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THE BIOLOGIC FUNDAMENTALS OF RADIATION THERAPY

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A Textbook

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This book is dedicated
to the memory of my father
ALEXANDER EHRLINGER, PH.D., M.D.
late Professor of Pharmacology
and Director of the Pharmacological
Institute of the University of
Frankfurt a.Main

Preface

Today, more than ever before, the use of Radiation for therapeutic purposes is coming into the foreground. The fundamental principles of this therapy are based on numerous careful investigations which have helped to replace empiricism by a more scientific approach to therapy. No physician today can give his patients optimal care if he is lacking in knowledge of the fundamentals of radiation biology. These problems are thoroughly discussed in this book which fills a particular need in the literature of Radiation Therapy. It is a comprehensive survey of the enormous mass of scattered information pertaining to the biologic fundamentals of Radiation Therapy. Not only the Radiologist and Physicist, but all Clinicians and Medical Students may profit greatly by reading it.

New York City, November 1940. Maurice Lenz, M.D.

Author's Preface to the English Translation

Two facts have chiefly inspired the English translation of this book, viz. the growing interest in the teaching of the basic science of Radiology as shown at the Fifth International Congress in Radiology in Chicago in 1937, and the very friendly comments concerning this book which were made in different parts of the world and especially in this country.*

Since its first appearance in 1935 kind suggestions for its further improvement have reached me. I wish to express my appreciation for the interest and support my work has received from all sides. In the present edition I have attempted to make the best use of the advice given. Typographical errors and obsolete portions have been eliminated and the latter replaced by more recent data. A short paragraph concerning the action of neutrons has been added. The list of recent pertinent literature has been brought up to date (essentially to April 1940). In quoting from collective reviews of the literature pertaining to various subjects, special attention has been given to American and English sources. A fairly extensive bibliography is given to facilitate and encourage individual source interpretation. This has been limited to papers which have appeared since 1930 to prevent the list from growing too long. Similar considerations made it impossible to list all recent papers. The author is fully aware that many papers could be used interchangeably with those quoted. The goal has been to give a well rounded picture of the biological facts which form the basis of radiation therapy. For complete literature the reader is referred to the systems of Radiology. From a didactic point of view it was found necessary to describe some therapeutic procedures and dosages. Since plans of treatment may vary markedly in the various clinics it may be emphasized that the doses mentioned in this book are merely for general orientation. Complete details may be obtained from the relevant publications.

The author wishes to express his sincere thanks to Dr. Maurice Lenz for the kind interest always shown to him and his work, to the publisher who made this translation possible in spite of difficulties caused by war in Europe, and to Dr. Reuben Gross for his fine co-operation in its preparation. The author further wishes to acknowledge the granting of permission by the American Medical Society to reprint illustrations 6, 8, 11; by the W. B. Saunders Company to reprint illustrations 25, 26, 27; by Charles C. Thomas, publisher of "The American Journal of Roentgenology and Ra-

* Radiology 1936 No. 6, Arch. Phys. Therap. X-ray, Radium 1936 No. 3.

dium Therapy" to reprint illustrations 10, 18, 36, 37; by the Radiological Society, publishers of "Radiology" to reprint illustration 16.

When this book was published in 1935 the hope was expressed that "it might serve as a useful adviser for the indications of radiation therapy, as an aid for the further study of the as yet unanswered problems and to open this branch of therapy to the students." Widespread use of this book as shown in quotations in a large number of papers throughout the world has fulfilled this hope. May the English translation add many new friends to the old.

If I may express today one further hope it is that, as Radiation Biology influences the development and progress of Radiation Therapy* more and more, may this book also contribute toward securing for the Radiobiologist the same rights, and last but not least the same working and teaching facilities, which the Physicist and Pathologist have already acquired in Radiation Therapy.

New York City, November 1940 Friedrich Ellinger
561 W. 141st Street

Preface to the German Edition

In this book I have attempted to gather in didactic form the results and problems of radiation biology in so far as they are of importance in the practice of radiation therapy. This has been done to help spread the knowledge in a form that would also be available to the general practitioner and student.

Undeniably, penetration into the problems of radiation therapy is not inconsiderably complicated by the essentially greater part played by technique, as compared to its role in the use of pharmaceuticals. The impression is therefore frequently given that the therapeutic application of radiant energy differs in principle from that of drugs.

With this presentation of the biological fundamentals of radiation therapy, I hope to demonstrate the equality of basic principles in the use of radiant energy and chemicals for therapeutic purposes, and thus simplify comprehension of the problems of radiation therapy. In order to emphasize this basic equality I have endeavored to divide the material as is customary in pharmacology texts. Physics and technique are discussed only where they aid the comprehension of biological problems. As an introduction there is a brief sketch of the nature and problems of experimental radiation therapy. Serving as a model for my efforts in many ways, was that masterpiece of

*cf. Sievert (1088).

textbook presentation in the field of materia medica by H. H. Meyer and R. Gottlieb.

Following their example I have included a list of recent pertinent literature (essentially up until 1934). This will facilitate individual source interpretation in spite of the textlike presentation. Recourse will have to be taken to systems of Radiotherapy for the older literature, else the list would become too unwieldy. Corresponding to the character of this book, an exhaustive survey of the literature was avoided, this also remaining the task of a system. For practical purposes authors have been listed alphabetically, and an attempt has been made not to entirely disregard the history of radiation therapy.

If this presentation of radiation biology accomplishes its purpose as a useful adviser for the indications of radiation therapy, as an aid for the further study of the as yet unanswered problems, and helps open this branch of therapy for the student, I would feel amply rewarded for my efforts.

I wish to thank here the William Kerchhoff foundation in Bad Nauheim for its support in making possible this long planned work, as well as my honored teacher, Prof. W. Friedrich, for his aid and advice. I am also very grateful to H. Meyer in Bremen, the editor of Strahlentherapie, and the publishers Urban and Schwarzenberg for their co-operation and interest. Finally, many thanks are due to my colleagues, whose friendly advice helped my efforts.

Berlin—Spring 1935 Friedrich Ellinger.

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FOURTH PART

FURTHER EFFECTS OF LIGHT

INTRODUCTION

1. Nature and Problems of Experimental Radiation Therapy

The use of radiation for therapeutic purposes is as old as the history of mankind. Yet it was not until the 20th century that radiation acquired substantial importance in therapy, a feature bound up with the development of physics.

Like other branches of therapeutics, radiation therapy is an empirical science, experience teaching that desirable as well as highly undesirable effects are brought about by its use. As a result, the necessity arose for studying the action of radiations upon normal and pathological tissues in order to control their effects, to bring the desired effects into the foreground, and, above all, to learn how to avoid the undesirable or even dangerous reactions.

The science directly concerned with the action of radiation upon living matter is *radiation biology,* which thus forms a subdivision of physiology. But in so far as interest is mainly focused upon the potentialities of radiant energy in therapy, *"experimental radiation therapy"* is spoken of. Under the latter heading therefore, are grouped all the effects of radiation which might also be designated as the pharmacology and toxicology of radiation.

The problems of experimental radiation therapy extend mainly into two fields (Friedrich and Ellinger (12)). First the primary processes in the action of radiation must be explained, i.e. the chemical, physical and biological processes set up at the site of application of the radiation. Relevant information is obtained from experiments upon non-living matter, examination of unicellular organisms, and recently, from tissue cultures. Occasionally the investigations are aided by experiments on plants (Ingber (72)). These throw light on the general laws of radiation (general physiology or pharmacology of the action of radiation). Secondly, based on the known general effects of radiation, the fundamentals of radiation therapy must be clarified by a study of the action of radiation upon individual organs, and the organism as a whole (experimental radiation therapy in the narrower sense). The solution to many problems in this sphere must of necessity be gained from animal experiments. Tests on human beings are, from experience, frequently ruled out owing to the risks associated with certain types of radiation. On the other hand, it is only by animal experimentation that many problems can be solved; a case in point being, as shall be seen, inherited injuries due to Roentgen rays. Even at this early stage,

however, it is well to draw attention to the difficulty of adapting the data of animal experiments to human conditions, especially where the action of radiation is concerned. This point will be frequently met with in the course of our remarks.

2. Physical Considerations

In the following, a short survey will be presented of the knowledge of the biological processes important in the therapeutic use of radiation.

An attempt will first be made to formulate a clearer definition of the nature of radiation. The question arises, what is radiation? Radiation is a type of energy which occurs in two forms, viz. as electromagnetic vibrations which include light and Roentgen rays, and as corpuscular radiation, the most notable examples of which are the α and β rays of radium and neutrons. It is not within the scope of this book to enter into the funda-

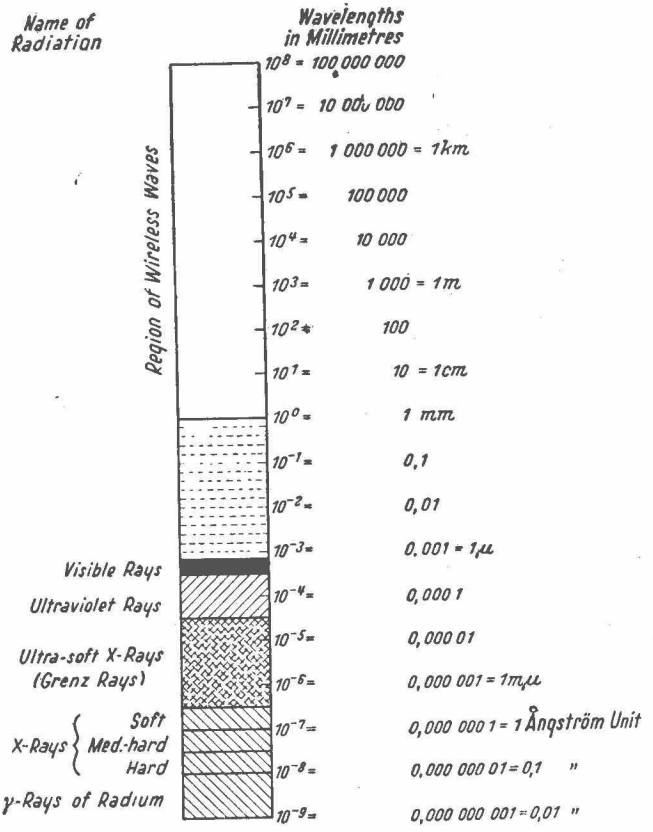

Fig. 1. Electromagnetic spectrum.

mentals of radiation physics, and a knowledge of the essential facts will therefore be assumed.

Figure 1 is a diagrammatic presentation of the natural phenomena included under the heading of electromagnetic vibrations. The arrangement of these rays according to wave length is called a spectrum. It can be seen that the rays most commonly used in medicine are those of short wave length (ultra violet and Roentgen rays as well as the gamma rays of radium). Visible light with a wave length 10,000 times greater than Roentgen rays, has only slight clinical importance. The connection between wave length and therapeutic value of the radiation as shown in figure 1 calls attention to a physical relationship between the wave length and the frequency of oscillation. This in turn paves the way to the understanding of many problems of radiation biology. The relationship is expressed by the equation $\lambda = c/\nu$. In this equation, c is the velocity of light (300,000 km. sec.) and is constant. All electromagnetic oscillations travel at this speed in a vacuum. Now the equation reveals:

1) The wave length of a radiation is directly proportional to the velocity of light and inversely proportional to the frequency of the radiation.

2) Wave length and frequency are reciprocal quantities. In other words, as the wave length decreases, the frequency increases.

Although the electromagnetic theory of radiation permitted classification of the various natural phenomena under a single physical concept, it did not prove satisfactory in all respects. Difficulties arose particularly in regard to the energy factor. The quantum theory formulated in 1900 by Max Planck overcame these difficulties. This theory postulated for radiant energy, as well as for matter, the existence of extremely minute particles, so-called "quanta." According to this theory, the energy of a radiation is always emitted in multiples of this very small elementary quantum. The symbol of the elementary energy quantum is h, where h is 6.55×10^{-27} ergs/sec. and a natural constant (Planck-Einstein constant). This is of great interest, since $h\nu$ represents the energy of the light quantum: $E = h\nu$ (E equals energy).

It has just been shown that the frequency bears a constant relationship to the wave length, namely that the frequency and wave length are reciprocals. Since it is customary in therapeutics to characterize radiations by wave length, we may replace ν in the above equation by the symbol of wave length. The equation is then written: $\nu = c/\lambda$ from which follows: $E = h \times c/\lambda$. This latter form of the equation reveals that:

3) The energy constant of a radiation is determined (according to the quantum theory) by the quantity h, and the wave length of the radiation.

4) Wave length and energy are in fact also reciprocals, so that a decrease in wave length is accompanied by an increase in the energy of