CHURCHILL LIVINGSTONE

Principles of Pathology for Dental Students

J. B. Walter Margaret C. Hamilton M. S. Israel

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Principles of Pathology for Dental Students

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Preface

The student embarking on a career in dentistry must achieve, within a period of five years, sufficient skill to recognize, diagnose correctly, and treat the diseases occurring in the oral cavity. In addition to becoming adept in many complicated practical procedures, the student must also acquire much theoretical knowledge. This knowledge should be based on sound general principles, and Part I of this book is intended to cover the principles of general pathology in a manner suited to the particular needs of the dentist.

The dental surgeon treats not only diseases of the oral cavity but also people—each patient as an individual with problems that may not be confined to the mouth. Dental treatment must be related to other diseases in so far as these may modify the treatment or necessitate the taking of certain precautions. Nowhere is this more pertinent than in a patient with heart disease. Although the dentist need not be medically qualified, there should be sufficient insight into common diseases to afford an appreciation of the patient's general condition, so as to allow an effective co-operation with the medical attendants.

The second part of this book is designed to cover the basic principles of pathology pertaining to some of the special systems. Of necessity this coverage is brief, but it is intended to be adequate, so that when time and opportunity arise, the dentist will be able to consult specialized texts without the feeling of venturing into foreign lands. When the student encounters pathology for the first time, many new words and concepts are met; these we have endeavoured to define when they are first introduced so that the learning may proceed by a series of graded steps. We have appended a list of references to each chapter in the hope of fostering the spirit of enquiry in our students. These references have been rigorously scrutinized in this edition, and most of those over ten years old have been omitted. The old references can easily be obtained from the previous editions and from standard texts of pathology as well as from the current reviews. For the first time the full title of each reference has been included, and it is hoped that this will stimulate the reader to consult the material cited, and to adopt a critical approach.

Six years have elapsed since the third edition was published, and although there have been no striking breakthroughs in medicine, the many advances that have been recorded have necessitated a complete revision. Four new chapters have been added; in Chapter 16, 'Some disorders of metabolism', the section on glucose metabolism is followed by an account of diabetes mellitus and gout. Chapter 17,

'Disorders of nutrition', encompasses the important topics of starvation, the role of vitamins, and the malabsorption syndrome. The topic of calcium metabolism has been expanded and added to the existing section of heterotopic calcification; this now constitutes a new Chapter 18. Chapter 19 is devoted to an account of the collagen vascular diseases. The chapters devoted to immunology have been thoroughly revised, and additions have been made to the chapters on diseases of the heart, gastrointestinal tract, and kidney. Other topics which have either been introduced for the first time or else considerably expanded include the mediators of acute inflammation, the granuloma, the bactericidal mechanisms in polymorphs in relation to immunity, viral diseases (especially the section on the oncogenic viruses and the viruses of hepatitis), axial regeneration in amphibians, the HLA system, the serology of syphilis, leprosy, chlamydial infections, and the clonal origin of tumours. In all, this has necessitated an increase in the size of the book by 153 pages.

One other departure from our previous custom has been the introduction of SI units. These are commonly used in many countries, but the traditional units have been retained alongside the SI units for those readers who are unfamiliar with the new nomenclature.

1981

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We wish to thank W B Saunders Company of Philadelphia for generously allowing us to use over 40 illustrations from *An Introduction to the Principles of Disease* (by J B Walter). A number of these figures have previously apppeared in the fifth edition of *General Pathology* by J B Walter and M S Israel and published by Churchill Livingstone. Many of the gross specimens illustrated are from the Wellcome Museum of Pathology, and we are grateful to the president and the council of the Royal College of Surgeons of England for permission to publish them. In accordance with their wishes each is acknowledged at the end of the caption, and their catalogue number is indicated. A number of specimens illustrated are from the Boyd Museum of the University of Toronto, and we thank Dr E Farber of that Institute for permission to use these.

We are indebted to a number of colleagues for providing valuable criticism and for assisting in the realms of their particular expertise: Dr Y Bedard (Toronto) for electron microscopy; Dr G T Simon (Hamilton) for electron microscopy; Dr Leslie P Spence for reviewing the section on virology, and Micheline Fauvel, lately of his Department of Virology at the Toronto General Hospital, for providing many of the new electron micrographs of viruses. We owe special gratitude to those who have given us unpublished material or have allowed us to modify their original work. Each figure is acknowledged separately under its caption.

Our thanks are due to Mrs Sonja Duda, librarian of the Banting Institute, Toronto, for valuable help in obtaining references, and to Mr A A Silcox and Mr J T Manders of the Pathology Department of the Royal College of Surgeons of England, London, for help with photomicrography.

Contents

PART ONE

General pathology

1

Introduction

In the practice of medicine it is soon apparent that the majority of patients who seek help do so because of some abnormality which is causing them distress. Often such *symptoms* can be dispelled by simple remedies—quite often by time and reassurance. Much of medicine is an art which its practitioners, whether doctors, dentists, nurses, or physiotherapists must learn. Nevertheless, there have always been individuals who were not content simply to observe disease and the effects of empirical time-honoured remedies upon it. They have attempted to describe and record the abnormalities in their patients in an objective manner; by introducing measurements they initiated the science which is called pathology.

Disease itself is as difficult to define as is the normal, from which it is a departure. As generally used, the term disease is employed to describe a state in which there is a sufficient departure from the normal for signs or symptoms to be produced. The variations from the normal are called *lesions,* and although generally structural in nature, the term may also be used to describe functional abnormalities, for example *biochemical lesions* (p. 55). The cause of the disease is called its *aetiology* and the development of the lesions its *pathogenesis.* Although aetiology and pathogenesis are generally described as separate entities, in practice it is often difficult to distinguish between them. Indeed, the aetiology of one era may become part of the pathogenesis of the next. An example will suffice. A patient takes a large dose of strychnine, develops convulsions, and dies. Clearly the aetiology of the disease is administration of strychnine. However, a closer consideration may reveal that the drug was self-administered during a phase of depression. The suicidal administration of strychnine would then be part of the pathogenesis of the fatal disease depression.

Although this instance may appear to be an exaggeration of the difficulty in delineating the cause of a disease, many other examples will be encountered. The great advances in bacteriology which started at the end of the nineteenth century fostered the concept that each disease had a single cause. To state that a boil is always caused by the *Staphylococcus aureus* is true, but nevertheless this is an incomplete statement. It is known that patients with diabetes mellitus are prone to develop recurrent boils. Which is the cause of the boils, the staphylococcus or the diabetes? Present doctrine would still favour the organism, but the diabetes would be labelled a major predisposing factor. Multiple causes are probably much more common than we think. The doctrine of one cause for one disease has certainly failed to be a profitable concept in the search for the aetiology of many

common diseases such as cancer, arteriosclerosis, emphysema, chronic bronchitis, and dental caries.

An attempt to avoid the difficulty in defining disease has been the introduction of the term *syndrome*. This is a condition in which there occurs a defined collection of lesions, signs, or symptoms which are not necessarily always caused by the same agent. Thus Mikulicz's syndrome is defined as bilateral painless enlargement of the lacrimal and salivary glands from whatever cause. It may be found in leukaemia, but frequently the cause is unknown and it is then said to be *idiopathic*. Clearly the diseases in which the cause is not known are difficult to distinguish from syndromes. Indeed, the two terms are frequently used quite indiscriminately and interchangeably.

Pathology is thus the scientific study of disease. It describes the cause, course, and termination of disease, and the nature of its lesions. In almost all diseases the lesions are of varying nature, and may be morphological, chemical, or functional. Anything which can be measured is within the domain of pathology. The height of the blood pressure, the rate of the heart, and the temperature of the patient are all valid measurements, which if accurately recorded are as scientific as are measurements of the size of a muscle fibre on a section or the amount of fat in a liver.

All good clinicians are thus practising pathologists, and it is for this reason that pathology is such an important part of the curriculum for both dental and medical students.

2

Normal structure

Introduction

The body is composed of innumerable cells which are bound together by a variable amount of intercellular material. Each cell is enclosed by an outer limiting membrane, the *cell* or *plasma membrane,* and contains a nucleus which is bounded by the *nuclear membrane.*

Development from the fertilized ovum is accomplished by two processes:

1. *Division,* whereby more cells are produced and
2. *Maturation,* or *differentiation,* whereby cells develop specific structures which enable them to perform specialized functions, e.g. contraction in the case of muscle fibres. Some highly specialized cells, e.g. neurons, lose their ability to divide as they become differentiated, but others do not, e.g. liver cells. What is lost during the process of maturation is the ability to differentiate along other lines. While the fertilized ovum is *totipotent,* i.e. capable of producing all the tissues of the body, its cellular progeny are not all alike and do not have this ability. Both cytoplasmic and nuclear factors are probably involved in differentiation, but the nature of this process, which may be regarded as a type of ageing, is not understood.

Early evidence of differentiation within the mass of cells composing the developing embryo is the formation of three distinct germ-layers. An outer layer of cells forms the *ectoderm,* while a tube develops within the mass and the cells lining it form the *endoderm.* This tube forms the basis of the future alimentary canal and the organs that bud from it—lungs, liver, pancreas, and others. The *mesoderm* consists of cells lying between the ectoderm and the endoderm. The primitive cells of each germ-layer can differentiate along two separate lines to form either epithelium or connective tissue. These are described later (see p. 31). It is evident that the cells of the body show a considerable diversity of structure and function, yet each is in fact remarkably independent. Each receives a supply of oxygen and foodstuff from the blood stream with which it must produce its own structural components and secretions, and from which it must release the energy required for mechanical, chemical, or electrical work. It is therefore not surprising that all cells are built upon a similar basic plan.

The number of chemical reactions known to occur inside the cell is so great that it would be difficult to understand how these could proceed in a structure as simple as the cell appears to be under the light microscope. The electron microscope has changed all this—from a barren wilderness, the internal structure

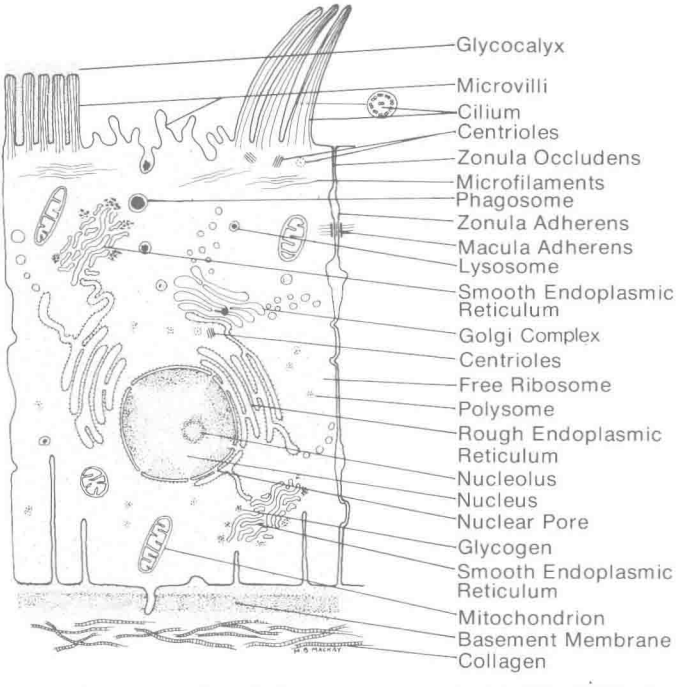

Fig. 2.1 Diagrammatic representation of a hypothetical typical epithelial cell. The free surface of the cell has projecting microvilli, which on the left are arranged regularly to form a brush border. In the centre the villi are irregular, and micropinocytotic-vacuole formation is depicted. On the right cilia are shown. The cell adjoins its neighbours with some interdigitation of their plasma membranes; one junctional complex is shown. The nucleus contains one nucleolus, and is surrounded by a double-layered membrane. Between the nucleus and the free border is the cell centre, or centrosome, and adjacent to this is one Golgi complex. There are two centrioles lying at right angles to each other. The base of the cell rests on a basement membrane, and adjacent to this collagen fibres are shown. The plasma membrane, like the other membranes of the cell, has a trilaminar structure. Ribosomes are scattered free in the cell cytoplasm, and are also attached to the rough endoplasmic reticulum and the outer nuclear envelope. (*Drawn by Margot Mackay, Department of Art as Applied to Medicine, University of Toronto*).

of the cell is now seen to resemble a large industrial city with its factories, warehouses, streets, power-stations, etc. (Fig. 2.1 and Fig. 2.6).

CELLS

STRUCTURE OF CELLS

Each cell possesses an outer limiting membrane (the cell or plasma membrane) and within its protoplasm there is another limiting membrane which encloses the nuclear material. Most cells possess a single nucleus which is centrally placed; the basal nuclei of some columnar epithelial cells and the eccentric nuclei of plasma cells are obvious exceptions to this rule. Cells with more than one nucleus are called *giant*, or *multinucleate cells*. The osteoclast is an example of such a cell normally found in the body. Giant cells that are formed under pathological conditions are described later.

The cell membrane[1,2]

The cell membrane is an extremely important structure, since it forms the interface between the cell cytoplasm and the interstitial tissue fluids, or in the lower forms of life, the exterior. Its functions may be listed as movement, cell recognition, adhesion, control of cell growth, and transfer function.

Cell movement[3]

Examination of living cells reveals that the plasma membrane is not a rigid structure, but is in constant motion. This motility is particularly well developed in certain cells, and permits them to move bodily through the tissues. The white blood cells—polymorphonuclear leucocytes, lymphocytes, and monocytes—behave in this way. The undulating surface of the macrophage is particularly characteristic. Folds of the membrane have been observed to entrap a droplet of fluid by a process known as *pinocytosis*.

Apart from locomotion, the surface movement of monocytes and polymorphonuclear leucocytes produces another effect. By pushing out projections, or *pseudopodia*, around particles, they are able to surround and finally engulf them. This process of ingestion is called *phagocytosis*.

Cell recognition

The membranes of the cell, including the plasma membrane, are associated with the antigens by which the body is able to recognize its own cells and tolerate them. Cells from another individual are regarded as aliens, and are attacked by the immune response which they provoke.

Receptor function. Many agents act on cells at specific points, or *cell receptors*. Thus influenza viruses attach themselves to specific receptors on the red-cell envelope (p. 260). Likewise drugs and hormones act on their own receptors. The presence of these specific receptors on particular cells is indeed the explanation of how hormones act only on their target cells and not on other cells. The mechanism of action of many non-steroid hormones is of great interest. The attachment of the hormone to its receptor activates the enzyme adenylate cyclase, which is situated in the cell membrane. This enzymatic activation causes ATP, which is present in abundance on the inner side of the cell membrane, to be converted into adenosine 3′,5′-cyclic phosphate—a nucleotide known more widely as *cyclic AMP* or simply *cAMP*.[4] This important compound has many actions. Thus in a liver cell acted upon by adrenaline, the formation of cAMP leads to the activiation of a phosphorylase that converts glycogen to glucose: this is then released from the cell. In other instances cAMP acts on the nucleus and stimulates the expression of some particular genetic information (Fig. 2.2). In this way cAMP acts as a *second messenger* for the action of glucagon, thyrotrophic hormone, ACTH, and other hormones. Insulin also acts *via* a specific cell membrane receptor, but another nucleoside, guanosine 3′,5′-cyclic phosphate or cGMP, is its second messenger. With the steroid hormones the specific cell receptors are in the cytoplasm (see Ch. 39).