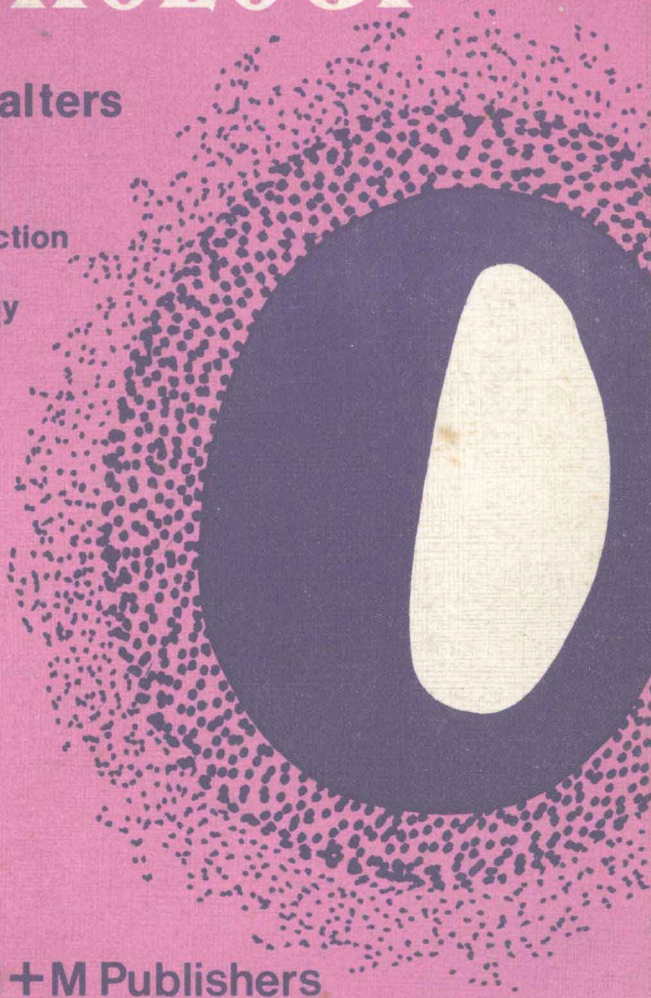
THE LANGUAGE OF PATHOLOGY

Glyn Walters

An Introduction to Medical Terminology and the Nature of Disease



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The Language of Pathology

An Introduction to Medical Terminology and the Nature of Disease

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Preface

Some years ago a biochemist colleague asked me, after a discussion with a physician, 'What is malignant hypertension – is it hypertension due to a malignant tumour?' This seems a perfectly reasonable question but, coming from a colleague who had shared with me for several years an interest in some aspects of hypertension, it made me appreciate for the first time just how difficult it is for the laboratory scientist to acquire an adequate background knowledge of medicine, without which he cannot appreciate the relevance of his work to clinical problems.

The many textbooks which cater for nurses, radiographers and physiotherapists might be expected to be useful in this respect. However, they are not ideal, for they contain relatively detailed accounts of anatomy or of the symptoms and signs of disease, whereas the prime requirement of the laboratory worker is a knowledge of the nature of disease. In the absence of suitable aids the acquisition of such knowledge is likely to be a slow process, and the purpose of this book is to assist the individual to attain a working knowledge of pathology early in his career.

The book is not intended to be comprehensive, nor is it concerned with the basis and interpretation of laboratory tests, which are dealt with in many other books. Its aim is to present an account of the language of pathology which, if assimilated, will enable the individual to acquire detailed knowledge from other sources without the inconvenience of frequent recourse to a medical dictionary.

It is my experience that graduates in chemistry and physics, unlike graduates in biochemistry, often possess little knowledge of biology, and the book therefore begins with an introductory chapter on the structural components of the body. The next four chapters introduce topics and terminology which recur throughout the book. The subsequent chapters dealing with individual systems all begin with a brief account of the relevant anatomy and physiology; new words are explained in context when they first appear.

Although written primarily for the clinical biochemist and other scientific officers, it is hoped that the book will be helpful to medical and nursing students and to others in allied professions.

My thanks are due to Clare Burford who drew the diagrams.

Bristol, June 1978 GLYN WALTERS

Contents

Chapter 1

Cells, Tissues and Organs

The unit of structure of the body is the *cell*. Cells differ widely in their functions, and cells of the same type are aggregated to form *tissues*, different tissues being combined to form more complex structures, i e. the *organs*. The term *histology* refers to the microscopic structure of the tissues, examination of which requires special preparation of the tissue beginning usually with *fixation*. The aim of fixation is to kill the cells while preserving their structure. Thereafter very thin slices or sections of the tissue are cut and stained with a variety of dyes to show up different structural features. Fixation is a slow process and rapid freezing of the tissue may be used instead. An additional advantage of the latter procedure is that enzyme activity and products of cell metabolism are preserved and may be studied in sections by appropriate chemical techniques which give a visible end-point; this constitutes histochemistry.

Although cells differ widely in their size, shape and other details they do have certain structural features (morphology) in common. All cells consist of *protoplasm* surrounded by a *cell membrane*. The protoplasm is subdivided into the *cytoplasm* which forms the bulk of it, and a dense ovoid body called the *nucleus* which is surrounded by a nuclear membrane and may contain one or two smaller *nucleoli*. The nucleus contains the genetic material of the cell and is responsible for transmitting this during cell division. It also governs protein synthesis and hence is necessary for the continued existence of the cell. There are other distinctive bodies or *organelles* in the cytoplasm including the rod-shaped *mitochondria* which are the sites of aerobic energy production in the cell, the *endoplasmic reticulum* concerned with protein synthesis, and the *lysosomes* which contain hydrolytic enzymes capable of destroying foreign particles such as bacteria. Extraneous matter may be engulfed by the cell by a process known as *phagocytosis* or, in the case of droplets of fluid, *pinocytosis*.

All multicellular organisms develop from a single fertilised ovum by successive cell division. At an early stage there is a

spherical mass of cells which during its later development forms three distinct layers, namely the *ectoderm*, the *mesoderm* and the *endoderm*. With further proliferation the cells become 'differentiated', i e. they develop into the specific varieties needed to form tissues and organs. The ectoderm gives rise to the skin, the nervous system and sensory organs, the mesoderm to the connective tissues, the muscles and the cardiovascular system, and the endoderm to the digestive tract. In the fully developed organism some cells are able, like the earliest cells during development, to proliferate and develop into a variety of other cell types (see Inflammation in Chapter 2). Most 'mature' cells however do not have this property and if they are capable of multiplying at all they give rise to cells of the same type. They exist, of course, in the tissues described below.

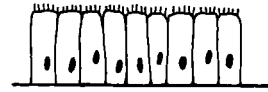
Epithelium

This is the name given to the tissue which is found covering the external and internal surfaces of the body. There are several varieties, which are classified according to the shape of the constituent cells and the number of layers (Fig. 1). An epithelium with only one layer of cells is a *simple epithelium* and one with more layers is a *stratified epithelium*. In all cases the bottom layer is attached to a basement membrane. Thickening or other change in the basement membrane is sometimes an important pathological change.

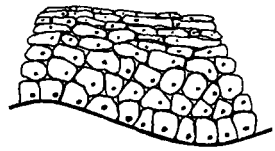
Squamous epithelium consists of flattened cells. A single layer of flattened cells lines the blood vessels and in this situation is known as an *endothelium*. A *stratified squamous epithelium* has several layers; the basal cells are not usually flattened but the cells become progressively flatter towards the surface. The superficial part of the skin, the epidermis, is an example of a stratified squamous epithelium; in this case, the surface consists of dead cells which have become hardened or cornified (see below).

Columnar epithelium consists of cylindrical cells standing on a basement membrane. In some cases the free surface of the cell shows many finger-like processes called *microvilli* which serve to increase the surface area through which absorption into the cell occurs; this type of epithelium is found lining part of the intestine. Another type of columnar epithelium is ciliated epithelium. *Cilia* are cellular processes capable of movement, and they wave rapidly in unison setting up a current of secretions in one direction; they are found, for example, in the air passages of the respiratory system.

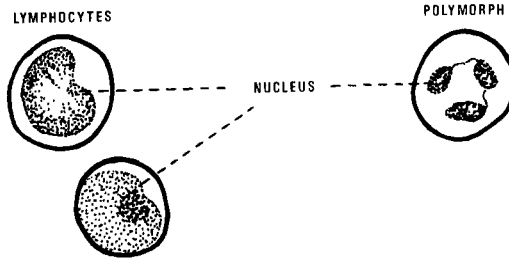
SQUAMOUS EPITHELIUM

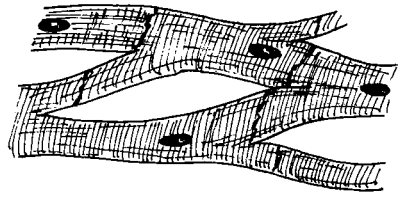


CILIATED COLUMNAR EPITHELIUM



STRATIFIED SQUAMOUS EPITHELIUM





CARDIAC MUSCLE

Fig. 1 Some examples of tissues

Cuboidal epithelium is commonly found in glands, where the division into columnar and cuboidal types is to some extent artificial, e g. in the thyroid gland the epithelium is columnar when the gland is active but changes to cuboidal in the resting state.

A *gland* is an epithelial structure which elaborates a secretion. Glands vary in their structure, and the secretory portion is called the *acinus* in some cases and the *alveolus* in others. The reader of this book should regard these two terms as synonymous.

There are two main varieties of glands, namely *exocrine* and *endocrine*. The exocrine glands secrete into a duct which conveys the secretion to a surface where it acts. The endocrine glands (Chapter 15) have no duct, i e. they are the *ductless glands*, and their secretion passes directly into the blood vessels, with which they are richly supplied. The substances secreted by endocrine glands are the hormones, which influence the activity of tissues far removed from the glands.

Connective tissue

There are several varieties of connective tissue, which differ in their structure and function. All are derived from the embryonic mesoderm and all consist basically of a mixture of cells, fibres and intercellular material called *ground substance*.

The most widespread form of connective tissue is known as *areolar tissue* and this is often referred to simply as connective tissue. It consists of a relatively large amount of ground substance composed of mucopolysaccharides, intermingled with which are many fibres and cells. The fibres consist of *collagen fibres*, which are bundles of *reticular fibres*, and *elastic fibres*. The characteristic cell of connective tissue is the *fibroblast*. This lays down the reticular fibres and, in keeping with the implications of the term 'blast' that the cell is not fully differentiated, it matures into inactive fibrocytes, and is also capable of transformation into other cells. Connective tissue also contains *histiocytes* and *macrophages* whose function is to phagocytose foreign particles, *fat cells* (also called *lipocytes* or *adipocytes*) which store fat as triglyceride, and *mast cells*. These last are specialised cells which release histamine in response to a variety of agents including certain antigens (see below). Connective tissue may be loose or dense according to whether the collagen fibres are relatively sparse or densely packed together. Tissue composed mainly of collagen fibres is referred to as *fibrous tissue*.

Adipose tissue is a connective tissue composed almost entirely of fat cells and is the storage depot for fat. In obesity there is an increased amount of subcutaneous adipose tissue.

The *blood* is regarded as a specialised form of connective tissue. It consists of approximately 55 per cent. by volume of liquid *plasma* (ground substance) and 45 per cent. of cells. The cells are a mixture of so-called *red cells* (erythrocytes), which are exceptional in that they have no nucleus, and *white cells* (leucocytes), the red cells being about a thousand times more numerous than the white cells. In addition there are other non-nucleated formed elements called *platelets* or *thrombocytes*. The red cells contain haemoglobin and serve as carriers of oxygen and carbon dioxide, the white cells are concerned with certain protective mechanisms, and the platelets with blood clotting. These are all described in more detail in Chapter 13, but some further account of the white cells is needed at this stage.

The leucocytes are divided into two main classes based upon the presence of granules in the cytoplasm. Thus there are non-granular leucocytes, also called *mononuclears,* and *granulocytes* which are also called *polymorphonuclear leucocytes* because their nuclei are lobulated; they are usually referred to simply as *polymorphs* (Fig. 1). The granules in the polymorphs stain variously with certain dyes. *Neutrophil* polymorphs are those which stain with neutral dyes; they account for about 95 per cent. of the granulocytes and have important anti-bacterial properties. The remaining 5 per cent. of granulocytes stain best with either acidic or basic dyes and the cells are known respectively as *eosinophils* or *basophils;* their functions are poorly understood. The mononuclear cells include the *monocyte, lymphocyte* and *plasma cell,* and of these the lymphocytes normally constitute about 95 per cent. and account for about one quarter of the total white cells.

Monocytes are relatively large cells and are the precursors of some of the tissue macrophages, migrating from the bloodstream when required.

The lymphocytes in the blood, which are produced in the lymphoid tissue (Chapter 14), are subdivided into small and large varieties. They differ not only in size but also in that the small lymphocyte has only a very thin rim of cytoplasm compared with a relative abundance in the large lymphocyte. (Fig. 1). The plasma cell has characteristic staining properties. It is derived from the small lymphocyte and is normally present in the blood only in very small numbers, but its production is greatly increased in certain

pathological states. Both lymphocytes and plasma cells are important as producers of antibodies.*

Bone and cartilage are two other specialised forms of connective tissue. They are described in Chapter 12.

Muscle

The characteristic of muscle cells is a highly developed power of contraction. There are three kinds of muscle namely, *skeletal muscle* responsible for locomotion, *cardiac muscle* which forms the bulk of the heart, and *smooth muscle* which is found in blood vessels and various other organs (viscera).

The cell membrane and cytoplasm of a muscle cell are known respectively as the *sarcolemma* and the *sarcoplasm*. Within the sarcoplasm there are many *myofibrils* composed of the proteins actin and myosin, interaction of which produces contraction. Both skeletal and cardiac muscle show cross striations when seen with the light microscope and are called striated or *striped muscle*. This appearance is due to the arrangement of the molecules of actin and myosin. *Smooth muscle* which lacks this arrangement is therefore called unstriped.

Skeletal muscle is also known as voluntary muscle because, unlike the other two, it is under voluntary control. An ordinary 'muscle' consists of numerous bundles or fasciculi of fibres enclosed within a muscle sheath of connective tissue. Each fibre consists of a single cell which has several nuclei at the periphery and runs the entire length of the muscle. At each end it is attached to bones through fibrous processes which collectively form the *tendons*. One attachment remains fixed when the muscle contracts and is called the *origin*, the other is called the *insertion*. Contraction of each fibre is stimulated by nervous impulses transmitted through the neuro-muscular junction or *motor end plate*. Each fibre that is stimulated contracts rapidly and maximally. A series of stimuli applied sufficiently close together will produce a sustained contraction or *tetanus*.

Cardiac muscle, the other form of striped muscle, has quite different properties. The muscle fibre in this case consists of a series of cells each with a single central nucleus, and the cells are joined end

* Antibodies are globulins which will combine with and render innocuous certain foreign agents such as bacteria. They are produced by small lymphocytes and plasma cells in response to stimulation by a noxious agent called an antigen, and each antibody reacts specifically with the antigen that stimulated its production. Antibodies produced by small lymphocytes remain on the surface of the cell whereas those produced by plasma cells are secreted into the plasma.

to end through an *intercalated disc*. Moreover, the cells branch, all the branches being joined end to end so that an interconnecting network or *syncytium* is formed (Fig. 1). It has the intrinsic property of contracting rhythmically even when cut into pieces but unlike skeletal muscle a contraction is followed by a short *refractory period* when it will not respond to further external stimuli.

Smooth muscle, also known sometimes as involuntary muscle, is also composed of large numbers of fibres each consisting of a single cell with a central nucleus. The cells vary enormously in length in different organs. Contraction of smooth muscle is slower and more prolonged than that of skeletal muscle, and it also has some powers of intrinsic contraction independently of its nerve supply.

An example of the integration of different tissues into an organ is the skin (or *integument*, or *cutis*). Its thickness varies in different regions from about 0.5 millimetres to several millimetres, but its basic structure is the same throughout. It is composed of two layers, namely the superficial *epidermis* and the deeper *dermis* or *corium*. Beneath the dermis is the subcutaneous fat or adipose tissue.

The epidermis is of ectodermal origin and consists of a stratified squamous epithelium, the most superficial cells of which are flattened, lay down the protein keratin and lose their nuclei (*stratum corneum*).

The dermis consists of connective tissue of mesodermal origin. It contains intermingled collagen and elastic fibres and numerous blood vessels, lymphatics (Chapter 2) and nerves (Chapter 6). The superficial part of the dermis is arranged in conical masses called the *dermal papillae* the apices of which project into the overlying epidermis. The dermal papillae are richly supplied with capillaries and sensory nerve endings.

The skin has a number of *appendages* comprising the nails, hairs, *sebaceous glands* and the *sweat* or *sudorific glands*. The nails are keratinous modifications of the stratum corneum. The hairs arise from invaginations of the epidermis into the dermis called hair follicles. The dermal part of the follicle is the *root* and the part projecting from the surface of the skin is the *shaft*.

The sebaceous glands occur in the dermis and discharge their secretion, *sebum*, through ducts which open into the hair follicles. The sweat glands are also found in the dermis but their ducts open onto the surface of the skin. The distribution of sweat glands, like that of hair follicles, varies in different areas of the skin.

Chapter 2

General Pathological Processes

A number of pathological processes are common to many different diseases and it is appropriate to describe them before discussing in more detail the pathological changes that affect specific organs.

All organs of the body are supplied with blood which picks up oxygen in the lungs and is then pumped to the organs by the heart. The blood is conveyed to the organs by the *arteries* and returned to the heart in the *veins*. The arteries divide progressively into smaller vessels terminating in the *capillaries*. These are microscopic in size and consist of a single layer of flattened endothelium. The capillaries then coalesce to form larger vessels, the *venules*, which ultimately form the *veins*.

All exchanges of gases, nutrients and waste products between the blood and tissues take place through the capillary walls. The pressure relationships in the capillaries and tissue spaces are such that fluid passes out of the capillary at the arterial end and returns at the venous end. Any fluid that does not return to the capillary enters another system of channels outside the blood vessels, called the *lymphatics*. The smallest lymphatics are also one cell thick but are more permeable to large molecules than the blood capillaries. Like the capillaries they join to form progressively larger channels ultimately forming the *thoracic duct* in the chest. This opens into one of the large veins near the heart, thus returning the contents of the lymphatics, the *lymph*, to the bloodstream. At intervals along the lymphatics will be found the *lymph nodes* (see Chapter 14) through which the lymph is filtered, thus enabling large particles such as bacteria to be trapped.

Alterations in blood flow

*Hyperaemia**and *ischaemia* are terms used to indicate respectively

* The prefixes *hyper-* and *hypo-* are used in many contexts to indicate greater than normal and less than normal respectively.

increased blood flow and inadequate blood flow. Hyperaemia must be distinguished from *congestion*, in which case there is an increased volume of blood in an organ owing to reduced flow out of it. When the blood contains less oxygen than normal there is said to be *hypoxaemia*. Inadequate oxygen supply to the tissues is *hypoxia*, and this arises either from ischaemia or from a normal flow of blood which is hypoxaemic.

Inflammation and repair

Of prime importance among the general processes is *inflammation*, generally indicated by adding the suffix *-itis*, e g. appendicitis is inflammation of the appendix. This may be defined as the local reaction to injury and in addition to being caused by infection with micro-organisms it may be provoked by a variety of other agents such as a heat burn or a chemical burn. The earliest change is dilatation of the small blood vessels in the injured zone and local hyperaemia. The permeability of the capillaries is increased so that more fluid and proteins exude into the tissue spaces. Leucocytes become adherent to the capillary wall and then pass through it. The exudate of fluid and leucocytes is the *inflammatory exudate*. This may be *serous* which is thin and watery, or *fibrinous* if it contains much fibrinogen* which forms fibrin clots. The exudate and the increased blood flow give rise to the clinical signs of inflammation, namely swelling, warmth and redness. The polymorphs kill bacteria and may themselves be killed by bacterial toxins. Liquefaction of dead tissue and polymorphs gives rise to *pus*.

Following soon after the polymorphs large mononuclear cells appear which engulf and remove the dead tissue. These are the histiocytes from the tissue, and monocytes from the blood, and they are known collectively as *macrophages*. The inflammatory process may resolve completely quite soon, but when it is prolonged the terms *sub-acute*† and *chronic inflammation* are used. During the sub-acute stage lymphocytes and plasma cells are prominent, and as this progresses to the chronic stage the macrophages become transformed into fibroblasts. These lay down collagen fibres, and blood vessels at the periphery proliferate and also

* Fibrinogen is a protein in the plasma which, in certain circumstances, becomes converted into insoluble fibrin to form a blood clot.

† In medicine the terms 'acute', 'sub-acute' and 'chronic' refer to the duration of a process (or a symptom) and they do not mean severe or continuous as they sometimes do in lay usage of the terms.

grow into the area. This process is called *organisation* and the new tissue is called *granulation tissue*. Ultimately it replaces all the dead tissue. The capillaries then gradually disappear and the fibroblasts become quiescent, the collagen contracts and finally the original tissue is replaced by a mass of fibrous tissue called a *scar*. Although scars are most familiar in the skin they also occur in the internal organs where the contraction of the scar often leads to an irregular depression on the surface of the organ.

It is this process of fibrous replacement of the original tissue which is known as *repair*. In some cases a tissue can regenerate to restore the original structure completely, e g. the epithelium of the skin or the healing of fractures of the bones, but with extensive tissue damage 'healing' is by the process of repair.

Necrosis

Necrosis is the term used to refer to the death of cells. There are many causes of necrosis, and the appearance of necrotic tissue varies to some extent with its cause. In *coagulative necrosis*, the outline of the cells and basic structure of the tissue is clearly preserved, sometimes for several weeks. It occurs when the blood supply to the tissue is suddenly stopped. The resulting zone of coagulative necrosis is called an *infarct*, specific examples of which will be dealt with in later chapters. The term *colliquative necrosis* is used when there is rapid liquefaction of the dead cells. *Caseous necrosis* occurs in tuberculosis, and the necrotic tissue in the centre of the lesion resembles friable cheese. In *fat necrosis*, which occurs in adipose tissue, the cells rupture, fatty acids are released and form white calcium soaps. Necrosis of any form will provoke an inflammatory reaction.

An *ulcer* is an area where the continuity of an epithelial surface such as the skin or the lining of the stomach is broken because some of it has become necrotic (Fig. 17, page 97). When the necrotic tissue separates from the surrounding healthy epithelium it is called a *slough*, the removal of which exposes the tissues underneath – and an ulcer is thus formed. The two processes that contribute to the healing of an ulcer are organisation and re-epithelialisation. Organisation begins by fibroblastic and capillary proliferation from the base, and the epithelium grows over the surface of any exudate that is present. Eventually the epithelial layer becomes stratified in the case of the skin or may develop a more complex structure as in the case of the epithelium lining the stomach.