an introduction to general pathology

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An Introduction to General Pathology

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Preface

This book is intended primarily for students of Medicine, Dentistry and Veterinary Science; it should also prove useful to workers in all branches of science who wish to learn about the essential disease processes.

Although relatively short, the book contains enough information to enable its readers to reach a satisfactory standard of knowledge of general pathology in all qualifying examinations of which the subject forms part. This includes the M.B. examination of English Universities or its overseas equivalents or its counterparts in dentistry and veterinary science. It also contains enough information to do so with respect to the general pathology component of specialist examinations in the various branches of pathology itself.

Although the aims and general layout of the book are conventional it contains some unusual features which need explanation. The photographs which usually accompany a text of this sort have been replaced by artwork which is intended to aid comprehension. Photographs are perhaps less useful in this respect.

Throughout the book pathology is related to broader aspects of biology, especially ecology and natural selection. This is not an attempt to be fashionable but again represents an effort to make the subject more understandable.

Finally, the chapters on psychological and social pathology were thought by me to be necessary to give the reader at least an intimation of the importance of these factors as causes of disability.

London, 1976 W.G.S.

Contents

1. Understanding Pathology

Pathology is the study of disease, but what is disease? It is often defined as disability, or in terms of visible changes in bodily organs, but to do this avoids the issue. In the normal, non-pathological state our existence depends upon thousands of adjustments which the homeostatic mechanisms of our bodies make every second, as our outside medium oscillates between over-heated rooms and cold windy streets and as our internal milieu changes from a need to conserve water due to thirst to a need to excrete water due to swallowing several pints of beer. This continuous process of monitoring and adjustment which lasts from our first to our last hours, is the substance of the science of physiology, the study of adaptation to the body's ever changing internal and external needs.

By contrast, pathology is the study of inadequate adaptation to changes in the external and internal environment. In simple terms, pathology is the scientific study of the way things go wrong.

Failure of adaptation as seen in pathology may take one of two forms. It may be a simple inability to respond adequately, for example in the face of a truly overwhelming infection for which the body has no answer. More usually, disease is partly the result of an adaptive mechanism being turned against the host instead of working to his benefit. The importance of this second type of mechanism is best illustrated by examples. Antibodies appeared in vertebrates as an aid to the destruction of harmful parasites such as bacteria. They are, however, a significant cause of disease, because if the host's tissues become in any way altered, they may be mistaken as alien and evoke a destructive antibody response as in various allergic maladies.

The major killing disease of Western man is atheroma in which the inner part of the wall of arteries becomes infiltrated by fat from the blood. This is an inevitable consequence of the fact that this part of the arterial wall normally receives its nourishment by diffusion of nutriments from the blood. If the wall incorporated tiny blood vessels the diffusion process would be unnecessary but the artery would be too weak to withstand the force of the blood pressure.

As table 1.1 shows cancer too, is a major cause of death. If the organs of the body contained no stem cells capable of mitotic division, cancer would be rare, but if there were no stem cells, cell renewal would be impossible and our life span would be enormously shortened.

Table 1.1 The major causes of death in England and Wales in 1973*

Total deaths	590,000
Ischaemic heart disease	150,000
Cancer	120,000
Cerebro-vascular disease	80,000
Other heart disease	70,000
Pneumonia	48,000
Chronic bronchitis	27,000
Accidental injury	18,000
Neurological disease	6000
Diabetes mellitus	5000
Kidney disease	5000
Suicide	4000
Infectious disease (including tuberculosis)	3000

* From the Registrar General's Statistical Review for 1973. H.M.S.O. London

Thrombosis allies itself with atheroma as a major cause of death and its essence is the formation of clumps of blood platelets. One might then ask why natural selection has not eliminated platelet clumping. The answer is that the aggregation of these little blood cells is one of the most important bodily devices for the arrest of bleeding. Any mutants not

able to produce platelets or to clump them would quickly die. In this instance, as in the other examples, fatal pathology is an unfortunate but inevitable consequence of a process essential for life.

This stress on disease as the other side of the coin of survival is deliberate. The main conceptual problem which medical students encounter in pathology is in attempting to reconcile opposites, such as the dual role of antibodies in defending and attacking the body. If it is accepted in advance that this duality is the hallmark of most disease processes, the subject becomes much easier to understand. The reason for the double-edged nature of many survival mechanisms is because natural selection can act only on individuals young enough to reproduce. What happens to such individuals in later life cannot be influenced by natural selection. So the young have antibodies against bacteria while in middle age the antibodies cause thyroid disease and rheumatoid arthritis. The young are saved from haemorrhage by having sticky platelets which in middle age may kill them by causing coronary thrombosis.

In middle age most disease consists of the unwanted side effects of homeostatic mechanisms. What ill effects nature fails to achieve, man introduces by way of environmental hazards such as cigarettes, industrial pollutants and medicines. In the young disease is more likely to result from a straightforward aberration of nature such as failing to provide some vital enzyme.

Pathology cannot be said to have laws, as thermodynamics has laws, but it does have recurrent themes. The first, already discussed, is that disease often originates from a perversion of a survival mechanism. The second theme is that failures of adaptation tend to be self-reinforcing and progressive. In other words, once a pathological process has started 'one damn thing leads to another'. This is best seen in long lasting illness and is often due to the inappropriate triggering of homeostatic mechanisms, e.g. unwanted retention of sodium in kidney disease. A third theme is that quick bodily responses to un-

favourable environmental events are often over-done. In normal circumstances if more leucocytes are needed the bone marrow produces the appropriate amount. In pathological circumstances a great excess is released from the marrow. A fourth theme is that pathological duels, e.g. between bacteria and man tend to be fought to a draw rather than outright victory. The reason for this paradox is that natural selection favours such a conclusion for both parasite and host.

Reflection on these themes provides the beginning of a conceptual basis for pathology but still leaves the student with a bewildering variety of diseases. It may be convenient for him to consider these as belonging to one of four broad categories. This simple classification is based primarily on the bodily defect or response rather than on the causation of disease. The classification consists of inflammation, degeneration and neoplasia, and a fourth group which cuts across the other three, namely congenital or inherited disease. These terms will be defined in their appropriate place.

2. Infection: Man and his Symbiotes

Everybody knows that much human disease is caused by infection with micro-organisms but the relationship between man and microbe is widely misunderstood. The relationship is not one of defender (man) and invader (microbe) but rather of symbiosis, a term meaning living together. The bodily contact between man and micro-organisms is one part of the broad interdependence between species that we call ecology, defined in 1959 by Odum as the study of the function and structure of nature. It is no longer consistent with the evidence to think of man defending himself against bacterial invasion. This error arose from scientific attitudes developed in the seventeenth century and reinforced in the eighteenth and nineteenth centuries in which man was placed at the centre of natural science while the observer stood back and recorded his relationship with his environment. We are now wary of imagining the body's reaction to microbes as a gift for the preservation of man. A look at the evidence shows us that nature is impartial and that its concern is as much for bacteria and viruses as for ourselves. Germs differ from man only in the level of organisation which they exhibit. Like man, some of their reactions are protective while others appear self destructive, depending, as we shall see, on circumstances. It follows that perjurative terms such as parasitism, no longer serve a useful function, merely describing a symbiotic situation in which no advantage to the host is apparent.

It is customary to speak of **pathogenic** and **non-pathogenic** organisms, the words implying a capacity to produce disease. Although bacteria do vary in this respect, the term is mean-

ingless in a general sense since almost any organism can produce severe disease if the conditions are right and almost any pathogen can live in peaceful symbiosis in a disease-free host. A word used sometimes synonymously with pathogenicity is *virulence* but this really means that an organism has an unusual capacity to invade and damage the tissues of its host. *Infection* itself is a word used in many different ways and this reveals confusion in our concepts of the relation between man and germs in areas normally germ-free (sterile). Sometimes it means that microbes have produced overt signs of damage. Sometimes it means the mere presence of micro-organisms whether they are normally present or not. For example, the urine is normally sterile but if bacteria are present a urinary infection is diagnosed even if evidence of damage or disease is absent. Secondly, if signs of disease are present one would speak of a bacterial infection of the skin even though it was known that this part of the skin in that individual normally harboured bacteria of the same strain. Thirdly, a surgeon would think of the normal large bowel as being infected simply because of the massive bacterial flora it invariably contains.

All infection is better thought of as a variation on the theme of symbiosis. Of these alterations the most important is a change in the population of the resident microbial flora and the second most important is a deficiency in those bodily mechanisms which normally limit the type and extent of microbial co-habitation with man.

When infection occurs in the sense of micro-organisms causing demonstrable disease it is obviously important to establish which particular organism is responsible. To do this with complete certainty Koch's postulates should in theory be fulfilled. These demand that the micro-organism be obtained from the pathological lesions it is thought to have caused, that it be isolated in pure culture uncontaminated with other forms of life which might complicate the experiment, that the pure culture be injected into animals and the predicted disease develop and that the micro-organisms be isolated again from

these experimentally induced lesions and be shown to be identical with those originally isolated from the human patient. However, it is not always possible to satisfy all Koch's postulates even in infections where no doubt exists as to the causative organism.

It is now appropriate to list the micro-organisms which are symbiotes of man and which may produce disease. In ascending order of complexity and degree of organisation they are as follows:

Viruses

These are very small organisms, seen only with the electron microscope. Their size ranges from 28 nm (a nm is one millionth of a mm) to 450 nm. They are composed of a core of either RNA or DNA but never both and with a protein coat called a capsid. They are obligatory intracellular symbiotes, i.e. they can only multiply within the cells of a host. They can, however, survive outside cells in a resting form for long periods even under very unfavourable conditions. They are the cause of many diseases of man ranging from smallpox to the common cold and are now widely suspected of a major role in the cause of cancer.

Rickettsiae

These are larger than viruses although a subspecies, the *coxiella*, are small enough to pass through fine filters like viruses and also like viruses are resistant to heat and disinfectants. Rickettsiae contain both RNA and DNA plus proteins, resemble viruses in being obligatory intracellular symbiotes but like bacteria, are visible under the light microscope and can reproduce by binary fission, i.e. by simply dividing into two. Rickettsiae can survive for months outside the body and cause many severe diseases, notably Typhus. Like viruses, they may spread disease with the aid of insect carriers, e.g. mosquitoes. *Chlamydiae* are similar to Richettsiae

but deserve special mention because they cause the important diseases, Trachoma and non-specific urethritis.

Bacteria

These are larger (0·5–8 μm) and more highly organised, containing DNA, RNA, a cell wall and a complete biosynthetic, respiratory and energy-yielding apparatus. With their complex chemical structure they have the capacity to proliferate outside cells by binary fission, i.e. they are not obligatory intracellular symbiotes although some species, e.g. *Mycobacterium tuberculosis* are facultative intracellular symbiotes, i.e. do better inside cells than outside. Many bacteria survive in a resting form in unfavourable environmental conditions, e.g. in dust. In Pathology it is traditional to divide bacteria into two broad categories of Gram positive and Gram negative on the arbitrary basis of whether they retain a Gram stain (gentian or methyl violet) after alcohol treatment (Gram positive) or whether they lose it and take up a carbol fuchsin counterstain (Gram negative). They are also subdivided by virtue of shape, e.g. the round cocci or the elongaged bacilli and in various other ways.

Mycoplasmae

These are closely allied to bacteria but less highly organised being facultative intracellular symbiotes. They can, however, like bacteria be grown on artificial cell free culture media.

Protozoa

These are highly organised but unicellular organisms of which the amoeba is the prototype. Disease producing protozoa include Plasmodia (malaria) Trichomonas, Toxoplasma, Leishmania (Kala-Azar) Trypanosomes (sleeping sickness) and entamoeba histolytica (amoebic dysentry). Protozoa are most important as causes of tropical diseases.

Fungi

These are plants devoid of roots, stem or leaf. Unlike the algae they have no chlorophyll so they are obligatory symbiotes. They reproduce by spores which germinate and send out branching hyphae. Fungi rarely produce more than superficial disease in man unless there is a major breakdown of host mechanisms which normally stabilise this form of symbiosis.

Helminths

These are worms. They may cause disease at a variety of stages of their life cycle. Their main categories are Nematodes, Cestodes and Trematodes. The most important diseases that they cause occur in hot non-industrialised countries, e.g. Schistosomiasis caused by a Trematode.

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3. The Stabilisation and Breakdown of Symbiosis Between Man and Microbes

A more conventional title for this chapter would be resistance to infection. However, although in every day terms infection means disease caused by micro-organisms, the phrase 'resistance to infection', gives, as we shall see, a misleading picture of the relationship between man and his microbial companions.

One of the many false images surrounding infection is that of man moving permanently through a cloud of dangerous germs as if the air we breathe were an aerosol of pathogenic bacteria. In fact, the microbes are present not in the air but on the surface of floors and furniture and especially on the surface of our bodies. The primary defence against invasion of the tissues by these bacteria is our intact, cornified skin. This is easily shown by a simple experiment commonly performed by nature in which children's knees are temporarily denuded of their cornified epithelium by physical injury, i.e. a graze. such a wound may become heavily colonised by bacteria which give rise to a local tissue reaction, including the formation of pus (p. 78). Two bacterial species, *staph. pyogenes* and *strep. pyogenes* are especially likely to participate but neither could have invaded the tissues and damaged them had the skin surface remained intact.

Apart from the mechanical barrier afforded by a tightly interlocked and cornified, stratified epithelium, the skin has at least two other mechanisms for controlling bacterial populations. There is normally a coating of long chain unsaturated