psycho-Neurological Clinic of the Institute of Paediatrics of the Academy of Medical Sciences of the U.S.S.R., directed by Corresponding Member of the Academy of Medical Sciences of the U.S.S.R. Professor B. N. Klosovskii.

From the point of view of its chemical composition and structure, the brain is a highly complex, organic formation. During the period of embryonic development of the brain the primitive mother cells undergo very complex processes of proliferation, transformation into various cell forms with different functions, migration of cells, combination of groups of cells and the formation of reflex arcs for the transmission of excitation from the extero- and interoceptors to the cells of the central nervous system and back again to the periphery, and so on. These processes have nutrient systems for supplying them with cerebrospinal fluid and blood.