PATHOLOGY ILLUSTRATED

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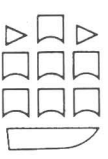

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PREFACE

We believe that communication by verbal and written methods is the fundamental basis for study and learning. Nevertheless, in the modern setting where knowledge is increasing so rapidly and in a subject such as pathology where morphological changes are a major component, we consider that the visual image has an important facilitating role. We therefore offer this book as a companion to its predecessors in the Illustrated Series on medical subjects.

The work has been sustained by the patience and understanding of our wives. In addition we acknowledge with pleasure our debt to numerous friends and colleagues in our working environment who have contributed informally to our understanding of pathology.

A. D. T. Govan
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Glasgow, 1981

INTRODUCTION

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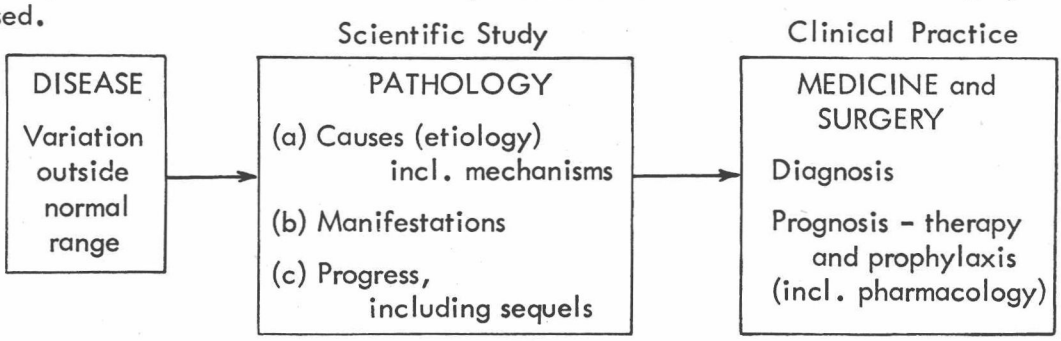
Anatomy and physiology represent the scientific study of the structure and function of the body in the process of normal living. At every level of measurement a range is established within which NORMAL structure and function are defined.

DISEASE occurs when there are variations of structure and/or function outside the normal range.

PATHOLOGY is the scientific study of DISEASE. It is concerned with the causes and mechanisms by which disease is produced, with the descriptions of the manifestations of disease and with its progress and sequels. It is therefore one of the important sciences on which the practice of clinical medicine and surgery is based.



Because of the close relationship between the subjects, anatomical and physiological resumés are given throughout the book.

MANIFESTATIONS of DISEASE are essentially a summation of the damage done by a harmful agent and the body's response to it.

DAMAGE done by HARMFUL AGENT + BODY'S REACTION = DISEASE.

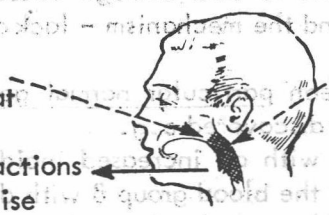
The components of this simple equation are themselves so very diverse and subject to modification by many factors that the spectrum of disease processes is very broad. Nonetheless scientific study demands analysis followed by resynthesis in the form of CLASSIFICATION.

The important broad groups of DISEASE are:-

INFLAMMATORY	DEGENERATIVE	NEOPLASTIC
(incl. infections)	(excl. ageing)	(tumours)

INTRODUCTION

Streptococcal sore throat is an example of a disease process caused by a single harmful agent.



Streptococcal infection of throat

1. 'Poisons' damage cells locally.
2. Local inflammatory response
3. Immune response

General body reactions e.g. fever, malaise

(a) Usual or (b) Abnormal

Cure of infection

Local abscess formation

Rheumatic fever

Nephritis

However in many diseases the harmful agents are multiple and the manifestations and progress of the disease very complex.

AGE AND DISEASE

In young subjects a single harmful agent may cause disease leading to death if a vital organ is affected. With increasing age the chances of several harmful agents each causing separate diseases are enhanced and death is often due to the cumulative effect of such independent disease processes.

Physiological ageing implies a gradual loss of cellular and body vitality usually associated with atrophy of tissues and organs. This process is accentuated and mimicked by the degenerative diseases of old age (particularly arterial disease) so that the physiological and pathological states tend to merge. Nevertheless the student should try to identify the distinctions between ageing and disease although in some instances they may prove difficult to define.

CAUSES of DISEASE There are 2 broad groups.

1. Genetically determined disease

   (a) Abnormalities of the chromosomes and component genes cause many diseases.

   The chromosomal changes are called MUTATIONS: the majority occur spontaneously (or without known cause): in some cases radiations, chemical or infective agents can be incriminated. The diseases produced range from serious defects incompatible with life to mild disorder presenting in adulthood. An important subdivision is the group of hereditary diseases in which family studies are particularly informative.

INTRODUCTION

(b) Susceptibility to some diseases has long been linked with particular genetic types. The susceptibility of blonds to skin damage caused by the ultra-violet rays in sunlight is well known and the mechanism - lack of the protective pigment mechanism - is obvious.

More recently, associations between particular normal genetic types and particular disease processes have been discovered e.g.

(i) The blood group A is associated with an increased incidence of gastric cancer and pernicious anaemia and the blood group B with duodenal ulcer.

(ii) The Human Leucocyte Antigen (HLA) system has been shown recently to have important associations with diseases - particularly infections and auto-immune processes. The system consists of protein substances on the surface of all cells (discovered first on leucocytes). The genetic control of the protein is on chromosome 6.

Chromosome 6

- genes on 4 loci, each with many alleles.

The important rôles so far discovered are:-

(a) a close connection with graft rejection : the better the HLA match between subjects the better the chances of graft survival.

(b) associations with disease processes of many types. The most striking association is of HLA B27 with ankylosing spondylitis (90 per cent of AS subjects are HLA B27).

The mechanisms by which these associations are effected are currently the subject of intensive study.

Chromosome 6

Locus concerned with the immune response - particularly lymphocyte function: implicated in auto-immune disease.

Loci concerned with infection and graft rejection - important implications in carcinogenesis and transplant surgery.

2. Acquired Disease

The many causes of acquired disease can be classified under the following general headings:-

(i) Physical Agents Among these are trauma, radiations, extremes of heat and cold, electrical power, i.e. the application to the body of an excess of physical energy in any form.

(ii) Chemical Poisons These are increasing in number particularly with the advances in industrial processing. Some act in a general manner, such as cyanide which is toxic to all cells. Others act locally, for example strong acids and caustics. Another group exhibit a prediliction for certain organs - paraquat affects the lungs; phosphorus and organic solvents cause damage especially in the liver and kidneys.

Iatrogenic disease is an important subgroup, not uncommon in present times due to the development of powerful drugs, many of which have undesirable side-effects.

(iii) Nutritional Deficiencies These may arise as a result of poor supply, interference with absorption, inefficient transport within the body or defective utilisation. In addition, the effects may be of a general nature as in starvation or lack of oxygen or they cause specific damage, for example, in vitamin deficiencies.

(iv) Infections and Infestations Viruses, bacteria, fungi, protozoa and metazoa all cause disease. They may do so by causing cell destruction directly as in certain virus infections e.g. poliomyelitis, or protozoal infections e.g. malaria. In many cases, however the damage is done by toxins elaborated by the infecting agent as in diphtheria and tetanus. As with poisons they may have a general effect or show a prediliction for certain tissues.

(v) Abnormal Immunological Reactions The immune process is normally protective but in certain circumstances the reaction may become deranged. Hypersensitivity to various substances can lead to alarming shock-like conditions - anaphylaxis or to more localised lesions such as asthma. In other circumstances the immune process may act against the body cells - autoimmunity. This can be seen in certain endocrine diseases such as thyroiditis.

(vi) Psychological factors cause and influence disease processes in several ways: (a) psychological stress may lead to mental illness; (b) their influence on the individual's symptoms and reaction to established somatic disease is apparent; (c) they are important components in disease caused by addiction, e.g. alcohol, tobacco; (d) finally it is thought that psychogenetic factors, by as yet ill-defined mechanisms, may be causally related to such diseases as hypertension, peptic ulcer, coronary arterial thrombosis and ulcerative colitis.

Although the causes of disease are divided into these two main groups, in most disease processes causes from both groups are operative. However in only a few diseases is the genetic component well defined.

A good example is the ability of subjects who have inherited a particular blood group (Duffy negative) to resist infection by Plasmodium Vivax (a type of malaria). The infection clearly occurs only in genetically susceptible individuals: the implications for survival in evolutionary terms are obvious.

Congenital disease is present at birth. It can either be genetically determined or acquired. An example of the latter type are the deformities caused by thalidomide taken by the mother during early pregnancy and it is becoming clear that environmental factors e.g. nutritional factors and smoking are very important environmental causes of congenital disease.

INVESTIGATION of DISEASE

In medical practice the objective of the study of disease is twofold.

1. To determine the nature of the disease process and if possible its causation i.e. to establish a diagnosis.
2. To monitor the extent and progress of the disease and provide an indication of prognosis.

Historically the study of disease was based on morphological observations, first at a gross level and from the nineteenth century at cellular level and MORBID ANATOMY and HISTOLOGY remain the corner stones of pathological study. The emergence of subspecialities e.g. biochemistry and haematology has led to greater understanding in depth. But it is important that such knowledge should not be compartmentalised and one of the tasks of the modern student is to integrate information about disease from various sources and thus acquire a breadth of pathological knowledge.

CONTENTS

INTRODUCTION

METHODS in PATHOLOGY

The traditional methods of careful naked eye and light microscopic examination of organs and tissues at autopsy have been supplemented by the much wider use in clinical practice of biopsy which is the removal of tissue during life for diagnostic purposes. With the development of modern instrumentation biopsies are obtained from many parts of the body.

In addition, numerous technological advances have been applied to pathological methods at various levels with advantage. The following is a brief outline of these levels:-

Level A. Morbid anatomy reveals the gross changes in diseased organs and indicates the secondary effects in other parts of the body.

Level B. Histology: diseases generally have a distinct pattern which can be recognised using the light microscope. Extensions of the method are histochemistry and immunohistochemistry by which the presence of various chemicals can be revealed.

Level C. Cytology: the study of cellular detail is of course a part of histology but the study of individual cells in detail is now important particularly in the diagnosis of cancer.

Level D. Electron-microscopy (EM) reveals the cellular organelles and various patterns of change found in disease.

Level E. The ultimate level, which is as yet beyond the scope of pathology in most cases, is in the field of molecular biology where form and function become one. At this level important advances in pathological knowledge can be expected.

These increasingly sophisticated methods tend to influence the student to focus on detailed mechanisms occurring at microscopic level. Without discouraging such an approach to the subject it must not be forgotton that the observations obtained over many years using the relatively simple methods of naked eye examination and histological assessment of routinely stained specimens are fundamental.

The following descriptions therefore begin with gross pathology and proceed stepwise to the detailed cellular changes where these are known. The student will find that such an approach is the basis of his learning and progress in clinical practice.

CHAPTER 1

CELL AND TISSUE DAMAGE

CELL DAMAGE

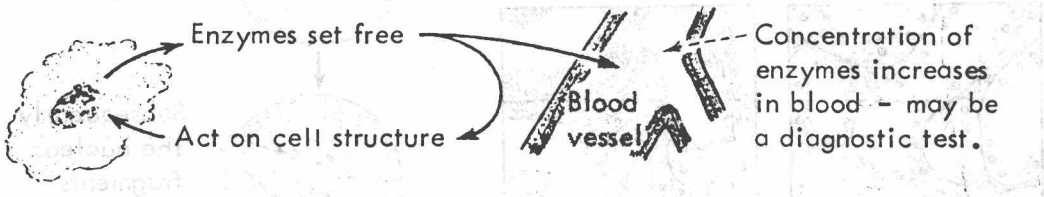
Visible changes occur in cells as a result of noxious agents, the degree of change varying with the severity and duration of the damaging process.

CAUSES OF CELL DAMAGE

1. Reduced Oxygen Supply -
   respiratory disease, cardiovascular disease, anaemia.
2. Physical Agents -
   mechanical trauma, excessive heat or cold, radiations.
3. Chemical Agents -
   these are innumerable and increase with the complexity of industrial processes.
4. Toxins
   bacteria, plants, animals e.g. snakes.
5. Viruses
6. Abnormal Immunological Reaction
   hypersensitivity states.

NECROSIS

This means death of cells while still forming part of the living body.
Following death of cells, enzymes are set free :-



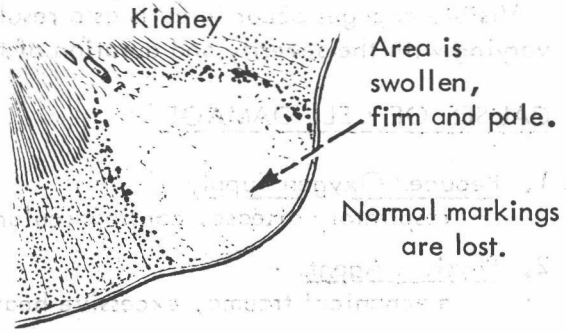
The enzymes induce visible changes in the tissue and these may take one of two forms :-

(1) Coagulative Necrosis
(2) Colliquitive Necrosis.

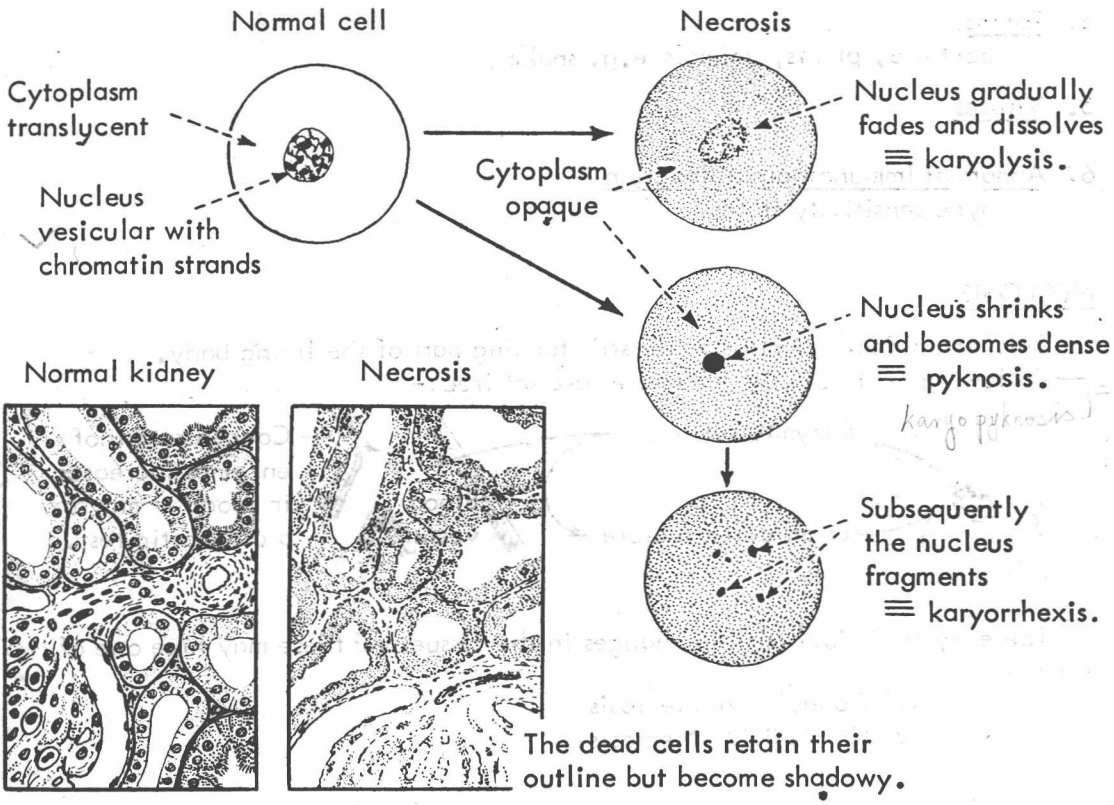
NECROSIS

1. COAGULATIVE NECROSIS

This is the commoner type of change and is frequently caused by lack of blood supply. Necrosis of this type is seen in infarcts of the heart, kidney and spleen (see p 132).



Microscopically the cytoplasm becomes opaque and reacts more strongly with dyes. The nucleus may undergo one of two changes, (a) Karyolysis or (b) Pyknosis.



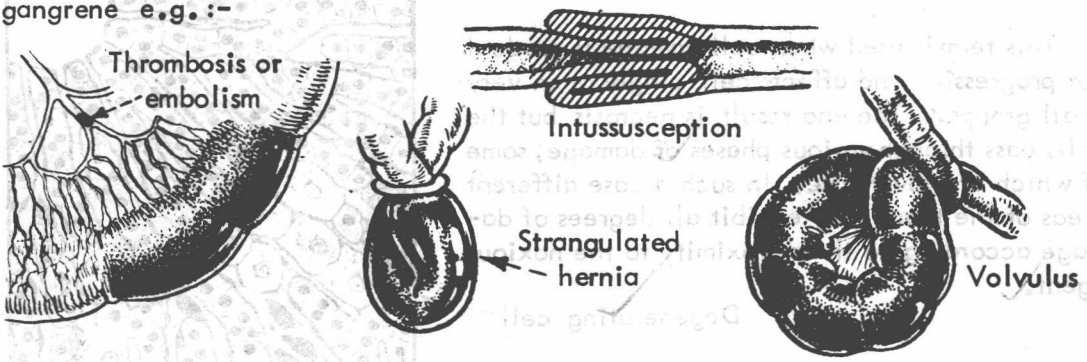
2. COLLIQUITIVE NECROSIS

In the brain consistently, and occasionally in other tissues when they contain a large amount of fluid, necrotic areas undergo softening and form collections of pigmented or turbid fluid, with complete loss of structure.

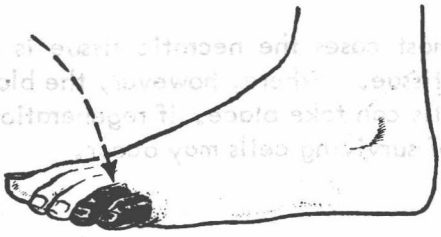
GANGRENE

This is a complication of necrosis. In certain circumstances necrotic tissue is liable to be invaded by putrefactive organisms which are both saccharolytic and proteolytic. Foul-smelling gases are produced and the tissue becomes green or black due to breakdown of haemoglobin.

Obstruction of the blood supply to the bowel is almost inevitably followed by gangrene e.g.:-



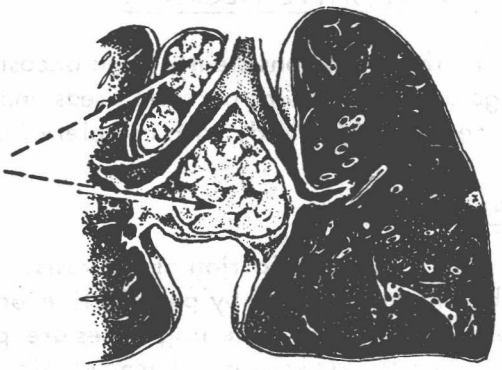
Gangrene also occurs on the skin surface following arterial obstruction. It is particularly liable to affect the limbs, especially the toes in diseases such as diabetes.



A special type of gangrene follows infection with clostridial organisms (gas gangrene; see p 56).

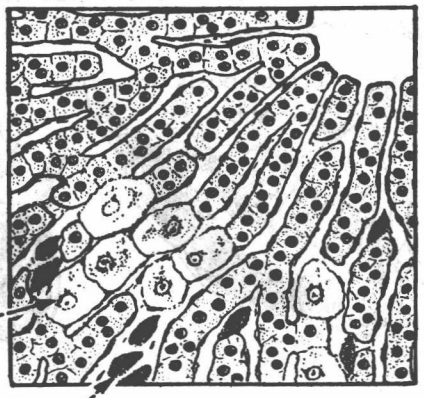
NECROSIS

CASEATION



This is a variation of the necrotic process. The necrotic tissue assumes a yellowish cheesy appearance, slightly greasy to the touch. Microscopically the material is amorphous and granular with odd flecks of chromatin. It is commonly seen in chronic tuberculosis.

NECROBIOSIS



This term is used when cell damage is gradual but progressive and affects cells singly or in very small groups. The end result is necrosis but the cells pass through various phases of damage, some of which are reversible. In such a case different areas of the tissue may exhibit all degrees of damage according to their proximity to the noxious agent.

HEALING OF NECROSIS

In most cases the necrotic tissue is eventually broken down and replaced by fibrous tissue. Where, however, the blood supply is intact regeneration of specialised cells can take place. If regeneration does not take place compensatory hypertrophy of surviving cells may occur.