



# AN INTRODUCTION TO PATHOLOGY

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**AN INTRODUCTION TO  
PATHOLOGY**



In 1858, just a hundred years ago, Rudolf Virchow published his *Cellular Pathology*—the most famous of his many contributions to medical literature. The work was revolutionary in its reconstruction of the concepts of pathology on the foundation of the then new 'Cell Theory' of living organisms. At once, the analysis of the morphology of lesions changed from the grossly anatomical to the more refined microscopical, and this new approach paved the way first to an understanding of the processes of infection and second to a better appreciation of the nature of neoplasms and their origins. Few medical works had greater influence on both contemporary and later thought than the *Cellular Pathology*.

An account of the life and work of Virchow as a pathologist, anthropologist and statesman has recently been written by Ackerknecht (*Rudolf Virchow*, Madison, 1953). Much, too, of interest for his early life as a student and young physician in Berlin is to be found in the charming letters to his parents that were collected by his daughter, Marie Rabl (*Rudolf Virchow: Briefe an seine Eltern*, Leipzig, 1906). The above portrait of Virchow was made shortly before the publication of his *Cellular Pathology* and about the time that he returned to Berlin to take up the professorship at the famous hospital of La Charité.

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## PREFACE TO THIRD EDITION

It is now generally accepted by medical educators that the student's study of the pre-clinical sciences should be designed with two purposes in view: first, to provide a training in the methodical collection of evidence and the drawing of warrantable inferences from it, and second, to carry out this education by making use of selected facts and theories that will themselves prove of value in the later and more applied portion of their professional training. Formerly, almost the whole of this preparatory education devolved upon teachers of chemistry, anatomy and physiology, and it is more for this historical than for any other reason that in this country these subjects still occupy a disproportionately large fraction of the medical curriculum. There has been insufficient appreciation of the contribution that general pathology can make in this dual programme of education and vocational training, and for a variety of reasons, among them competition with ward work for the student's time and interest, it has never been accorded the status of these more securely established preliminary sciences. Yet as regards both education in scientific method and in factual content, it has much to offer, especially at a time when the integration of the entire curriculum is more needed than ever. Indeed, in regard to factual material capable of holding the interest of the medical student, with his natural urge to the practical, it has manifest advantages over sciences whose growing points appear to be carrying them further and further from the main body of medicine. The time seems to be approaching when, without seriously minimizing the contribution made by the conventional pre-clinical sciences, a more realistic proportion of the curriculum might advantageously be allotted to the study of those general pathological questions that ultimately bear so closely on the further practical training of the student.

Before he can justify a claim to a larger share of the student's limited time, however, the teacher of pathology must design a course that is directed realistically towards the important problems that he will meet with during his clinical work. It is no longer sufficient to regard the subject as self-contained, and to restrict it almost wholly to its morphological aspects: it is essential to present it as a dynamic course which incorporates experimental findings whenever they throw a clarifying light, and is alive to current discoveries in related branches of science. The course should, in brief, be a synthetic one, bringing to a focus the previous two or three years' work—the value of which the student at that stage often fails fully to appreciate—and amplifying it in the many ways that can illuminate clinical problems. It should supply the student with confidence in a method of thought at a critical time in his career, when he is tempted by the very vastness of the mass of factual knowledge confronting him to abandon

scientific principles and adopt a frankly empirical attitude in their place. It is to help him when he is faced with this parting of the ways—by providing a broad survey of future clinical experience in the light of past academic studies—that this book has been written. Moreover, the title *An Introduction* was not—as some reviewers seem to suppose—an unconsidered choice but was made deliberately. For general pathology provides an introduction, which no other basic science can do so well, to a rational approach to those clinical problems to which most medical graduates devote their professional lives.

The earlier editions of this book have included a selected collection of references to original papers or comprehensive reviews; in the present one, I have removed many earlier and introduced numerous more recent ones. Of those newly appearing, many are British or Continental, and it is hoped that by so doing it may be easier for American readers, who are naturally much occupied with their own valuable and expanding literature, to become better acquainted with some of the contributions currently made by their professional contemporaries elsewhere.

In conclusion, I should like again to express my gratitude to many nameless colleagues and correspondents for the help and encouragement they have given me. The enlargement of his circle of friends—even if only friends by correspondence—is one of the more gratifying rewards of an author's work.

G. P. W.

LONDON, *November*, 1957

## PREFACE TO FIRST EDITION

**PATHOLOGY** is rapidly extending its fields of interest in the direction of Laboratory Medicine, and in the training of students there is a tendency for an increasing emphasis to be placed on its practical applications in diagnosis. For obvious reasons, such a development has much to recommend it, for the scope of Medicine and Surgery has been so greatly widened by new knowledge acquired in the laboratory that an appreciation of its potentialities forms an essential part of modern clinical education. But there now seems to be a serious danger that in the teaching of Pathology to undergraduates—and to post-graduate students also—these practical aspects may be over-emphasized, and that the more detailed knowledge of its current clinical applications in diagnosis is now being gained at the expense of an adequate understanding of the mechanisms that underlie disease processes. The present book—which is based upon the author's undergraduate teaching course—has been written in the belief that any further curtailment of the study of what is conventionally known as General Pathology would not only be detrimental to Pathology itself, but would, by starving the student of a training in principles, ultimately have undesirable repercussions in clinical subjects also. The better the student, the more likely it is that this handicap will be felt in later professional work.

In a branch of knowledge that is advancing as rapidly as modern Medicine, it is becoming increasingly difficult to draw any distinction between its academic and its practical aspects. The present generation of clinicians has seen whole fields of Medicine radically transformed as a result of discoveries that only a few years before had seemed to be quite divorced from any likelihood of practical application. It thus becomes more than ever desirable to provide medical students not only with a knowledge of current practice, but also with an intellectual background which will enable them to make effective use of the advances of the future. What direction such advances will take is, of course, wholly unpredictable, but whatever lines they may follow, a grasp of the general principles underlying the body's defences against infection, the repair and replacement of injured tissues and the main features of tumour formation, will all be necessary for their proper comprehension.

The present book is designed to provide an approach to the study of disease from two essentially dynamic points of view. Firstly, emphasis is placed on ætiology—the scientific study of causation in disease. The era in which Pathology was primarily a branch of morphology, and studied by the same technical methods, has passed, and a period is opening in which increasing attention will be directed to integrating studies on pathogenesis with those on preventive medicine. In the past, too, prophylaxis



has centred chiefly round the discovery and elimination of the extraneous agent; in future it will pay greater attention to those intrinsic factors that can modify the resistance of the tissues of the threatened host. Thus consideration of ætiology must come to occupy a larger place in Pathology. Secondly, the book is intended as an introductory exposition of the principles of Pathology in terms of the more fundamental sciences of Biology and Physiology. In so doing, it is hoped that students who have found satisfaction in the experimental display of how the organs of the body work in health will find an equal interest in how these organs react to the noxious agents that excite diseases. While this functional approach to Pathology forms one of the main themes running through the present book, it must be emphasized that such knowledge only supplements and can never supplant a proper knowledge of morbid anatomy and histology. Though a book like the present one can set out the general principles of Pathology, it can never take the place of personal experience in the post-mortem room, the museum and the practical class-room. Neither morbid anatomy nor morbid physiology can be satisfactorily studied alone; it is only when the two are brought into relation to one another that their full significance becomes apparent.

It is becoming more and more accepted that no professional training can now be considered satisfactory which fails to impress students with the rapid advancement of present-day Medicine, and the need for them to develop those critical faculties which will enable them to make prompt and proper use of the major discoveries that will undoubtedly take place within their own lifetimes. This mental attitude can only be reached by bringing undergraduate students into familiar contact with medical literature of an original kind, so that they may early acquire the judgement needed for the appraisal of newly published work. Fortunately, the standards of the libraries available in medical schools in this country have improved so much in recent years, that it is now possible for almost every student to receive his education at a university level. To assist such readers to follow up any aspect of the subject that may interest them, therefore, a selection of representative references, most of which have been taken from readily-available sources, has been included in the text.

G. P. W.

LONDON, *January*, 1950

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## CONTENTS

Frontispiece	ii
Preface to Third Edition	v
Preface to First Edition	vii
Acknowledgements	ix
I Introduction	1
II <i>Ætiology: The Causes of Abnormalities and Diseases</i>	9
III The Inheritance of Abnormalities	26
IV Infection: The Early Phases	46
V Infection: Its Establishment	75
VI Infection: The Dissemination of Micro-organisms within the Body	84
VII The Inflammatory Reaction	99
VIII Therapeutic Modifications of the Inflammatory Reaction	130
IX Inflammation in Allergic Reactions	142
X <i>The Effects of Injurious Agents upon Cells: Degenerations and Necrosis</i>	161
XI Tissue Reactions in Virus Infections	180
XII Tissue Reactions to Ionizing Radiations	200
XIII Reparative Processes in Connective Tissues	222
XIV Chronic Inflammation and Amyloidosis	243
XV Regeneration of Parenchymatous Cells	267
XVI General Reactions to Trauma and Infection : Endocrine, Pyrexial, Leucocytic and Immune	290
XVII Thrombosis	317
XVIII Ischæmia, Embolism and Infarction	339
XIX <i>Hæmorrhage and Hæmostasis</i>	373
XX <i>Œdema</i>	395

XXI	Hypertrophy and Atrophy: Morphological Adaptations to Functional Requirements	416
XXII	Neoplasia: Introduction and Nomenclature	432
XXIII	The Modes of Spread of Malignant Tumour Cells and the Formation of Metastases	450
XXIV	The Morphology and Metabolism of Tumour Cells	474
XXV	The Ætiology of Tumours: Hereditary Factors	486
XXVI	The Ætiology of Tumours: Exogenous Factors	495
XXVII	The Ætiology of Tumours: Endogenous Factors and General Discussion	524
XXVIII	The 'Precancerous State'	537
XXIX	The Pathology of Some of the More Common Tumours	549
	Index of Names	619
	Index of Subjects	631

## CHAPTER I

### INTRODUCTION

A STUDENT beginning the study of Medicine today is entering it at a period of unparalleled progress. Never in its history has any generation seen such rapid advances in the treatment and prevention of diseases. Nor has progress been confined only to certain aspects of medicine: every major branch of the subject, whether concerned with infectious diseases, nutritional deficiencies or endocrine disorders, has undergone similar revolutionary changes. Even in cancer research, although the final goal of control over the development and course of the disease has not yet been reached, fundamental advances have been made in the understanding of the ways in which many kinds of tumours arise, and how precautionary measures against them may be taken. Such progress has naturally exacted its price, for the practice of medicine today is much more elaborate, both as regards diagnosis and treatment, than was that of a generation ago. But the successes achieved have been worth far more than their cost both to the investigator and the practitioner; today the clinician who is able and willing to use the resources of modern scientific medicine can often feel a gratifying sense of power over diseases before which, even a generation ago, his predecessor merely experienced the consciousness of frustration. No longer are medical men concerned almost solely with the alleviation of their patients' symptoms; they are now in a position to prevent or cure many of the pestilential diseases from which human beings suffer.

It is natural to enquire why the rate of advance in medicine has quickened so much in recent years. The answer to this question applies equally to all the major applied sciences, for medicine occupies no exceptional position in this respect. Progress at this accelerated pace has resulted from the application to the solution of technical problems of the theoretical principles of the basic physical sciences whose growth began in the 16th century with the Revival of Learning. In earlier times, every technical advance in engineering, agriculture, industry or medicine was only made slowly, and more often by chance than by design. Only in recent years has it become possible to replace empiricism as the guiding principle in technology by the rational and experimental methods of the abstract physical and biological sciences.<sup>1</sup> In comparison with the long history of narrowly utilitarian efforts, 'the pursuit of knowledge consciously and for its own sake is a thing of yesterday; it is almost the last product of civilization.'<sup>2</sup> This is

<sup>1</sup> Conant, J. B., *On Understanding Science*, New Haven, Conn., 1947.

<sup>2</sup> Ritchie, A. D., *Scientific Method*, London, 1924, p. 1.

not the place to discuss the motives of the Renaissance scholars who recovered the essential spirit of the ancient cultures—an interest in promoting knowledge by independent research.<sup>1</sup> It is sufficient to note that their efforts to satisfy their scientific curiosity have made possible the modern era of rapid material progress.

During the early 19th century, while medical practitioners were still largely dependent upon the traditional methods of mediæval medicine for coping with the practical problems of the diseases they met with daily in their patients, the great pioneers of medical science—amongst them John Hunter, Bassi, Claude Bernard, Virchow, Mendel, Pasteur and Lister—were sowing the seeds of the great growth of theoretical knowledge in various fields of biology closely bordering on medicine. Today modern clinical medicine is reaping the results of their work. No longer are the practical investigators of technical problems forced to rely almost wholly on the precarious method of trial and error: in the planning of any new work, they can now draw upon an immense store of relevant scientific facts and principles, and the whole *tempo* of progress in medical research has been quickened accordingly.

Although the contents of these introductory paragraphs are for the most part common knowledge, there are two good reasons for reiterating them here. Firstly, the belief that medicine is still primarily an 'art' dies hard. How far the holding of this view is likely to advance clinical practice in the future may be judged from the fact that for centuries in the past the stereotyped treatment of diseases lay exclusively in the hands of 'artists'. In the past three generations, the transformation of clinical medicine into an applied science—integrated with the more fundamental sciences of physiology, chemistry, pathology and bacteriology—has effected incomparably more for human welfare than all the centuries of 'art' that have gone before. To refuse to recognize the essentially scientific character of modern clinical medicine, merely because the transformation is still incomplete, is to persist in an attitude of mind that has done much to retard progress in the past, and cannot fail to cause further harm in the future. The modern clinician must be thoroughly imbued with the scientific spirit of the age if he is to take advantage of all the resources now at his disposal.

Secondly, these few preliminary remarks serve to emphasize the debt that clinical medicine owes to the fundamental physical and biological sciences. During its recent era of rapid progress more particularly, medicine has drawn heavily upon branches of knowledge that are often rather disparagingly referred to as 'academic'. Many technical procedures which are now of great practical importance were in the academic stage of development only a generation ago, as innumerable instances can exemplify, and this application of theoretical knowledge to the ordinary pursuits of life will undoubtedly gain greater momentum in the future. To value some knowledge for its usefulness is reasonable, but to stigmatize other

<sup>1</sup> Willey, B., *The Seventeenth Century Background*, London, 1934.

knowledge as useless and academic merely because it has as yet found no applications is to misunderstand the whole history of science and of the forces which have been responsible for its present immense technical successes.

*Pathology as One of the Basic Medical Sciences*

Although today it has become tacitly assumed, it is by no means self-evident that the cure and prevention of disease can only be rationally approached through an understanding of the structure and function of the body in health. It was only during the Renaissance, in the 15th and 16th centuries, that this point of view became at all widely appreciated, but once it had been realized, its acceptance was soon followed by a lively interest in the medical sciences. First came the rapid growth of normal anatomy—the simplest and most easily studied of all the medical sciences. Within a few generations, Vesalius, Fallopius, Fabricius, together with their pupils and contemporaries, had provided a remarkably complete account of the structures of the human body, so far as these could be discovered by the help of naked-eye dissections. The functional activities of the various organs presented problems of much greater complexity, for, unlike those of the more self-contained science, anatomy, they were often dependent for their solution upon the help of other branches of knowledge, especially physics and chemistry, which themselves were then still in their infancy. But in spite of its greater intrinsic difficulties and slower start, physiology has now reached a stage at which it can provide a coherent account of the ways in which healthy organs function both separately and in conjunction with one another in maintaining the vitality of the body.

In his two pre-clinical years, the medical student has brought before him the main discoveries of anatomy and physiology of the last three or four centuries. On this essential foundation, derived from the study of the normal, he must now build his knowledge of the facts and principles of the third great medical science, pathology. Pathology is commonly defined as the 'Science of Disease', though its more lengthy description as the scientific study of 'any condition of the organism which limits life in either its powers, enjoyment or duration'<sup>1</sup> is in many respects to be preferred. Its province is extremely broad, for it deals simultaneously with the structural changes found in the organs of diseased persons both before and after death, with the functional disorders that these may bring about, with the adaptations often made by other organs to compensate for such defects, and lastly with the causes which are responsible for these changes and disorders. Pathology is thus primarily concerned with disease states and processes and their pathogenesis—in short with what Bacon called the 'footsteps of diseases'<sup>2</sup>—and leaves to clinical medicine and surgery the task of discovering how these may be detected and treated at the bedside.

<sup>1</sup> Russell Reynolds, J., *System of Medicine*, London, 1866, Vol. 1., p. 1.

<sup>2</sup> Francis Bacon, *The Advancement of Learning*, Everyman Library, London, 1915, p. 114.

Any description of pathology solely in terms of disease, however, would be too restricted to be entirely satisfactory for the purpose of a modern definition. Although disease in its conventional sense is much the most important, it is in fact only one of a number of relevant conditions studied in this science. For in addition, such very varied disorders as congenital deformities of all kinds and degrees, mechanical injuries that result in the laceration of tissues and the fracture of bones, chemical intoxications such as those that are appearing with increasing frequency in industry through the use of new materials and methods, and finally, special susceptibilities, either inborn or acquired, that affect resistance to other agents of disease, all need to find their places if the full scope of the science is to be properly defined. Because all these latter conditions, in addition to those conventionally regarded as diseases, may be classed together as *abnormalities*, or deviations from the normal, pathology in its more modern and inclusive connotation may be better described as the *science concerned with abnormal states of the body, the functional disorders that accompany them, and the causes that bring them about*. This last aspect of pathology, which has no corresponding counterpart in the sciences of anatomy and physiology, is in many respects the most significant of all, because it is only after the causes of an abnormality or disease are known that appropriate steps can be taken to prevent their effective operation, and *prevention of disease is the goal of modern medicine*.

### *The Scope and Methods of Pathology*

Until the beginning of the last century, medicine was based almost wholly upon the study of symptoms, and these subjective phenomena provided the foundations for all attempts at the systematic classification of diseases. Diagnosis was directed to the elucidation of the major symptoms, and therapeutics to their alleviation. Diarrhœa, for example, whatever its cause, was a 'flux', to be stopped if possible by some combination of the many remedies in the elaborate polypharmacy of the period. Pain was regarded as a sensation to be abolished by some drug, not as an indicator to lead the clinician to the identification of the underlying, often progressive, lesion, that gave rise to it. The practice of medicine was directed to the treatment of symptoms—not to the recognition and eradication of their underlying causes.

The latter part of the 18th century saw the emergence of modern medicine, and so far as any single date can be set to a revolution in any great branch of learning, it may be said to have been born in 1761, when Morgagni published in Venice his famous book entitled *On the Seats and Causes of Diseases as Disclosed by Anatomical Dissections*. The Greeks and Romans had carried out occasional post-mortem examinations on patients who had died of unusual diseases or under more than usually suspicious circumstances, and, so far as ecclesiastical permission allowed, their example had been followed by a few of the physicians of the Renaissance. But Morgagni was the first who attempted systematically to connect and



correlate the symptoms suffered by his patients with the anatomical changes found in their bodies after death.<sup>1</sup>

The great value of this new approach to the problems of disease was immediately recognized, and the next two generations of physicians were actively engaged in the combined roles of clinician and pathologist. They sought to discover in the post-mortem room the morbid anatomical lesions present in their patients at death, for comparison with bedside observations made during the final illness. In these efforts at clinical-pathological correlation, no medical school was more active than that in Paris, and the revolution initiated by Morgagni was soon exploited rapidly and skilfully by Bayle, Laënnec, Bretonneau, Louis and others. Under the influence of these leaders, a profound change in outlook took place there and soon spread elsewhere. Whereas previously the aim of diagnosis and the basis of systematic classification had both been the symptom, it now changed to the anatomical lesion: a 'flux' became an enteritis and an 'angina' a pharyngitis. Strongly though this current of thought in the direction of morphology was running at this time, the abler clinician-pathologists of the period, such as Matthew Baillie,<sup>2</sup> were never misled into believing that morbid anatomy constituted an end in itself; they had the foresight to recognize its growth as a necessary step forward in the final unravelling of the *causes* of diseases. In the first sixty days of his first clinical appointment, every medical student recapitulates the change in outlook that took place in sixty years of a very active period in the history of medicine, for he is introduced to the mental viewpoint which consists in the attempt to translate the signs and symptoms elicited from the patient into the objective anatomical realities that lie beneath them. But in so doing he must not fall into the error against which Matthew Baillie warned, of regarding a correct anatomical diagnosis as the primary aim of clinical medicine—it is merely a prerequisite step in the right direction.

The remarkable improvements in the microscope that were made in the early part of the 19th century opened up entirely new fields in morphology. Two of these have been of major importance in the subsequent development of medicine: the first was the '*Cell Theory*'—the realization that all tissues and organs are immense aggregations of minute, highly specialized

<sup>1</sup> Bacon's remarkable prescience in this matter can be seen from the following quotation from *The Advancement of Learning* (1605): 'And as for the footsteps of diseases and their devastations of the inward parts, imposthumations (abscesses), exulcerations, dis-continuations, putrefactions, consumptions, contractions, extensions, convulsions, dislocations, obstructions, repletions, together with all preternatural substances, as stones, carnosities, excrescences, worms and the like; they ought to have been observed by multitudes of anatomies (post-mortems), and the contribution of men's several experiences, and carefully set down, both historically, according to the appearances, and artificially, with a reference to the diseases and symptoms which resulted from them, in case where the anatomy is of a defunct patient; whereas now, upon opening of bodies, they are passed over slightly and in silence.' Little attention seems to have been paid to Bacon's suggestion; the first serious exposition on these lines was Morgagni's book, which appeared nearly two hundred years later.

<sup>2</sup> Baillie, M., *Morbid Anatomy of some of the most important Parts of the Human Body*, London, 1795.