

GENERAL PATHOLOGY

EDITED BY
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Fourth Edition



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PREFACE TO THE FOURTH EDITION

THIS edition of *General Pathology* was almost completed when Lord Florey died suddenly on 21st February, 1968. The chapters for which he was responsible are thus the last writings to issue from his pen. Some of his pupils had hoped to produce a Festschrift for his 70th birthday, but have been deprived of that pleasure. This book must serve instead. It remains a lasting memorial to Lord Florey's conception of the subject of Pathology, a conception which, by his instruction and by his example, he succeeded in diffusing throughout the world. The book has been extensively re-written, but its structure, style and scope remain the same. A new chapter on pathological consequences of chromosomal abnormality has been added.

June, 1969

PREFACE TO THE FIRST EDITION

PROGRESS in the medical sciences is now so rapid that even those who confine themselves to relatively narrow specialities find it increasingly difficult to master, or indeed to read, the great volume of literature that appears. Nevertheless, the student must try to grasp what is known of the general principles underlying the pathological changes that he will be called upon to diagnose and treat.

For many years it has been the custom at Oxford for every medical student to spend one year studying for an Honour School; in practice this is usually the Honour School of Physiology, which includes a good deal of biochemistry. The aim in the Honour School is not merely to teach facts, but to encourage students, both in the laboratory and by individual tuition, to think about the principles and problems of physiology and biochemistry, an appreciation of which is unquestionably required for the sound building of future clinical knowledge. Thus, it is hoped to give students early in their medical work some training in the deductive and inductive reasoning associated with experimental methods.

It is primarily for those who have read the Honour School of Physiology that a course in General Pathology and Bacteriology is given in Oxford. At present the course lasts for two terms of eight weeks each, and caters particularly for the better student. It is taken at the same time as the study of pharmacology, and immediately before clinical work begins. The lectures in this book are drawn from this course, but they may be of value to those more advanced in their medical work than the students for whom they were prepared; with increasing specialisation the more general aspects of pathology tend to become lost in the details of the subject.

It is to be emphasised that the lectures do not form a complete survey of General Pathology. For the most part they deal with subjects in which one or other of the authors has had a special interest. In particular they attempt to treat of some of the fundamental changes that take place in the body in response to injury, using this word in a broad sense, and to discuss some present-day views about the nature and causes of such changes.

It is hoped that some students will find sufficient stimulus from the lectures to carry an experimental outlook into clinical medicine and surgery, for these subjects have suffered, and continue to suffer in this country, from an approach that pays too little attention to experimental science. At the present day nearly all significant advances in the diagnosis, treatment and prevention of disease depend on the application of experimental methods.

H. W. FLOREY

December, 1953

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Chapter 10 is a revised version of the chapter originally written by Sir Roy Cameron (deceased). Chapter 31 originally written by Dr. F. Kingsley Sanders has now been rewritten by Dr. M. L. Fenwick.

We are again grateful to Miss Christin  Court for half-tone and line drawings and copies of many graphs; and to Mrs. P. B. Loder for helpful criticism and proof reading of Chapters 14, 15, 25, 26, 32, 33, 27, 39 and 40.

The completion of this edition of the book, interrupted by Lord Florey's death, would not have been possible without the help rendered in many ways by Mrs. D. G. Finch-Mason and Miss D. Mackay.

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Chapter 1

THE HISTORY AND SCOPE OF PATHOLOGY

By H. W. FLOREY

TO-DAY we are perhaps more conscious than ever before of our debt to our predecessors, and not only to those of the immediate past but to those also of relatively remote times. The study of medical history is both interesting in itself, and may help to modify the view sometimes expressed that medical students and doctors are lacking in culture of any sort. Moreover some historical perspective is often advantageous when one is considering the multitude of advances that are now taking place in the theory and practice of medicine. I do not therefore consider it a waste of time to bring before you what seem to me to be some of the more important events in the development of pathology. Krumbhaar¹ when writing on the history of pathology remarked that "when we consider one of the broader definitions of Pathology—such as 'The study of the causes of and the effects (both structural and functional) produced by disease', we at once realise that a consideration of its history might properly be almost co-terminous with that of medicine."

Early Studies

The study of disease has no doubt been going on since the time that mankind emerged as a thinking animal, for many of its manifestations are easily seen and felt. There is evidence from mummies, bones, carvings and paintings of antiquity that pathological lesions similar to those of to-day existed, and certain ancient literary fragments contain recognisable descriptions of disease.² An Egyptian papyrus of about 2160 to 1788 B.C. notes diseases of women and cattle, and the Edwin Smith papyrus of 1600 B.C. describes fractures, dislocations, infections of wounds, tumours and a number of other conditions. The Ebers papyrus of about 1550 B.C. mentions "coryza, dysentery, mastoiditis, diseases of bones and joints, tumours, cysts, parasitic diseases, abscess, many diseases of the eye, gastro-intestinal tract and female genitalia". It is perhaps surprising that the Egyptians did not construct a firm foundation of anatomical knowledge, for their practice of embalming might be thought to have given them great opportunities for observation of the viscera. The internal organs were, however, apparently removed through small incisions and the Egyptians did not, in fact, contribute anything substantial to the knowledge of human anatomy. There are many references to disease in other ancient writings, for instance those of the Jews, the Assyrians, the Indians and the Chinese.

Though some cultures had well-developed pathological theories which to a certain extent controlled ancient medical practice, it was the Greeks who most profoundly influenced Western medicine. They invaded Greece and Asia Minor from the north, conquering the preceding Minoan civilisation, and not only came into contact with the medicine of their conquered subjects, but in

Asia Minor were influenced by doctrines coming from Mesopotamia and from Egypt. The nimble-witted Greeks absorbed other people's ideas and, as in all they did, added greatly to them by accurate observation and by a new philosophical outlook. They recorded the appearances of many disease conditions that can be recognised by careful clinical examination and such descriptions are still valid, but their studies of pathology were severely handicapped since, except for a short period in Alexandria, they made no systematic examinations of the body after death. The Alexandrian writings have apparently all been lost. With the lack of background founded on post-mortem observation there flourished physiological and pathological theories that had little foundation in ascertained fact. These theories, which may have originated with the Hindus before 2000 B.C., dominated physiological and pathological thought in Europe until the re-awakening of inquiry during the Renaissance began to make its effects felt in the fifteenth and sixteenth centuries.

The Greek views on pathology, based on "humours", to which "spirits" and other elaborations were later added, cannot detain us now, but as they dominated medical thought and paralysed rational progress in western medicine for at least 1500 years, they can rightly be deemed of great importance, perhaps historically the most important pathological theories yet propounded. Greek medicine came down to mediæval times partly through the works of the non-medical patrician Roman, Cornelius Celsus (about 30 B.C. to A.D. 38), who collated much of the knowledge of the time. But it was a Greek, Galen (A.D. 130–200) from Pergamum in Asia Minor, who, besides making many original observations, some of an experimental nature, put the pathological doctrines of the time into a form that was treated as authoritative until well after the Renaissance. It was not until the sixteenth century that a serious breach was made in the teachings of Galen, which had been erected into a dogma which no one challenged by further observation.

The ancient humoral theories still persist in some of the words that we commonly use, indeed much of medical terminology is of Greek origin. The humour, or fluid, that predominated was thought to govern, amongst other things, a man's temperament. Thus one was *sanguine* (from predominance of blood which was hot), another *phlegmatic* (phlegm was thought to be a product of the brain), another *jaundiced* (yellow bile from the liver) and a fourth *melancholic* (black bile from the spleen). Certain expressions such as "to vent one's spleen" come from the same era.

Though the theories that underlay the use of these words have gone, certain aspects of Greek medical thought survive to this day. In particular the oath of dedication that was taken by the followers of Hippocrates set a high standard of moral behaviour for the medical man towards his patients and their relatives. The fact that all medical practitioners to-day are expected, in addition to having professional skill, to adhere to a code of ethics in their practice is a continuance of the ideal that was first clearly formulated by Hippocrates. Though some of the original Hippocratic oath to which Greek medical men subscribed seems outmoded to-day, medical schools given to symbolic rites still use it, and from time to time an attempt is made to formulate an "international oath" for medical practitioners that would bear a close resemblance to the oath of the Greeks.



1/FIG. 1.—Vesalius (1514–64), from *De humani corporis fabrica*, 1543.

The Rise of Morbid Anatomy

With the Renaissance the scientific and medical atmosphere altered completely. The great sixteenth-century anatomists who worked for the most part in Italy, among whom the Belgian Vesalius stands supreme, founded the modern study of anatomy by their careful dissections and observations, their work often being illustrated by engravings of the greatest beauty (FIGS. 1–3). It was largely through their work that a beginning was made in challenging Galenic dogmatism.

It is worth recalling that Leonardo da Vinci (1452–1519) dissected some thirty corpses and made remarkable drawings of his observations. Unfortunately his great collection of drawings and notes, which he never published, passed into private hands at his death and was not seen for the next fifty years,

If his work had been known, there is little doubt that Leonardo would have been hailed as the originator of modern anatomical studies.

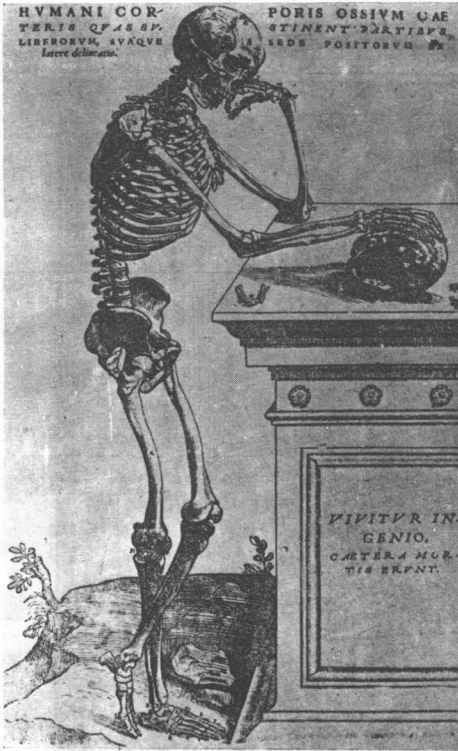
The word "anatomy"—literally a "cutting up"—first denoted the function at which the corpse was dissected. FIGURE 4 shows the somewhat feverish atmosphere to be found when Vesalius and others were examining a body, and one can perhaps glimpse the eagerness of the gathering of students before the revelations of the new method of exact dissection and the disregard of what the ancients had said. Just as hangings were public functions, so during the rise of interest in scientific matters anatomies attracted gatherings of laymen, often people of rank and education, for whom science in all its aspects was a fashionable hobby. The study of anatomy by dissection was fairly widespread in Europe by the end of the sixteenth century. FIGURE 5 shows an anatomy of the period in this country, and FIG. 6 one in Holland, a country which was to assume the lead in medicine during the seventeenth century. FIGURE 7 shows a dissection in eighteenth-century Holland, marked by the elegance of the participators—an elegance which might perhaps be copied by present-day anatomists and pathologists without harm. The illustration of an anatomy by Hogarth shows how by the eighteenth century the professor sat with a wand and somewhat disdainfully pointed out parts of the body laid bare by a bewigged attendant (FIG. 8).

As the dissection of bodies became more frequent, deviations from the usual were often noted, and in time substantial additions were made to pathological anatomy. Some information about disease conditions had been obtained by sporadic post-mortem examinations before the fifteenth century (FIG. 9), but it is in the writings of Antonio Benivieni (ca. 1440–1502), a Florentine surgeon, that we first encounter a description of some twenty post-mortem examinations "made specifically to determine the cause of death and explain symptoms".¹ Benivieni has been called the father of pathological anatomy and his book has been described as "the only book on pathology that owes nothing to anyone".

It was, however, Giovanni



1/FIG. 2.—Second muscle tabula from the *Fabrica*.



1/FIG. 3.—From the *Fabrica*. Note that the skeleton is depicted in a living position.

how 'the symptoms were the result of the lesions. Morgagni is justly said to have introduced the 'anatomical concept' into the practice of medicine. This concept is one of the main elements in modern diagnosis, and a modern physician, in reflecting on a case, considers first whether he is able to express the symptoms in terms of the lesion."³

In England John Hunter (1728–1793) (FIG. 11) and to a lesser extent his brother William (1718–1783) contributed greatly to pathology, as well as to normal and comparative anatomy. The great Hunterian Museum, with John Hunter's specimens, was almost completely destroyed in the second world war, but he made a lasting contribution to museum technique which still endures. A nephew and pupil of John Hunter—Matthew Baillie (1761–1823) (FIG. 12), a Balliol man—wrote the first systematic text on pathological anatomy in which the matter was arranged according to organs rather than by symptoms, which had been Morgagni's method.

Krumbhaar¹ has summed up the position as follows: "... By the end of the eighteenth century we find gross pathologic anatomy established as a firm basis for medical science; chiefly by the vast number of Morgagni's observations, on the whole well correlated with clinical records, and a beginning made with Baillie's text of systematic treatment of the subject as an independent discipline.

Battista Morgagni (1682–1771) (FIG. 10) who really put the scientific study of gross morbid anatomy on a firm foundation. He was a professor at Padua for no less than fifty-six years, during which time he made a vast number of morbid anatomical observations and added important facts to descriptive anatomy. His principal contribution was to correlate his post-mortem findings with the symptoms exhibited by the patient before death. His great book *De sedibus, et causis morborum per anatomem indagatis* was published in 1761. It takes the form of a series of letters to a friend, whose name is now unknown,² and describes some 700 reports of patients and post-mortem examinations. "The life-history of the patient, the history of his disease, the events in connexion with his final illness and death, are all recounted with detail and care. The condition of the organs at the post-mortem examination is minutely described and an attempt is made to explain