Pathological Histology

By

ROBERTSON F. OGILVIE

M.D., F.R.C.P.(Edin.)

Lecturer in Pathology, University of Edinburgh
Senior Pathologist, Royal Infirmary, Edinburgh
Pathologist, Deaconess Hospital, Edinburgh
Examiner in Pathology for the Triple Qualification

FOREWORD

by

A. MURRAY DRENNAN

M.D., F.R.C.P.(Edin.)

Professor of Pathology, University of Edinburgh

With 220 Photomicrographs in Colour by

T. C. DODDS

F.R.P.S., F.I.B.P.

Senior Technician, Pathology Department,
University of Edinburgh

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PATHOLOGICAL HISTOLOGY

PREFACE

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.

The 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 Edinburgh 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.

1940. ROBERTSON F. OGILVIE.

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.

TO

MY FATHER

IN

GRATITUDE AND AFFECTION

MADE AND PRINTED IN GREAT BRITAIN

CONTENTS

CHAPTER I

DISTURBANCES OF NUTRITION

The *causes* of cell-degeneration are mainly:—

(1) Poisoning
- (*a*) Organismal toxins, *e.g.* streptococcal.
- (*b*) Metabolic products, *e.g.* acetone bodies in diabetes.
- (*c*) Chemicals, *e.g.* phosphorus, chloroform.

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

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

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. In the earlier stages the cut-surface is pinkish from congestion, but later it becomes uniformly grey and opaque owing to occlusion of the vessels by swelling of the tubules. Engorgement affects longest the straight vessels of the medulla. For a time, therefore, this zone remains distinct, but with the disappearance of congestion it 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 exhibited by the convoluted tubules and ascending limbs of Henle's loops (Fig. 1). The cells lining these tubules are swollen and, in addition, often 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 and as further consequences the lumina of the tubules have been rendered unusually small and somewhat star-shaped. There is, moreover, a striking alteration in 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 granules which stain pink with eosin. In the earliest phases of the condition these granules are localised in the basal region of the cells, *i.e.* in the area originally occupied by the mitochondrial rods. But as the cells proceed to swell the granules drift increasingly inward toward the lumen until they become widely and more or less uniformly distributed throughout the 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. Where this has occurred the lumina of the tubules have naturally been rendered still more irregular. In cases of prolonged cloudy swelling, the result of moderately severe toxic action, there appear in the cells of the convoluted tubules relatively large granules which are strikingly hyaline and acidophile. 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 which have been described as a feature of cloudy swelling in its earlier phases. 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. 11) make their appearance. Such changes indicate that the stage of cloudy swelling has, in reality, progressed to that of necrosis.

Apart from perhaps slight swelling the cells lining the descending limbs of Henle's loops and the conducting tubules are normal. Absence of granularity in them is associated with their comparative poverty in mitochondrial elements. In the conducting tubules there may be 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 precipitation-product of protein-material that has passed through the glomerular capillaries.

If the cause of the cloudy swelling has been toxic the earlier stages of the tubular changes described above are accompanied by variable congestion of the glomeruli, intertubular capillaries and vasa recta. In the more advanced stages the intertubular capillaries and later the straight vessels of the medulla are compressed and so in varying degree occluded by the swollen tubules in their neighbourhood.

Heart.

Macroscopically, the myocardium is abnormally pale, particularly in its inner zone, and of soft consistence.

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). Although nothing definite can be stated regarding their origin it is probable that as in the kidney these granules are derivatives of the mitochondria. The nuclei are normal. The capillaries supplying the tissue may be congested, but in severe cases they are in varying degree compressed and occluded by the swollen cells.

Liver.

Macroscopically, the organ is swollen, abnormally soft, and on section exhibits a pinkish, opaque surface in which there is commonly some vascular mottling from cardiac failure.

Microscopically, the liver-cells are swollen and contain granules which stain pink with eosin (Fig. 4). Mitochondrial in character these granules differ from those of the normal cell in being less numerous, often larger and uneven in distribution. Sometimes they are scattered irregularly throughout the cytoplasm, but not infrequently they are gathered mostly at the margins of the cells adjacent to the capillaries. Instead of being finely and uniformly granular the swollen cells have thus a granularity which is as coarse as it is irregular. Despite these cytoplasmic changes the nuclei are normal or at most swollen with fluid. In the earlier stages the hepatic sinusoids may be congested, but later they are in varying degree occluded by the swollen cells.

(2) Fatty Degeneration

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

Kidney.

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

On *microscopical examination* of a frozen section stained with Sudan III and haematoxylin it is seen 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 show a content of fat (Fig. 5). This fat occurs in globular form and varies in amount both in different cells and different tubules. Thus, in some cells there is but a sprinkling of minute granules and then, as a rule, only a proportion of the cells lining a tubule are affected. In other cells the globules are numerous and often of relatively large size and in such circumstances it is common for all the cells of the tubule to be involved. 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. Sometimes, however, the cells are more or less uniformly packed with globules of various sizes. Despite the presence of even large amounts of fat in their cytoplasm the cells may show no distinctive nuclear changes so that their condition can be regarded as recoverable. On the other hand, the nuclei may be degenerated in one or other of the ways which indicate that the cells are actually dead (see necrosis). As already stated, only a proportion of the convoluted tubules are affected and these, it is seen, are distributed in wholly irregular manner, singly or in groups, throughout the cortex. Sometimes, fatty degeneration of the convoluted tubules is accompanied by a similar affection of the ascending limbs of Henle's loops and occasionally the fatty state is actually restricted to the ascending limbs, while the convoluted tubules merely exhibit the features of cloudy swelling. As in

the latter condition 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 and in origin is traceable to the minute mitochondrial granules which appear in cloudy swelling. Regarding the chemical composition of these granules information 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. It is, therefore, generally thought that the granules consist of a protein-lipoid complex. Thus combined with protein the lipoid part of their structure is unstainable by ordinary fatty dyes such as Sudan III and Scharlach R. This fat is, therefore, 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 in the kidney is therefore a liberation or unmasking of previously combined or hidden fat. This is corroborated by the experimental finding that the kidney contains the same amount of fat after as before degeneration. As already stated, the fat in the degenerated tubules consists of glycerol-esters. This means that after its liberation the complex lipoid of the mitochondria must undergo further reduction to fat of simple neutral type.

Finally, it should be added that as in cloudy swelling the glomerular tufts are commonly congested, but that 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 myocardium is soft and may even be greasy. It is yellow or yellowish brown in colour, the pallor being most marked in the inner third of the heart-wall. In a severe case, moreover, there are

seen under the endocardium, particularly in relation to the papillary muscles and columnae carneae, narrow transverse or irregular streaks of opaque appearance and more distinctly yellow colour. To this characteristic mottling which is seen most commonly in the left ventricle, but occasionally also in the right, the term " thrush-breast-heart " is popularly applied.

Microscopically, the condition is found to be an essentially patchy one affecting the muscle-cells only in groups. The myocardium is sometimes affected diffusely, but even then there is always a superadded patchy element, groups of fibres showing more severe degeneration. The condition involves the appearance in the muscle-cells of small globules of neutral fat disposed in longitudinal rows (Fig. 6). In the middle of a patch where the condition is most developed the globules are larger and more closely arranged than at the periphery where they are smaller, scantier and more widely separated. The globules of fat are similar in size, shape and distribution to the granules of cloudy swelling and, therefore, like them are presumably related to the mitochondria. The lipoid of the mitochondria has, in other words, been separated from combination with the protein-part and thereafter been reduced to fat of neutral type. That liberation of originally combined fat is wholly responsible for the appearance of fat in the muscle-cells is corroborated by the experimental finding that there is little or no difference in the quantity of fat extractable from the myocardium before and after degeneration has occurred. The phenomenon does not apparently involve the deposition in the cytoplasm of any fat from without. In this respect, therefore, the heart resembles the kidney. The nuclei in the muscle-cells may be normal or show degenerative features indicative of actual necrosis.

The patchy affection of the myocardium is explained by the fact that the degenerated areas lie at the terminations 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. If either of these states is sufficiently profound the myocardium may show diffuse fatty degeneration, but always the areas which are pararterial in distribution exhibit degeneration of more advanced degree.

Liver.

Macroscopically, the organ is swollen, somewhat increased in weight, and abnormally soft and friable. Its capsular aspect is smooth and on section it exhibits a surface the yellow colour of which is either mottled or uniform in distribution according as the affection of the lobules is zonal or diffuse. The depth of yellow varies considerably and is in itself no gauge of fatty change the actual occurrence and degree of which can only be confirmed by the examination of stained frozen sections. When the cut-surface of a fatty liver is scraped the material removed with the blade is definitely oily in character.

On *microscopical examination* of a frozen section stained with Sudan III and haematoxylin a proportion of the liver-cells are found to contain fat (Figs. 7 and 8). As in the similar affection of kidney and heart this fat occurs in globular form and is present in variable amount in different cells. Thus, while in some there are only a few minute droplets other cells contain numerous globules of which a proportion are slightly, but distinctly, larger than the others. In the cells of either of these types the distribution of the globules may be uniform, but is more often irregular and in the latter case the droplets are not infrequently situated at the cell-margins adjacent to the capillaries. Yet other cells contain only a small number of globules, but these are of such size as to be contiguous, while the cytoplasm is completely obscured. The final stage is seen in the case of cells each of which is distended by a single large globule of fat. In cells containing multiple globules the nucleus is still centrally placed and may either be normal or show one or other of the degenerative changes indicative of actual cell-death. In cells distended by a single

large globule the nucleus, on the other hand, is commonly pushed to one side and flattened out so that in general each resembles an ordinary adipose-tissue cell.

The fat in the liver-cells consists of glycerol-esters. The multiple minute globules are identical in shape, size and distribution with the mitochondria of the liver-cells and are, therefore, to be regarded as being derived from these structures by a process of unmasking. To this extent the process in the liver is thus merely one of fatty degeneration as obtains in the kidney and heart. But in the case of cells laden with large globules the fat is so abundant that it is not all attributable to a mitochondrial source. A proportion of this abundant fat has, in reality, been absorbed from the blood-stream. As is well known, it is one of the functions of the liver to absorb fat from the blood with a view to oxidising and later discharging it for use by the peripheral tissues. While retaining their ability to absorb fat from without, the cells in a state of fatty degeneration are unable to oxidise and discharge what they have absorbed. Consequently, the absorbed fat accumulates in the cytoplasm and is possibly laid down round the original minute globules of fatty degeneration. Large globules of fat thus form in the cytoplasm and ultimately each cell becomes distended by a single large globule. The process whereby fat is absorbed from the blood is known as *infiltration*. The condition in the end thus involves a deposition in the cell of fat from two sources—fat from the mitochondria by degeneration and fat from the blood by infiltration. The condition might, therefore, be conveniently designated *fatty change* of the liver to distinguish it from simple fatty degeneration and to indicate its more complex character.

According to the nature of the causative agent the fatty change may affect the lobules diffusely or focally, but is more often limited to a particular zone. Most frequently it is the central zone that is affected, less commonly the peripheral and only rarely the intermediate zone. In a case of central zone involvement the cells immediately round the intralobular vein are