

BLOOD GROUPS IN MAN

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PREFACE TO THE FIRST EDITION

SINCE the last edition in 1943 of Wiener's excellent text-book *Blood Groups and Transfusion* (Thomas, Springfield), the number of known blood group systems has doubled. This advance is due mainly to the attention of necessity given to blood groups in the huge wartime transfusion services, and to the investigation of innumerable blood samples for the Rh groups.

The present book concerns itself with the blood groups and with their inheritance. Other volumes shortly to follow in the same series will deal with the ethnological and clinical aspects of the subject. While attempting to give a reasonably full account of all the groups the emphasis is on the work done since 1940.

The authors regret that they have felt themselves quite unfitted to write of the chemistry of the ABO groups. The subject needs a book to itself.

The deep debt which the authors owe to Professor Fisher is apparent throughout this book. Wherever the sun of genius may have illuminated the English blood group work it has been of Fisher's shining.

The authors wish to thank Miss Sandra Flett for the very large part she played in preparing the manuscript for the press; they are also greatly indebted to Mr. J. D. Race (the father of the senior author) who has devoted much time to the reading of proofs and to the preparation of the author's index; and to Miss Helene A. Holt who has given much thought to the difficult problem of the subject index.

Both the authors have, for some time, been indebted to Dr. A. E. Mourant of the Ministry of Health (now Medical Research Council) Blood Group Reference Laboratory for most of the antisera used in their work.

We would like here to acknowledge the kindness of Dr. L. K. Diamond in making it possible for the junior author to work for some fruitful months at the Blood Grouping Laboratory, Boston.

We are indebted to innumerable authors and publishers for permission to quote published work, acknowledgement of which has been made in the text, but we would like here particularly to

thank the Editors of *Annals of Eugenics* and of *Heredity*, and the publishers, the Cambridge University Press and Messrs. Oliver & Boyd, for the loan of several blocks.

Finally we would like to record our appreciation of the skill and good humour of our publishers and printers in face of rather fearful odds.

PREFACE TO THE SECOND EDITION

SINCE the first publication of this book a ninth blood group system has been discovered and clearly defined, contributions have been made to the knowledge of the other eight systems, and there have been notable successes in the application of blood groups to genetics and to medicine. Because of all this each chapter has been added to and two new ones have been written—on the *Kidd* groups and on linkage.

Now that there are so many systems of blood groups we find that some rigid parochial order of recording them is essential: in pedigrees and lists we write them in the order of their discovery and in this way also the chapters have been arranged.

We thought that a table showing the distribution of χ^2 would be useful and we are very grateful to Professor Sir Ronald Fisher, of Cambridge, to Dr. Frank Yates, of Rothamsted, and to Messrs. Oliver & Boyd, Ltd., of Edinburgh, for permission to reprint Table IV from *Statistical Tables for Biological, Agricultural and Medical Research*.

We would like to thank those responsible for the most useful bibliographies in *Blood Group News* (Copenhagen), in the *Revue d'Hématologie* and in the *American Journal of Human Genetics*. Other acknowledgements will be found above in the Preface to the first edition.

FOREWORD

I AM extremely glad that Race and Sanger have been induced to undertake the heavy labour of preparing a modern book on the blood groups, giving especial attention to their inheritance. The need for an exact and comprehensive text-book has been increasingly evident during the rapid progress of the last decade, and no authors could be better qualified for the task. Both are, however, fully occupied by new researches in the fields which they themselves have to a great extent opened up, and great self-discipline was surely needed to bring themselves to sacrifice so much of their time as this book needed.

Research people are usually so conscious of how much remains to be done that they sometimes underrate the extent of what has been already accomplished. In particular this seems to be the case with respect to the future use of blood-grouping as the principal tool of a comprehensive study of the human germ plasm. To have established, in a short time, nine usable marked loci is surely to have gone a long way towards establishing that 'basic triangulation' by which in due time the whole will be surveyed. There are in man only twenty-three autosomes, and to have at least one good marker on nine of these puts the future study of the numerous Mendelian factors known in man, through the transmission of rare anomalies, in a position very advantageous compared with that when I left the Galton Laboratory. Many new linkages must be already within reach of detection, when family studies can be combined with comprehensive serological tests.

On matters once controversial (and still so occasionally) the senior author has exercised a commendable restraint. No one would judge from the text how often his personal contributions have been ignored, and when verified have been published without acknowledgement of his priority. Our present understanding of the complex *Rh* situation owes much to the good temper with which, in spite of irritants, he steadily pushed on with his own problems.

It is fortunate that the authors can command a simple and lucid style, for much that is to be expounded is really intricate. Those

who have followed the work during its development will often be surprised at the simplicity with which an adequate account can now be given. They may also be amused at the 'evasive action' occasionally taken by the authors when anything heavy in the way of mathematics seems imminent.

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BLOOD GROUPS IN MAN

CHAPTER I

INTRODUCTION

Blood groups

IN 1875 Landois noticed that if red blood cells of an animal of one species were mixed with serum from an animal of another species clumping, or agglutination, of the red cells usually occurred. The phenomenon was recognized as being similar to that which followed the mixing of bacteria with appropriate immune sera. The similarity suggested that the agglutination of the red cells was due, like that of the bacteria, to antigens on their surface uniting with antibodies in the serum. Had there been no knowledge of bacterial immunity already in existence the basic principles of the science of immunology could have been discovered from the behaviour of red cells and serum. As it was, the knowledge of bacterial immunology could be directly applied to the understanding of the nature of red cell agglutination.

The first observation of the agglutination of human red cells by serum belonging to the same species was made by Landsteiner in 1900, when he found that the sera of some of his colleagues agglutinated the red cells of others. Thirty years later he received a Nobel Prize for this discovery of the *ABO* groups. Until his death in 1942 Landsteiner was the leading figure in this field of biology which he had discovered.

The recognition of the part played by the *ABO* groups in blood transfusion soon followed and from that time transfusion began to be safe.

The discovery that the blood groups were inherited characters greatly increased their biological interest. Ottenberg and Epstein suggested in 1908 that the groups were inherited, but Bateson writing in 1909 could still say: 'Of Mendelian inheritance of normal characteristics in man there is as yet but little evidence.'

In 1910 von Dungern and Hirsfeld established beyond doubt the Mendelian inheritance of the groups, though it was not till

1924 that the exact manner of their inheritance was elucidated by the mathematician Bernstein.

The rigid manner of their inheritance made the groups of interest in another field—that of the law—where they are being used in more and more paternity cases each year.

The blood groups were found to contribute to yet another field of science when, during the first world war, Hirszfeld and Hirszfeld discovered that there were racial differences in the distribution of the groups. Blood groups now supply the physical anthropologist with what is probably his most useful tool.

The discovery of further systems of blood groups followed that of the *ABO* by a quarter of a century. In 1926 Landsteiner and Levine discovered the *MN* system and the *P* system. These two systems though of genetic and anthropological interest did not influence blood transfusion.

In 1939 and 1940 blood group investigation entered a new phase of interest when the work of Landsteiner and Wiener and of Levine and Stetson resulted in the discovery of the *Rh* groups and of their fundamental role in causing a disease called *erythroblastosis foetalis* or *haemolytic disease of the newborn*. Blood groups had now entered the field of scientific medicine.

Within the last ten years the *Rh* and the *MN* groups have been subdivided and five more systems of groups have been discovered, called *Lutheran*, *Kell*, *Lewis*, *Duffy* and *Kidd*. All of these systems are of genetical and anthropological importance: most of them have been blamed as the occasional cause of haemolytic disease and of haemolytic transfusion reaction.

Blood grouping

In this section an attempt is made to give those readers who are not serologists a general idea of the tests used in blood grouping. The tests most commonly used are, in principle, very simple, and it is a matter of surprise that they have contributed so much to biological knowledge.

The great bulk of blood group knowledge has been gathered from the results of simple agglutination tests. A serum containing a known antibody is added to a saline suspension of red cells. If the cells carry the equivalent antigen they are agglutinated; if no agglutination occurs it is concluded that the cells lack the antigen.

The converse procedure is the identification of the type of anti-