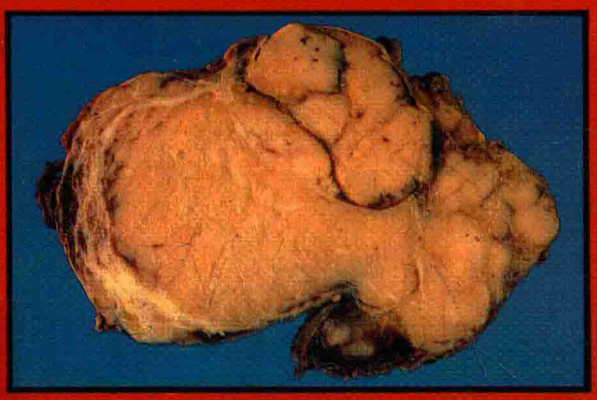
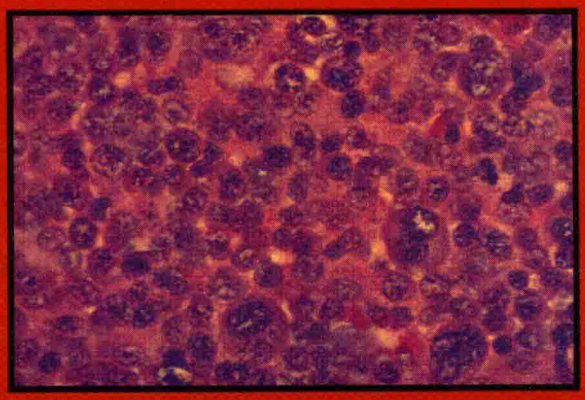
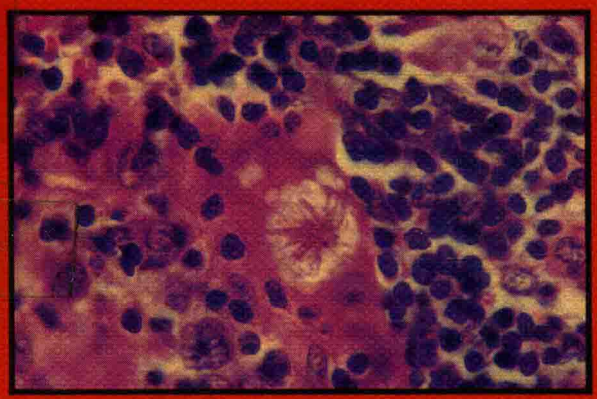
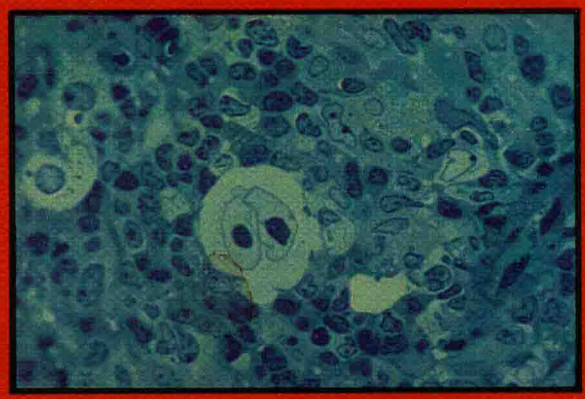
# A Colour Atlas of Thymus and Lymph Node Histopathology

Kristin Henry and
Geoffrey Farrer-Brown









A Colour Atlas of

# Thymus and Lymph Node Histopathology

with Ultrastructure


Kristin Henry

MBBS, MRCP, FRCPath

Reader in Pathology, Westminster Medical School,
Honorary Consultant Pathologist, Westminster Hospital,
London SW1

Geoffrey Farrer-Brown

MA, MB, BChir, MD, FRCPath

Consulting Pathologist at the Nightingale BUPA and
Fitzroy Nuffield Hospitals, London NW1



Wolfe Medical Publications Ltd

Published by Wolfe Medical Publications Ltd, 1981
Printed by Royal Smeets Offset b.v., Weert, Netherlands
ISBN 0 7234 0743 6

This book is one of the titles in the series of Wolfe Medical Atlases, a series which brings together probably the world's largest systematic published collection of diagnostic colour photographs.
For a full list of Atlases in the series, plus forthcoming titles and details of our surgical, dental and veterinary Atlases, please write to Wolfe Medical Publications Ltd, Wolfe House, 3 Conway Street, London W1P 6HE.

General Editor, Wolfe Medical Atlases:
G. Barry Carruthers, MD(Lond)

# Contents

# A Colour Atlas of Thymus and Lymph Node Histopathology with Ultrastructure

Published by Wolfe Medical Publications Ltd, 1981
Printed by Royal Smeets Offset b.v., Weert, Netherlands
ISBN 0 7234 0743 6

This book is one of the titles in the series of Wolfe Medical Atlases, a series which brings together probably the world's largest systematic published collection of diagnostic colour photographs.
For a full list of Atlases in the series, plus forthcoming titles and details of our surgical, dental and veterinary Atlases, please write to Wolfe Medical Publications Ltd, Wolfe House, 3 Conway Street, London W1P 6HE.

General Editor, Wolfe Medical Atlases:
G. Barry Carruthers, MD(Lond)

A Colour Atlas of

# Thymus and Lymph Node Histopathology

with Ultrastructure


Kristin Henry

MBBS, MRCP, FRCPath

Reader in Pathology, Westminster Medical School,
Honorary Consultant Pathologist, Westminster Hospital,
London SW1

Geoffrey Farrer-Brown

MA, MB, BChir, MD, FRCPath

Consulting Pathologist at the Nightingale BUPA and
Fitzroy Nuffield Hospitals, London NW1



Wolfe Medical Publications Ltd

*To*
*K.F.W.H. and A.C.T.*

# Contents

# Acknowledgements

Much of the material used in this Atlas results from research projects supported by the Cancer Research Campaign and the Muscular Dystrophy Group of Great Britain, and from our many colleagues participating in the British National Lymphoma Investigation Trial: to all of them we extend our thanks. We should also like to thank the following friends and colleagues for allowing us to photograph their slides/specimens – Professor J. G. Azzopardi, **819**, **820**; Dr M. H. Bennett, **16**, **165**; Professor A. H. Cameron, **292**, **293**, **670**, **671**; Dr K. M. Cameron, **813**, **814**; Dr Jonathan Gluckman, **821**, **822**; Professor M. S. R. Hutt, **329**, **330**, **364**, **365**, **638**, **641**, **823**; Dr G. Frizzera, **277**, **278**; Dr B. C. Morson, **334**, **335**, **336**; Dr K. Namba, **791**, **792**; Professor K. G. Naik, **288**, **289**; Dr G. Slavin, **184**; Professor A. C. Thackray, **344**, **345**, **346**, **347**; for providing photographs from their collections – Dr N. Byrom, **860**; Professor M. A. Epstein, **861**, **862**; Professor D. A. G. Galton, **579**; Dr P. D. James, **790**; to Dr B. Achong for the electronmicrograph, **643**. Diagrams **0** and **50** are reproduced from The Lymphocyte by K. Henry and J. Goldman in *Recent Advances in Pathology, 9* (1975), Ed. C. V. Harrison and H. K. Weinbren, by kind permission of the publishers, Churchill Livingstone. Figure **714** is reproduced from *Primary lymphomas of the gastrointestinal tract* by K. Henry and G. Farrer-Brown, Histopathology I Ed. R. E. Cotton, by kind permission of Blackwell Scientific Publications Ltd.

We gratefully acknowledge the expert help of Medical Laboratory Scientific Officers in our respective Histopathology Departments, particularly those at the Westminster Hospital and Medical School, who prepared the majority of the sections. We especially wish to thank Miss Phyl Brock and Mr J. Patel for their dedication in the provision of the wide range of special stains and enzyme/immunocytochemical preparations, and Mr S. J. Kee for his expertise in the printing of the electronmicrographs. The photographs of the macroscopic specimens were largely prepared by members of the Department of Medical Photography at the Westminster Hospital and we gratefully acknowledge their help.

We thank also past and present colleagues at the Royal Postgraduate Medical School, London, the Bland-Sutton Institute of Pathology, Middlesex Hospital Medical School and the Westminster Medical School and Hospital. Finally, we owe a very great debt of gratitude to Mrs Norma Jackson and Miss Joan Carter for their patience in typing and retyping the text, and to Mrs Shirley Jones for her meticulous preparation of the Index.

# Preface

This colour Atlas is intended as a visual aid to the interpretation of the difficult field of thymus and lymph node histopathology, and is designed for use by both practising and trainee pathologists, final year clinical students, research workers and clinicians active in this field.

The sections on thymus pathology include involution, aplasia, thymitis (inflammation) and neoplasia; with the emphasis on the thymitis associated with myasthenia gravis and on thymic tumours including thymomas. The largest individual sub-sections on the lymph node are devoted to Hodgkin's disease, lymphomas other than Hodgkin's disease, and to infectious conditions. Other major sections are concerned with common reactive conditions and reactive processes with characteristic features, which may be confused with lymphomas. The histopathology of extra-nodal sites, such as spleen, skin and gastrointestinal tract are only included where they relate to lymph node pathology.

Since the interpretation of reactive and neoplastic lesions is helped by the understanding of the normal, we have considered it essential to describe and illustrate *normal* thymus and lymph node structure. Many sections also include examples of plastic processed material and electronmicrographs since they, too, greatly facilitate the interpretation and diagnosis of thymus and lymph node pathology. Technical aspects include a short description of the handling and processing of surgical material and the final illustrative section is devoted to routine and special staining techniques and certain immunocytological and histochemical reactions.

Essentially this Atlas is a synthesis of the authors' experience in this field. Information relating to clinical data and aetiology have either been extracted from recent publications or reflect the personal views of the authors. Introductory texts have been kept deliberately brief. However, it is hoped that the more comprehensive legends to the selected illustrations – labelled where appropriate – taken with the introductory texts, will describe adequately the salient features of the normal and pathological conditions covered. A short list of books for recommended reading and an extensive Index are included.

In compiling this Atlas one of the biggest problems dictated by space and cost has been the limitation of the number of colour illustrations considered necessary to cover all aspects of this large and important area of pathology. Also, it has not always been possible to provide consistency in colour because of the different origins of material, and the variability in the routine and special stains used. The colour illustrations represent a very wide range of magnifications; from × 3 for whole-section mounts, through × 30 for low power views and up to × 940 for the oil immersion (high power) fields. However, in view of the differences in absolute size induced by routine fixation and processing procedures, and because we consider it more important for the reader to assess cell size in relation to normal cellular constituents (e.g. small = red cells, large = endothelial or macrophage nuclei) magnifications are indicated only for the macroscopic specimens and the electronmicrographs.

The majority of photomicrographs were taken with a Wild M20 camera microscope using Agfachrome 50L, a minority being taken with a Zeiss Ultraphott II camera microscope with Kodachrome 2. The electronmicrographs were taken either with the Hitachi 12U or the AEI 801 electron microscopes.

# The Lymphoreticular and Mononuclear Phagocytic System (LRMPS)

The lymphoreticular and mononuclear phagocytic system of cells – collectively called the LRMPS – is now known to be of prime importance in immunological function, with the cells of the lymphoid series closely collaborating with those of the mononuclear phagocytic system. It has been shown that in the lymphoid series there are at least two classes of lymphocytes – the thymus (T), dependent lymphocytes, and the bursa/bone marrow (B), dependent lymphocytes – both of which derive initially from bone marrow precursors. There has been clarification of the anatomical and functional distribution of the mononuclear phagocytic cells which are a constant component of lymphoreticular tissues. Mononuclear phagocytic cells are given different names according to their site and, though they may function independently in a purely phagocytic capacity, they are extremely important in many immunological reactions. The LRMPS can be conveniently divided into three functional compartments, as shown in figure **0**.

1 Stem cell compartment represented by yolksac, foetal liver and bone marrow which is responsible for the generation of the various populations of stem cells.
2 Primary or central lymphoid organs responsible for the production and control of immunologically competent cells such as thymus.
3 The secondary or peripheral lymphoreticular tissues which function in an executive capacity. (See also page 78, 109.)

# The thymus gland

The thymus(s) arises from the entoderm of the third and possibly fourth branchial pouches during the sixth week of gestation. It is thus a paired structure sharing a common origin with the inferior parathyroid glands. With continued growth there is downward migration into the anterior mediastinum. Only the upper poles of the left and right thymuses remain in the neck and, unless the connective tissue investing the two portions of the thymus are dissected away, the organ appears as one. The two thymus (lobes) are, however, quite separate, (**1** and **2**). Failure of normal descent results in ectopic thymic tissue which may be found anywhere from the neck down to the diaphragm. The lymphoid nature of the thymus is not evident until around the ninth week of gestation when lymphocytes derived from bone marrow populate the epithelial thymus. At about the same time the thymus assumes a lobular configuration.

The thymus gland achieves its greatest weight proportional to body weight at birth and its greatest absolute weight at puberty. With increasing age there is involution with loss of thymic parenchyma and replacement with fat. This normal involutionary process is known as age or physiological involution (see **37–39**), and should be distinguished from the very rapid involution known as stress or accidental involution which can occur in response to a number of different agents (see **40–47**) and which is mediated through the pituitary adrenal axis and is better referred to as steroid-induced involution.

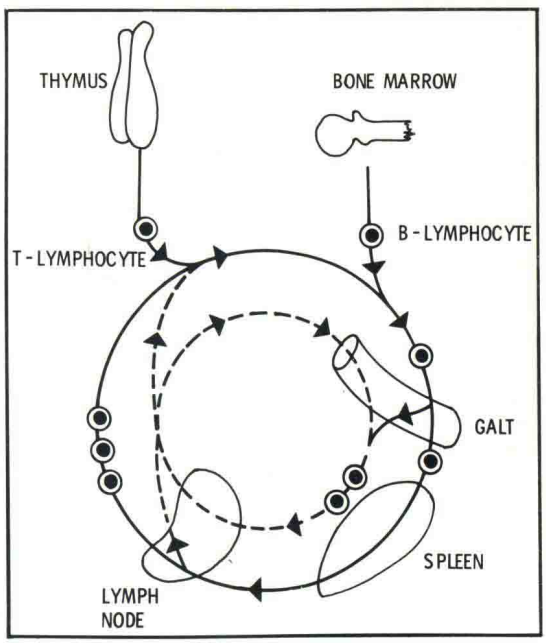
The thymus is a central or primary lymphoid organ responsible for the production, differentiation and direction of a population of small lymphocytes concerned primarily with cell-mediated immunity. Such thymus-dependent lymphocytes are known as T-lymphocytes in contrast to bone marrow dependent B-lymphocytes with which they intimately co-operate. There is thus a vertical division in the immune system dividing the thymus-dependent functions of cell-mediated immunity from that of the bone marrow function of controlling humeral antibody (immunoglobulin) production. Failure of development of the thymus and/or defective T-lymphocyte

function are recognised clinically by a number of immune-deficiency syndromes and histopathologically by the absence of T-lymphocytes in certain well-defined areas of lymph nodes, spleen or other extra-nodal lymphoreticular tissues.

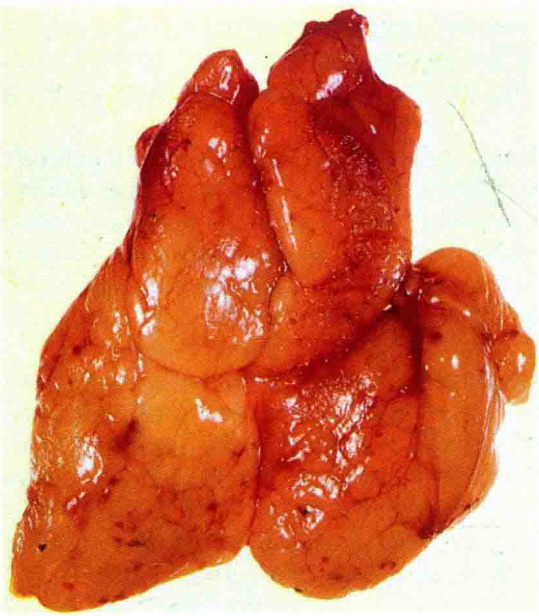
The basic unit of the thymus is the thymic lobule composed of a lymphocyte-rich outer cortex and an inner medulla with numerous epithelial cells, fewer lymphocytes and the unique structures known as Hassall's corpuscles (see **8–11**). It is the epithelial component – in addition to secreting mucosubstances – which is responsible for the production of the thymic hormones including thymosine. Among other cell types which are a normal constituent of the thymus, are eosinophils, mast cells and the striated muscle or myoid cells (see **28–36**). In contrast to lymph nodes and other secondary (peripheral) lymphoid tissues, only occasional lymphoid follicles with germinal centres are found in the *normal* thymus. The frequency of these structures increases, however, in certain conditions such as myasthenia gravis (see **54–66**). The thymus is also an important site in neoplastic transformation, not because thymic tumours are common but because there is a very high incidence in these neoplasms of an associated immunologically orientated disease.

**1 and 2 Normal foetal thymus** During intrauterine life the left and right thymus glands migrate downward into the anterior mediastinum where they come to lie in apposition, simulating one organ. When the loose connective tissue has been dissected away the two distinct and separate parts are clearly visible, **1**. The upper portions of each gland represent the cervical extension which, when present, remains in the neck and is accessible to biopsy. The rest of the organ overlies the base and the greater vessels of the heart. Figure **2** shows the thymuses viewed from behind. The two glands have been artificially separated and it can be seen that the only point where there is communication is via the venous drainage (the great vein of Keynes). In some individuals there may be failure of normal descent of each part into the mediastinum or there may be over descent. Abnormalities of descent account for the finding of ectopic thymic tissue anywhere from the neck to the diaphragm.

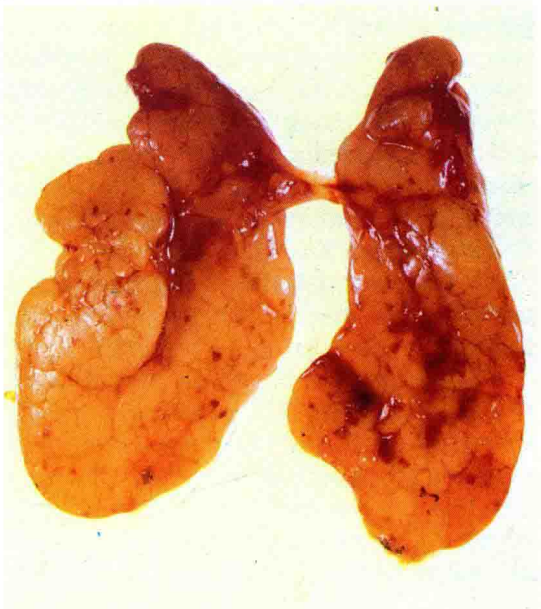
**0**




**1**

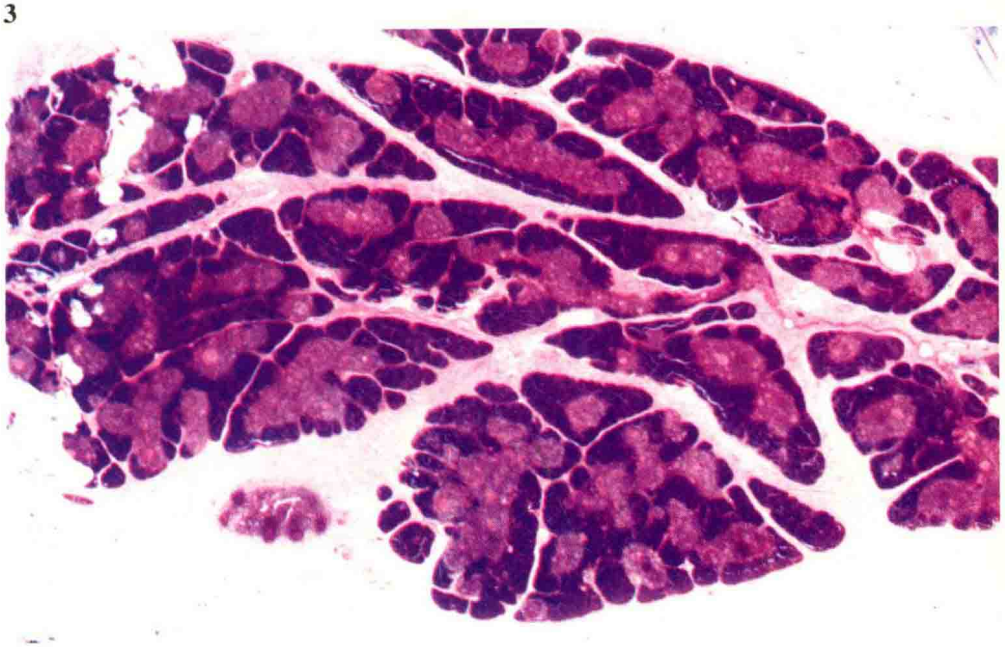


**2**



× 2

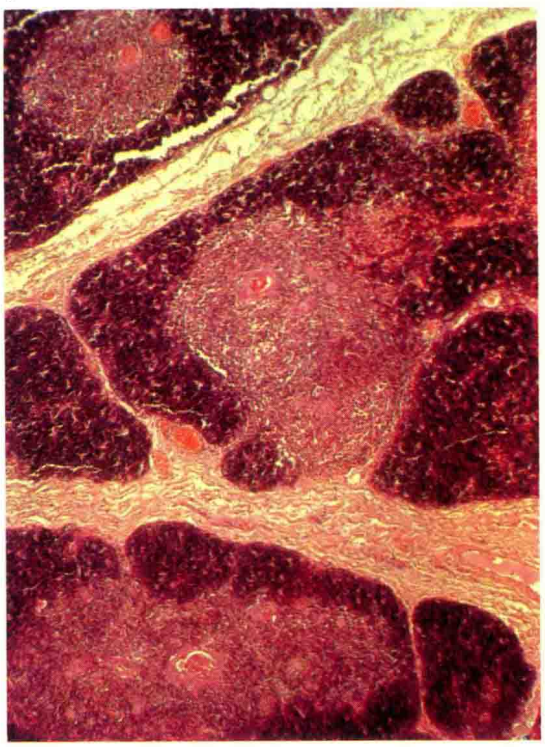
3



**3 Normal child's thymus** The thymus is derived from the entoderm of the third and probably fourth branchial arches, with a probable contribution from the cervical sinus. The thymus is, therefore, essentially an epithelial organ and may be viewed as a foregut derivative. The characteristic lobular structure as shown here is not evident until the third intrauterine month; until then the rudimentary thymus appears as an epithelial organ. The periphery of the lobules is bounded by a capsule from which are derived the connective tissue septa. Each lobule is composed of an outer darkly-staining cortex and an inner paler-staining medulla which is continuous throughout each half of the gland. *(H&E)*

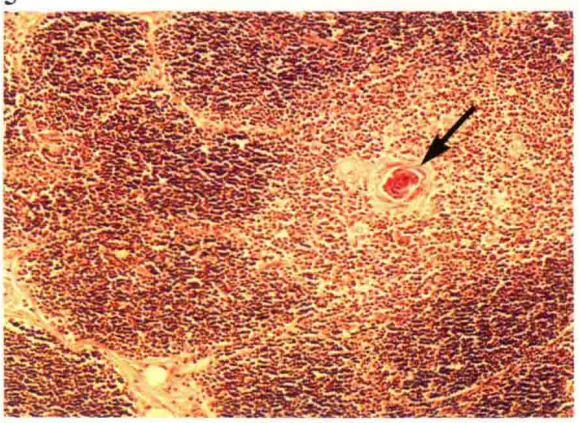
**4 Normal child's thymus** The outer cortex is composed of numerous densely-packed small lymphocytes (thymocytes) and the inner medulla consists of fewer lymphocytes admixed with the thymic epithelial cells. The lymphocytes are derived from bone marrow (stem) cells which migrate to the thymus at about the third intrauterine month. Scattered throughout the medulla are elongated or rounded epithelial structures known as the Hassall's corpuscles which are unique to the thymus. The epithelial component is essential for the normal maturation and competence of the lymphoid component, and is the source of the various thymic hormonal/ humeral factors now being defined. *(H&E)*

4



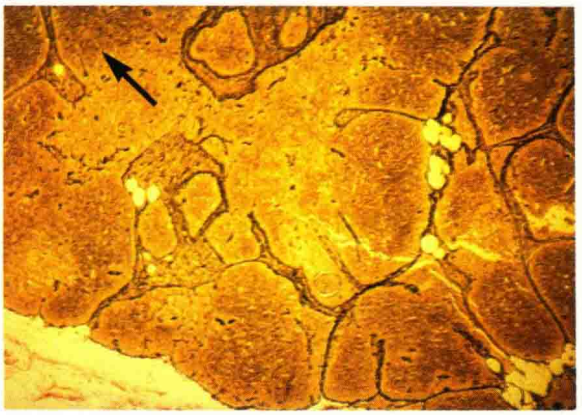
**5 Normal child's thymus** The inner part of the lobule, the medulla, consists of a loose cytoplasmic network formed from processes of the epithelial cells, among which are scattered the lymphocytes. Epithelial cells are also present in the cortex but are not usually evident because they are obscured by the closely-packed cortical lymphocytes and, at this site, they tend to be more attenuated. The rounded structure is a Hassall's corpuscle (*arrow*) which has undergone cystic change – a common finding. The red material seen at its centre consists of cell debris mixed with keratinous material. *(H&E)*

5



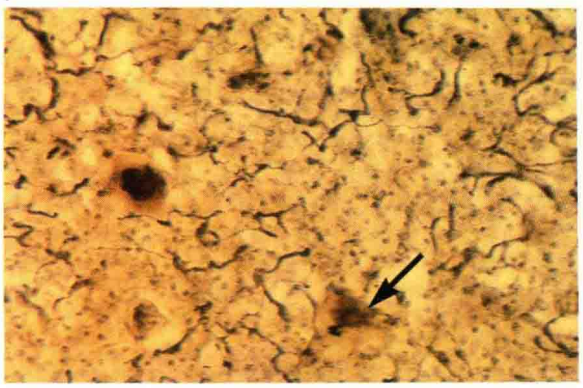
**6 Normal child's thymus, reticulin content** This figure demonstrates the sparse reticulin fibre pattern, which is in marked contrast to the rich reticulin network present in lymph nodes (see **194**). Fibres are confined to the capsule and vascular septa and to the small vessels which penetrate the parenchyma; in particular, there is an absence of reticulin fibre at the cortico-medullary junction (*arrow*). *(Gordon & Sweets)*

6



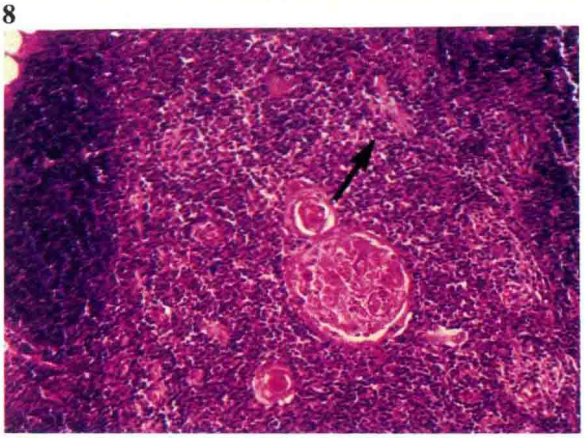
**7 Normal medullary epithelial cells** The processes of the thymic epithelial cells are shown here by a silver impregnation technique. This network of elongated branching and ramifying epithelial processes enclosing the lymphoid population is a normal characteristic of thymus. The darkly-staining bodies (*arrow*) are Hassall's corpuscles. This technique does not stain the reticulin fibre. *(Lithium carbonate)*

7



**8 Normal medulla, Hassall's corpuscles** Hassall's corpuscles are found in the medulla and are composed of aggregates of epithelial cells. These aggregates are not always rounded and may be elongated as shown here. Around the Hassall's corpuscles are a network of epithelial cells (*arrow*) and a population of lymphocytes showing some variation in size. The epithelial cell nuclei are pale and vesicular with a centrally placed nucleolus. The cytoplasm, though abundant, is poorly defined and forms communications with the cytoplasm of other epithelial cells. *(H&E)*

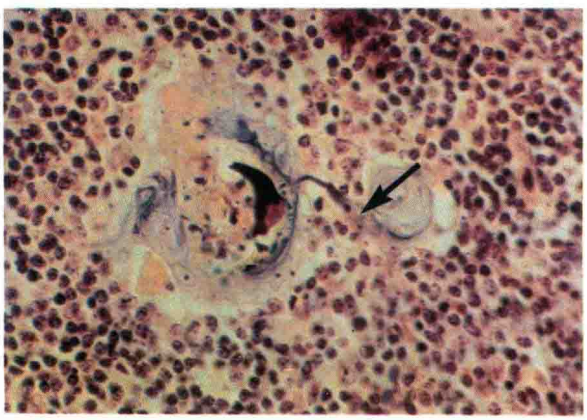
8



**9 Normal Hassall's corpuscles** Very often, the central portion appears cystic. The contents of the 'cyst' or lumen include degenerate, keratinised epithelial cells and other cellular elements such as myoid cells, lymphocytes and eosinophils. Trichrome stains are very useful in enhancing the different components of Hassall's corpuscles, and of the thymus gland in general. The keratin of the epithelium stains red as do some of the degenerate cells within the lumen, in contrast to the orange-brown granularity of the myoid cells (see **28–31**). *(Masson's trichrome)*

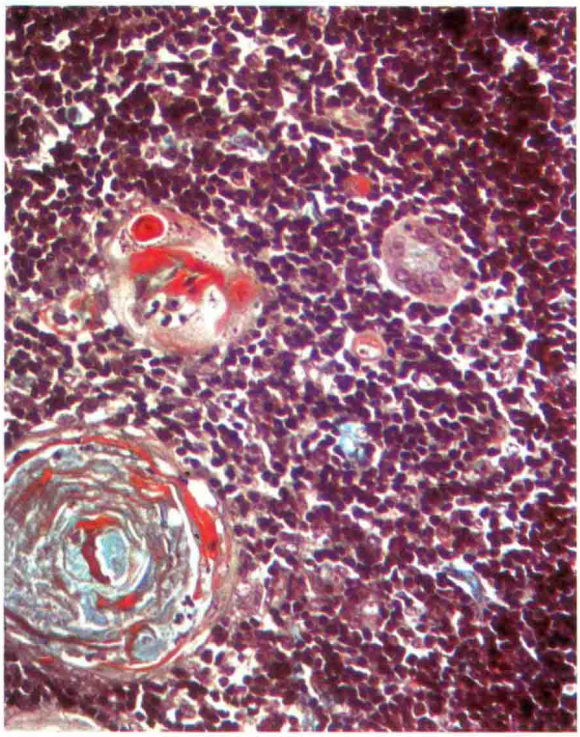
**10 Normal Hassall's corpuscles** The section has been specially stained to show the tonofibrils which are now seen as dark blue-staining fibres (*arrow*). The epithelial cell nucleoli of the Hassall's corpuscles and of the epithelial cell population in the surrounding medulla are also well demonstrated by this particular stain, and contrast with the lymphoid cells which show a densely aggregated chromatin pattern. *(Phosphotungstic acid/haematoxylin (PTAH))*

**10**



**11 Normal Hassall's corpuscles** In this section of resin-embedded material the features of a typical Hassall's corpuscle are emphasised. Note the concentric arrangement of the epithelial cells around the central cavity, and the dark blue staining keratinous material which consists of both tonofibrils and keratohyalin. *(Toluidine blue)*

**9**



**11**