Pathological Histology

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Examiner in Pathology and Forensic Medicine for the Triple Qualification

FOREWORD

by

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THIRD EDITION

With 260 Photomicrographs in Colour

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PREFACE TO THE THIRD EDITION

THE appearance of a third edition has afforded another opportunity for revision. The text of the last edition accordingly has been extensively rewritten and amplified and, where necessary, modernised by the addition of recent advances. Some of the illustrations have been replaced by superior samples, while a few others have been inserted to demonstrate important features.

Fifteen new subjects and plates have been added in this edition. These have been chosen particularly with a view to extending the range of pathological processes and are distributed among the alimentary, haemopoietic, reproductive, nervous, locomotor and endocrine systems. The text has thus been increased to 447 pages, while the illustrations now total 260.

Grateful acknowledgment is made to Mr. T. C. Dodds, F.R.P.S., F.I.B.P., who, as in the first two editions, was responsible for the fine Finlay transparencies; to Professor J. W. S. Blacklock, Professor Stanley Davidson, Professor R. W. Johnstone, Col. W. F. Harvey, Dr. Agnes R. Macgregor, and Dr. W. Blackwood for illustrative material; to Miss E. Johnston for compiling the index; and to Messrs. E. and S. Livingstone for constant attention in matters of publication.

ROBERTSON F. OGILVIE.

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PREFACE TO THE FIRST EDITION

THIS volume is designed to act as a companion to a standard textbook of Pathology and to meet the need of the student in the class of morbid histology and of the graduate seeking more specialised knowledge in pathological processes.

Its text is based on a series of lectures in pathological histology delivered at Edinburgh University and gives an account of the tissue changes produced by those diseases most commonly encountered in Great Britain. Following a scheme adopted by many textbooks of Pathology, the earlier chapters deal with the phenomena of degeneration, vascular disturbances, inflammation, repair and tumours, while the later chapters are devoted to special diseases of the systems. That its value might be enhanced, each microscopical description is introduced by a macroscopical account of the diseased tissue or organ and, in particular instances, brief space is also given to the etiology of the condition and to the significance of the microscopical findings in relation to the nature of the disease.

A feature of the book is the illustration of its text by 220 photomicrographs in colour. Of the superior appeal of colour there is no manner of doubt and it is, therefore, hoped that compared with monochrome prints these coloured pictures will convey a much more realistic impression of what the microscope reveals in stained preparations. The illustrations were made from Finlay colour transparencies. These were the work of Mr. T. C. Dodds, F.R.P.S., F.I.B.P., Senior Technician in the Pathology Department of Edniburgh University, of whose skill in colour photography the perfection of the illustrations is abundant proof. An equally high measure of praise is due to the blockmakers of Graphic

Arts Ltd., London and Woking, for having in design as in colour so faithfully reproduced the Finlay transparencies.

To Professor A. Murray Drennan for suggesting numerous improvements in the text and illustrations, to Dr. A. C. P. Campbell for his critical opinion of the chapters on Diseases of the Haemopoietic and Nervous Systems, and to Dr. W. Melville Arnott for advising me on the clinical aspects of Nephritis, I would express a deep sense of gratitude. For the use of material to illustrate the text I am indebted to the following: Professor A. Murray Drennan, Professor M. J. Stewart, Professor J. H. Biggart, Dr. A. C. P. Campbell and Dr. Agnes Macgregor. The preparation of this material was carried out in the Pathology Departments of the University and Royal Infirmary, Edinburgh, to the technical staffs of which it is, therefore, a pleasure to record my acknowledgment of their willing co-operation.

Finally, my grateful thanks are due to my publishers, Messrs. E. & S. Livingstone, for their constant advice in matters relating to production.

ROBERTSON F. OGILVIE.

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FOREWORD

It must be the experience of all those who have to teach students the histological appearances resulting from disease that certain difficulties arise. The teacher describes in detail the changes to be seen in the particular section of tissue, but he is never quite sure that the student has applied this description to the correct area. Where individual teaching is possible this uncertainty may be corrected by personal demonstration under the microscope, but where a large class is being taught and when time is limited such instruction is almost impossible. To overcome this difficulty it has been the custom of recent years in this school for the lecturer to project on the screen a magnified image of the section of tissue, of which samples are issued to the class, and to point out the features to be studied in that section. The students then examine their own sections taken in series from the same block. But when a student wishes to revise his slides he often finds that he is uncertain what were the features that were to be noted in a particular slide. The graduate who has occasion to return to morbid histology has the same difficulty; he has forgotten the salient features and may fail to recapture them from the sections without aid.

To help both groups of students, graduate and undergraduate, Dr. Ogilvie has produced this book wherein will be found representative histological pictures in colour. These have the advantage that they show not only the morphology of the lesion but the staining reactions of the tissues, a feature of importance where *e.g.* staining for fat or amyloid is necessary. Pigmentary changes such as those due to blood-pigment or melanin are also clearly seen in the coloured picture just as they appear in the prepared section of tissue.

Without some method of recording accurately the form and colour of microscopical preparations the illustrations of this book would have been impossible and its distinctive feature lacking. Fortunately, in the Finlay process of colour photography as interpreted by the skill of Mr. T. C. Dodds, Fellow of the Royal Photographic Society, of this Department, an ideal medium was to hand for the work. The pictures are reproduced from actual colour photographs of the stained sections and both original photograph and reproduction faithfully represent what may be observed with the microscope.

In the text Dr. Ogilvie has included brief descriptions of the macroscopical appearances of affected organs and tissues in order to remind the student of the morbid anatomy of the lesion he is studying microscopically and to impress upon him the need to correlate the gross and the minute. From an extensive experience as a teacher of pathology Dr. Ogilvie has selected those subjects which are most suitable to illustrate and describe in order to give a comprehensive view of morbid processes. Within the scope of the book it is obviously impossible to include all the variants of such processes and examples of the rarer diseases; such matters belong to larger works or special monographs.

No book on morbid histology can ever replace study of the actual specimen, but a book may so vividly represent and interpret the original that its study is greatly facilitated and revision of knowledge simplified. Dr. Ogilvie has succeeded in presenting such a volume.

A. MURRAY DRENNAN.

CONTENTS

CHAPTER I

DISTURBANCES OF NUTRITION

The *causes* of cell degeneration are mainly:—

(1) Poisons
- (*a*) Organismal toxins, *e.g.* streptococcal, spirochetal.
- (*b*) Metabolic products, *e.g.* ketone bodies in diabetes mellitus.
- (*c*) Chemicals, *e.g.* phosphorus, chloroform.

(2) Deficient oxygenation
- (*a*) Anaemia.
- (*b*) Inadequate circulation.

(3) Physical agents, *e.g.* light, heat, radium rays.

The *phases* of cell degeneration are:—

(1) Cloudy swelling.
(2) Fatty degeneration.
(3) Cell death or Necrosis, and
(4) Calcification.

(1) Cloudy Swelling

All cells are liable to cloudy swelling, but by reason of their specialised nature and complicated structure gland-cells as of kidney, liver and pancreas, muscle cells and nerve cells are especially prone to be affected and, in general, show most clearly the histological characters of the condition. Kidney, myocardium, and liver will, therefore, be considered in turn.

Kidney.

Macroscopically, the kidney is swollen and softer than the normal. Section allows its tissue to bulge and

exposes a cortex which is slightly increased in depth. The cut surface is pinkish from congestion initially, but later becomes uniformly grey and opaque owing to occlusion of the vessels by the swollen tubules. Engorgement affects longest the straight vessels of the medulla. This zone consequently remains distinct for a time, but with the disappearance of congestion ultimately merges into the pale cortex. The capsule can be stripped with ease and on removal leaves a smooth, pink or grey surface.

Microscopically, the principal changes are found in the convoluted tubules and ascending limbs of Henle's loops (Fig. 1). The cells lining these tubules are swollen and frequently also separated from each other, sometimes even as far as the basement membrane. The cells thus project inward in the manner of tall, dome-like structures, while the lumina of the tubules are unusually small and somewhat star-shaped. A striking change, moreover, has overtaken the mitochondria which occur normally as delicate rods in the basal half of the cells. They have undergone fragmentation and been replaced by a host of minute, faintly acidophile granules. These elements are at first localised in the basal region of the cells, *i.e.* in the area originally occupied by the mitochondrial rods, but are later widely and more or less uniformly distributed throughout the swollen cytoplasm. In many tubules the superficial parts of the cells have actually been shed off and are to be found in the lumina as variable amounts of granular debris. The lumina then are naturally more than ever irregular. Prolonged cloudy swelling, the result of moderately severe toxic action, is sometimes characterised by large, hyaline, acidophile granules in the cells of the convoluted tubules. These hyaline droplets vary in distribution, but occur, as a rule, at some distance internal to the basement membrane and often in immediate relation to the nuclei (Fig. 2). They have been formed by coalescence and further degeneration of the minute granules of early cloudy swelling. Despite these cytoplasmic changes, the

nuclei in the cells of both convoluted tubules and ascending limbs are normal or at most swollen from fluid intake. It is only when the action of the causative agent has been particularly severe that the nuclear changes detailed later (p. 12) make their appearance. Such changes indicate that the stage of cloudy swelling has, in reality, progressed to that of necrosis.

The cells lining the descending limbs of Henle's loops and the conducting tubules are normal or at most slightly swollen. Absence of granularity in them is associated with their comparative poverty in mitochondrial elements. The conducting tubules may contain occasional casts of epithelial, granular or hyaline structure. Of these, the first type consists of fused cells and the second of shed cytoplasm, both elements being possibly imposed upon hyaline casts as a basis. The third may be the result of complete hyaline degeneration of either of the previous varieties, but more probably represents the condensation product of protein material that has passed through the glomerular capillaries.

Cloudy swelling due to toxic causes is initially accompanied by congestion of the glomeruli, intertubular capillaries and vasa recta. The intertubular capillaries and thereafter the straight vessels of the medulla are later compressed and so in varying degree occluded by the adjoining swollen tubules.

Heart.

Macroscopically, the heart tends to be globular in shape, while its chambers, especially ventricles, are in varying degree dilated. The tricuspid and mitral valves are also commonly enlarged, but the pulmonary and aortic orifices usually remain average in size. The distended condition of the heart and auriculo-ventricular valves is related to the character of the myocardium. This tissue is abnormally soft and, in consequence, tends more readily than usual to pit or even disintegrate under pressure. It has also an opaque appearance and in colour is yellowish brown or frankly yellow, this pallor

being most marked in the inner third of the wall of the left ventricle.

Microscopically, the muscle cells are swollen. Their longitudinal striations are preserved, but in many areas no trace is discernible of their normal cross striations. Each cell, moreover, now contains numerous granules varying somewhat in size and disposed in parallel, longitudinal rows (Fig. 3). As in the kidney, these granules are probably derived from the mitochondria, although no definite statement can be made about this. The nuclei are normal. The capillaries supplying the tissue may be congested, but in severe cases are in varying degree compressed and occluded by the swollen cells.

Liver.

Macroscopically, the liver is distinctly swollen, while its borders are more rounded than usual. It is also abnormally soft and, in consequence, pits or disintegrates readily under pressure. Whereas its capsular aspect is smooth, its cut surface is dull, opaque, pink, grey or yellow, and commonly mottled from associated venous congestion.

Microscopically, the liver cells are swollen and contain many pink-staining granules (Fig. 4). These are of mitochondrial origin and differ from the granules of the normal state in being less numerous, often larger and unevenly distributed. They are scattered throughout the entire cytoplasm in some cells, but in others are gathered mostly at the margins adjacent to the capillaries. The fine, uniform granularity of the normal cytoplasm is thus replaced in the swollen cells by a coarse, irregular granulation. Despite these changes, the nuclei are normal or at most swollen with fluid. The hepatic sinusoids may be congested in the earlier stages, but later are partly occluded by the swollen cells.

(2) Fatty Degeneration

Fatty degeneration is the sequel of cloudy swelling and consequently the second stage in cell degeneration. It is a condition which may develop with comparative rapidity. Thus, it has been produced in the kidney of the experimental animal within two hours by the injection of oxalic acid. As in cloudy swelling, the phenomena of fatty degeneration will be considered as observed in the kidney, heart and liver.

Kidney.

Macroscopically, the features are essentially those of cloudy swelling with the addition that many distinctly yellow spots and streaks are distributed throughout the pale cortex and subcapsular surface.

Microscopically, a frozen section stained with Sudan III and haematoxylin shows that as in cloudy swelling the cells lining the convoluted tubules and ascending limbs of Henle's loops are swollen, granular and often separated from each other. In addition, the cells of many of the convoluted tubules contain fat (Fig. 5). This fat occurs in globular form and varies in amount both in different cells and different tubules. Thus, some cells contain but a few minute granules and the affection then usually involves only a proportion of the cells lining a tubule. Other cells exhibit numerous, relatively large globules and the condition in such circumstances is commonly found in all the cells of the tubule. As a rule, moreover, the globules are distributed most abundantly in the basal region of the cells, while in the cytoplasm adjacent to the lumen there are either none or only a few small granules. The cells may, however, be more or less uniformly packed with globules of various sizes. Despite the presence of even large amounts of fat in their cytoplasm, the cells sometimes show no distinctive nuclear changes, so that their condition can be regarded as recoverable. The nuclei, on the other hand, may be degenerated in one or other of the ways which indicate that the cells are

actually dead (see necrosis). The condition, as already stated, affects only a proportion of the convoluted tubules and these are distributed in wholly irregular manner, singly or in groups, throughout the cortex. Fatty degeneration sometimes involves not only the convoluted tubules, but also the ascending limbs of Henle's loops and may occasionally be restricted to the ascending limbs, while the convoluted tubules merely exhibit the features of cloudy swelling. As in the latter, the descending limbs of Henle's loops and the conducting tubules are more or less normal.

The fat in the degenerated tubules consists of glycerol esters, but the question of its origin is still controversial. On the one hand, the fat is thought to be derived from the minute, mitochondrial granules of cloudy swelling. Information regarding the chemical composition of these granules is afforded by two observations. First, their solubility in dilute acids and alkalies proves that they contain protein. Secondly, the fact that they are stainable by Weigert's method for myelin sheaths indicates that lipoid also enters into their composition. The granules, therefore, are generally thought to consist of a protein-lipoid complex. Thus combined with protein, the lipoid part of their structure is unstainable by ordinary fat dyes such as Sudan III and Scharlach R. The fat is consequently said to be in a masked or hidden state. But when cloudy swelling is followed by fatty degeneration, the fat in the granules is split off from combination with its protein partner and thus liberated can now be stained by Sudan III. The essence of fatty degeneration, according to this view, is thus a liberation or unmasking of previously combined or hidden fat. As already stated, the fat in the degenerated tubules consists of glycerol esters. This means that, after being liberated, the complex lipoid of the mitochondria must undergo further reduction to fat of simple neutral type.

Living cells, on the other hand, are continually absorbing from the circulation fat which has been mobilised from the fat depots to nourish the peripheral

tissues. In cloudy swelling, they continue to infiltrate this fat, but are unable to oxidise and use it. The fat consequently accumulates in the cells and becomes visible as a series of globules. According to this theory, the appearance of fat in damaged cells is thus wholly a matter of infiltration from the fat depots. The explanation, of course, may combine these views and involve a deposit in the cell of fat derived in the earlier stages from the mitochondria by unmasking and later also from the fat depots by infiltration. While each postulate has its supporting evidence, the most recent work on the subject definitely rejects the idea of unmasking in favour of the theory of fatty infiltration.

Finally, the glomerular tufts (as in cloudy swelling) are commonly congested, but owing to compression by the swollen tubules in their neighbourhood the capillaries of the intertubular plexus and the vasa recta of the medulla are, as a rule, more or less inconspicuous.

Heart.

Macroscopically, the heart shows features similar to those in cloudy swelling. It tends to be globular, while its chambers and auriculo-ventricular valves are commonly distended. The myocardium, besides being soft, friable and sometimes even greasy, is abnormally opaque and yellowish brown or yellow, especially in the inner third of the wall of the left ventricle. A severe case, moreover, is characterised under the endocardium, particularly on the surface of the papillary muscles and columnae carneae, by narrow transverse or irregular streaks of more opaque appearance and more distinctly yellow colour. This peculiar mottling which is seen most commonly in the left ventricle, but occasionally also in the right, is the basis for the popularly applied description of " thrush breast heart ".

Microscopically, the condition characteristically affects the muscle cells in groups. The myocardium is sometimes damaged diffusely, but even then groups of fibres always show more severe degeneration. The condition

entails the appearance in the muscle cells of small fatty globules (Fig. 6). The globules are disposed in longitudinal rows and are more numerous, larger and more closely arranged at the centre than at the periphery of a patch. The nuclei in the muscle cells may be normal or show degenerative features indicative of actual necrosis.

The fat in the muscle cells consists of glycerol esters and is accounted for by the same theories as in the kidney. First, the fat may be a product of the mitochondria by unmasking. This view is favoured by the observation that in size, shape and distribution the globules of fat are very similar to the granules of cloudy swelling. Secondly, the condition possibly represents a transportation to the cells by the blood of fat from the subcutaneous and other fat depots. Thirdly, the fat may be derived both from the mitochondria by unmasking and from the fat depots by infiltration. As stated above, the theory of infiltration is, on the grounds of recent experimental work, preferable to that of unmasking.

The patchy affection of the myocardium is explained by the fact that the degenerated areas lie at the termination of the arterioles. So situated, these areas are last to be supplied with oxygen and nutritive substances and consequently show first and most severely the effects of any anaemic or toxic state of the blood. The myocardium may be affected diffusely, but the areas which are pararterial in distribution always exhibit more marked degeneration.

Liver.

Macroscopically, the condition of the liver is similar to that in cloudy swelling with some additional features. The organ is definitely swollen and has more rounded borders than usual. Slightly increased in weight, it is also abnormally soft, so that it readily pits or tears. Its surface is smooth and its tissue on section is dull, opaque and yellow. The central or peripheral zone of the lobules, moreover, is often distinctly more opaque and

yellow than the tissue elsewhere. Fatty degeneration, however, cannot always be inferred from a yellow surface and is properly assessable only by examining stained frozen sections. Finally, the organ in advanced degeneration may actually be greasy, while material scraped from its cut surface is unmistakably oily.

Microscopically, a frozen section stained with Sudan III and haematoxylin shows that a proportion of the liver cells contain fat (Figs. 7 and 8). This material, as in the kidney and heart, occurs in globular form and is present in variable amount in different cells. Thus, while some contain only a few minute droplets, others show numerous globules of which a proportion are slightly larger than the rest. The distribution of the globules in the cells of either of these types may be uniform, but is more often irregular and then the droplets are not infrequently situated at the cell margins adjacent to the capillaries. Still other cells contain only a few globules, yet these are of such size as to be contiguous and completely obscure the cytoplasm. The final stage is seen in cells, each of which is distended by a single large globule of fat. The nucleus in cells containing multiple globules is still centrally placed and may be either normal or show one or other of the degenerative changes indicative of actual cell death. The nucleus of cells distended by a single large globule, on the other hand, is commonly pushed to one side and flattened out so that, in general, each resembles an ordinary adipose tissue cell. Further, according as the cells are swollen with fat, so the sinusoids in relation to them are compressed and occluded.

The fat is usually localised mainly in one zone of the lobules, while less often it occurs focally or diffusely. As a rule, it is the central zone that is affected, less commonly the peripheral and only rarely the intermediate zone. When those in the most affected zone contain only minute fat globules, the cells in the other regions are usually devoid of fat, but in the event of the principally affected region showing an abundance of