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# AN INTRODUCTION TO MEDICAL GENETICS

BY

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## PREFACE

THERE is probably no teacher of medicine who does not stress the importance of hereditary constitution as one of the factors to be considered in discussions on the causation of disease, and for nearly forty years now the science of genetics has been advancing with smooth and rapid strides. Yet it is to be feared that many medical men and many senior students are acquainted with vague generalities only, or are equipped with a somewhat uncertain knowledge of Mendelian laws which they would find it difficult to apply with confidence.

The medical student, during his pre-clinical work, receives instruction on elementary genetics. It is not at this stage that the trouble arises (except, to express a personal view, that it is very difficult, if the traditional and historical approach is adopted, to expound the subject adequately in the limited time available). What is so often lacking, during the clinical and post-graduate years, is guidance in the application of what was initially learned to the practical problems of the causation of abnormality and disease. This book is an attempt to remedy the deficiency. It is addressed primarily to the senior student and the clinician, but it is hoped that it may also be of interest to some of those who are concerned with other aspects of human biology. And it would be a source of particular satisfaction if any research worker were to decide, as the result of reading it, to incorporate a genetic inquiry in his investigations.

This book follows the accepted plan of clinical teaching. A recollection of what was previously learned is not taken for granted. Basic principles are restated fully and on this foundation is built up, not a recapitulation of the science of genetics, but an exposition of the applied science of *medical* genetics, dealing with the human subject as observed in the community, in medical practice, and in hospital. It is my belief that it is the neglect of established principles of medical teaching which has been largely responsible for much of the failure to assimilate and utilize genetic advances in the past. For a text-book of genetics is no more a substitute for one on medical genetics than is a text-book of physiology a substitute for one on medicine.

The historical approach has been entirely abandoned. In my experience it is highly unsuitable for imparting the essentials of the subject with a reasonable economy of time. An historical approach is rarely adopted in books on applied science, and after forty years a book on applied genetics need not be made an exception.

The basic principles of the subject, the alphabet of heredity, simple Mendelism, must be thoroughly and firmly grasped. Unless this is achieved any subsequent discussion is valueless. The attempt has been made to reduce these essentials to their simplest form by grounding them firmly upon chromosome behaviour, and then appealing to first principles in every instance. The attempt has also been made, by treating each topic in turn from the point of view of the phenomena presented in a human population, not only to stress and re-stress these basic principles, but at the same time to unfold the first part of the story of medical genetics.

Plant and animal examples have been completely excluded. This may seem an unduly rigid limitation. But the expounders of genetics to medical men have gone so far to the opposite extreme that it seemed wiser to deny oneself the luxury of an occasional plant or animal example, if only to show that the subject can be explained without any of them. A medical friend remarked recently: 'At the first mention of *Drosophila* I close the book.' It is to be feared that this ungrateful sentiment is widely shared. And undoubtedly no one could acquire a reputation as a brilliant teacher in the wards if he could hardly ever be induced to talk of anything but rats or guinea-pigs.

It has, of course, been unnecessary to include numerous genetic topics which have no present human application. The subject-matter is accordingly confined to the medical genetics of the present day, with a few references to what appear to be the probable advances of the near future. Certain sections, however, have been printed in smaller type, together with the whole of Chapter VI on genetic linkage. These sections include some further explanations, and also topics which are theoretically important but which have at present no wide practical application, topics a knowledge of which is not vital to an understanding of the essentials of the subject. It is hoped that the

book, without these portions, will present, for those who desire it, another and a simpler unity.

A general text-book of genetics includes far more than is required by the medical man, but it also includes far less. A human population differs in a number of important respects from a laboratory population, and any presentation which omitted to take this circumstance into account would remain academic. There does exist a science, an applied science, of human and medical genetics, presenting special features of its own and requiring the use of special methods. This science has made striking progress in recent years. But many of the methods of human genetics are the reverse of simple and a considerable mathematical knowledge is required if they are to be completely understood. The difficulty of explaining the subject in non-mathematical, or almost non-mathematical, terms has, however, to be faced. By the use of analogies and convenient approximations, by explanations of the nature of some problems, by occasional indications as to the methods of solution, above all by pointing out the practical consequences, I have tried to give the non-mathematical medical reader a picture of the present state of medical genetics. Naturally, the research worker in this field needs to know much more, but I believe it is easily possible for any medical man to learn enough to acquire what might be termed genetic intuition, just as he acquires clinical intuition; he will then be enabled to draw sensible conclusions from what he observes, and to appreciate the possibilities and probabilities in regard to the problems before him.

Many of the conditions used as examples, though fascinating, are rare, and the student or clinician would be fortunate if he personally encountered more than a small proportion of them. Few of us care to think entirely in terms of abstract symbols, and it is dull work tracing the transmission of something which is little more than a name. Accordingly, in the case of rare conditions, descriptions are included, with illustrations where appropriate. These descriptions do not pretend to be either complete or systematic, but it is hoped that they will provide some substitute for the vivid impression which would be made by the leading features of each condition, if it were studied in the wards or the out-patient department.

I have to admit that as a student of genetics from the time when the chromosome theory was being finally and triumphantly established, I could not entirely avoid some feelings of remorse as this book took shape. For it seemed sinful to omit all reference to the beginnings of the science and to the stages through which it has grown. And although in a book on an applied science it is not necessary to explain, as an exercise in scientific method, the steps by which conclusions are reached, it seemed revolutionary that I should describe linkage relations and chromosome maps as a simple consequence of a postulated linear order of the genes, instead of establishing that linear order with a flourish on the basis of observed ratios. But this is not a text-book of genetics and to such text-books the reader must be referred for a complete exposition of genetics as an integral part of biological science. Text-books of genetics, however, are weighty volumes and the time of the medical student and clinician limited; accordingly, it was with great pleasure that I read a very small book which appeared while this book was being written. This is E. B. Ford's *Study of Heredity* (Thornton Butterworth. Home University Library of Modern Knowledge, 1938). Any reader of my book who feels that he would like to have a short, straightforward account of the present position of the science of genetics, particularly in relation to biology as a whole, cannot do better than read this concise and lucid essay.

It will, of course, be realized that no attempt has been made to write an encyclopaedia. Examples have been chosen from the point of view of their suitability as illustrations of particular topics. Many important inherited abnormalities, and many important diseases in whose causation heredity plays a significant part, are not mentioned. I believe that the time has now passed when it was possible to present in a single volume, system by system, an adequate account of even the chief inherited human abnormalities. This book deals with principles and is intended to be an introduction to those works which give long lists of inherited conditions and expound the role of heredity in the production of numerous diseases. Many of these books of the present day are good, but progress is so rapid that the encyclopaedias of the near future will greatly surpass them. In the not distant future the medical man, having learned the

principles of the subject from a book somewhat like this one (but doubtless greatly improved), will be able to look up in the appropriate specialist volume any condition in which he is interested and there find a crisp, clear, and adequate summary of what is then known in that particular instance. I should have liked, however, had it been possible, to have included more examples of inherited abnormalities; in this connexion may I advise the reader to glance through (not read, for it is primarily a work of reference) E. A. Cockayne's *Inherited Abnormalities of the Skin* (Oxford University Press, 1933). I know of no other work in English which gives so good an impression of the immense number and endless variety of inherited conditions.

In view of its primary purpose every effort has been made to simplify the text by the avoidance of footnotes and details of the source of work quoted, apart, of course, from the names attached to borrowed illustrations and reproductions of pedigrees. It is desired, however, to associate authors' names with their work, and it is realized also that some readers may wish to have references to the sources of the material used. In the section 'Sources of Material' (page xix) will be found full details of the source of illustrations, pedigrees, quotations, and of statements and results given in the text. They are arranged in order opposite the appropriate page number. The reader who wishes to discover the source of any material has only to turn to this section and look up the number of the page he is reading. The references are intended to serve as a starting-point to the literature and have been limited as far as possible. Consequently in most cases only one is given for each topic; this is usually the most recent and is not necessarily the one principally consulted; actually a few very recent ones were substituted after the manuscript was written. Where possible, comprehensive reviews have been chosen.

No attempt has been made to include references for the general background of the book. Of course my indebtedness to such writers as R. A. Fisher and J. B. S. Haldane, to mention two of the most eminent in this country, will be sufficiently obvious to every student of the subject. But apart from the difficulty of giving specific references for general statements, I have refrained for another reason. It may well be that owing to a failure in comprehension on my part, or because of unwise

attempts to draw further deductions, or to attain undue simplification, I have on occasion misinterpreted those distinguished authorities, and, were I to quote their names in connexion with general statements, I might appear to attribute to them opinions of which they would not approve, and for which I alone am responsible.

It is a pleasure to acknowledge my indebtedness to those who have helped me in the preparation of this book. My friend Dr. A. L. Taylor was good enough to read through the manuscript and I owe far more to his keenly critical and helpful suggestions than I can persuade him to admit. Three friends contributed certain admirable illustrations, hitherto unpublished; Dr. H. G. Garland provided Fig. 14, illustrating Osler's disease (together with some observations quoted on page 32, also unpublished hitherto); Dr. J. T. Ingram Figs. 67 and 68, illustrating epidermolysis bullosa; and Dr. R. M. Norman those of Fig. 32, illustrating juvenile amaurotic idiocy. I am indebted to Dr. R. J. A. Berry for many helpful suggestions, and to Miss Joan Nethercot for her careful work throughout all stages of the preparation of the book. The form of the pedigrees is, with certain differences, essentially that suggested by the Eugenics Society, and published by them under the title of *How to Prepare a Family Pedigree*; for permission to use their scheme in this way I am much indebted to the President and Council of the Society. Finally, I owe a special debt of gratitude to Mr. G. T. Hollis, Medical Editor to the Oxford University Press, for resolving many problems and for doing so much to make the production of this book a pleasant task.

BRISTOL, *January*  
1940

J. A. F. R.



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I AM greatly indebted to the following authors and publishers for permission to reproduce illustrations; in each case full bibliographic details will be found opposite the appropriate page number in the section 'Sources of Material':

Dr. P. C. Koller and the Royal Society of Edinburgh for Fig. 1 (a) and Fig. 35, from the *Proceedings* of the Society.

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Dr. H. Rischbieth, Miss A. Barrington, and the Cambridge University Press for Fig. 93, from *The Treasury of Human Inheritance*.

## SOURCES OF MATERIAL

PAGE

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H. M. Evans and O. Swezy. *The Chromosomes of Man*.  
Berkeley: University of California Press. 1929.
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p. 35. 1908.
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p. 14. 1909.
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<sup>1</sup> A large collection of records and photographs relating to mental deficiency was made by Dr. Brushfield, and is available for study at the Library of the Royal College of Surgeons of England.

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