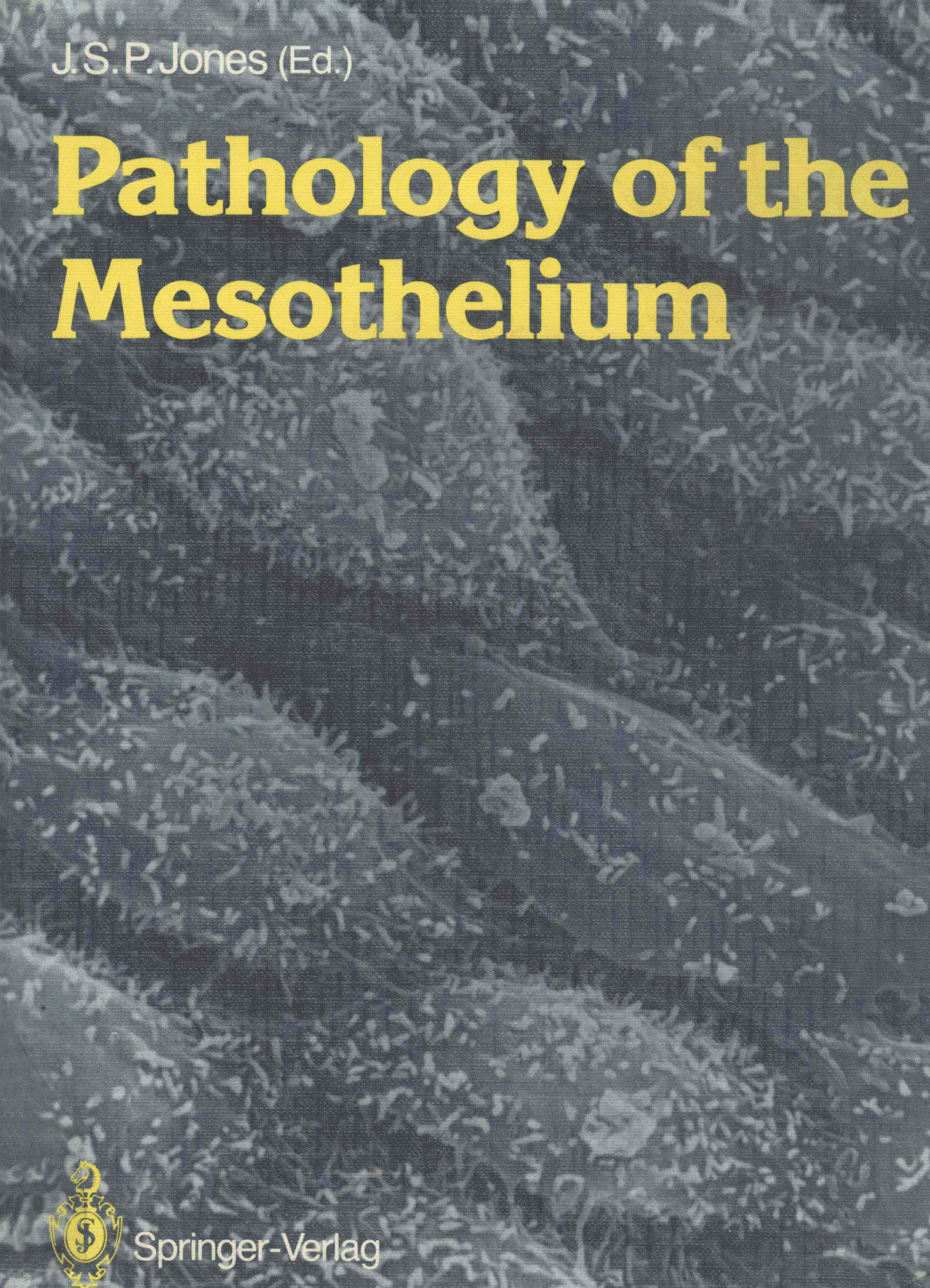
J. S. P. Jones (Ed.)

Pathology of the Mesothelium



Springer-Verlag

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Pathology of the Mesothelium

With 173 Figures

Springer-Verlag
London Berlin Heidelberg New York
Paris Tokyo

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ISBN 3-540-16208-9 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-16208-9 Springer-Verlag New York Berlin Heidelberg

British Library Cataloguing in Publication Data
Pathology of the mesothelium.
1. Mesothelium—Diseases
I. Jones, J.S.P. II. Brachet, E.A.
617'.55 RC665.5
ISBN 3-540-16208-9

Library of Congress Cataloging-in-Publication Data
Pathology of the mesothelium
Includes bibliographies and index. 1. Mesothelium—Diseases. 2. Physiology, Pathological. I. Jones, J.S.P., 1929–II. Brachet, E. [DNLM: 1. Epithelium—cytology. 2. Mesoderm—pathology. QS 532.5.E7 P297] RC665.5.P38 1987 617'.55 87–9590
ISBN 0-387-16208-9 (U.S.)

Printed in Great Britain

Filmset by Computerised Typesetting Services, Finchley, London N12 8LY
Printed by Butler and Tanner Limited, Frome and London

2128/3916 543210

Preface

Many books have been written about the pathology of the major organs of the body such as the lungs, heart, gastrointestinal tract etc. Included in these are descriptions — often with a minor emphasis — of pathological conditions which affect their serosal surfaces. In this book I have endeavoured to reverse the process and treat the mesothelium as an organ in its own right, rather than being the "no man's land" between various major structures. A number of pathological conditions are common to the coverings of the three major body cavities — the pleura, pericardium and peritoneum — while some abnormalities are exclusive to one or other sites.

I hope that the contents of this book cover a broad enough spectrum of mesothelial diseases to be of help to service pathologists, who are ever increasingly being asked to make diagnoses, particularly on small biopsies of pleural and peritoneal tissues. It is also my hope that the various aspects of the subject have been dealt with in sufficient depth to be of use to pathologists engaged in teaching and research, and to those whose interests lie in the structure and function of the mesothelium.

There is still much to be learned in understanding the way the mesothelium behaves in the realm of both inflammatory response and tumour formation. If this book provides a stimulus to furthering research in these fields I feel it will have achieved its objective.

I would like to thank Professor J.C.E. Underwood for his original suggestion that a book be written on the pathology of the mesothelium. I am grateful to Mr Michael Jackson of Springer-Verlag, not only for his confidence in asking me to write the book, but also for his endless patience and encouragement throughout its preparation. The scope of the book has been greatly enhanced by the contributing authors — Dr Norman Thomas (Embryology and Structure), Dr Eugenio Rasio (Physiology), Dr Etienne Brachet (Pathophysiology), and Dr Blanche Butler (Cytology) — and I thank them for their invaluable expertise and help. I am also grateful to Professor Brian Corrin for his advice and illustrations in the electron microscopy sections. I thank all my colleagues who have over the years provided me with the material that forms the basis for this book.

Dr Dewi Davies, Dr Hans Planteydt and Mr Gerry Hooton have kindly read the manuscript and have made helpful and constructive comments. I have had the enormous benefit of a detailed bibliography service from Dr Mike Pelnar of the Canadian Asbestos Information Centre, Montreal, and this has proved invaluable in the writing of this book. I have also received the greatest assistance from the Cancergram Service of the International Cancer Research Data Bank.

For the photographic illustrations I am indebted to Mr Geoffrey Gilbert of the Photography Department at the City Hospital and to Mr Bill Brackenbury of the Microphotography Department at the University Hospital, Nottingham. Illustrations from other sources have been individually acknowledged in their respective legends. I would also like to acknowledge the contribution of my secretary Mrs Valerie Bolton in typing the manuscript and the technical help and expertise of Mr Keith Miller.

Finally I would like to thank my wife for her tolerance during the past two years while the book has been written and I have monopolised the dining room table every weekend!

Nottingham, 1987 Stephen Jones

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Introduction

The mesothelium is a membranous structure consisting of a single layer of cells which lines the serosal cavities of the body — the pleural, pericardial and peritoneal cavities. In the male it also lines the sac which invests the testes.

The mesothelium has two layers:

1. A *visceral* layer which covers the outer surface of various organs — the lungs, the heart, the abdominal viscera and the testes.
2. A *parietal* layer which is in continuity with the visceral layer. The parietal layer lines the various body cavities.

In this book the mesothelium is considered to be an organ of the body in the same way as the skin could be described. However, in order to study its functions and its various pathological changes it is necessary to include also the *submesothelial structures* — connective tissue, blood vessels, lymphatic vessels and nerves. This concept is similar to the way in which the functions and pathological changes of the skin need to include not only the epidermis and dermis but also the subcutaneous structures.

Technical Note. Unless otherwise stated the staining used in the microscopy illustrations is haematoxylin and eosin.

Contents

1. Embryology and Structure of the Mesothelium

N. W. Thomas

Embryology of the Mesothelium

During the third week of embryonic life, segmentation of the paraxial intraembryonic mesoderm commences and the embryo enters the somite period of development. At the same time clefts appear within the lateral plate mesoderm, and gradually they coalesce to form a 'U' shaped intra-embryonic coelom. The arms of the cavity lie within the lateral plate mesoderm and meet in the midline, within the cardiogenic area of mesoderm, at the rostral limit of the embryonic disc. The cells that line the primitive coelom and its derivatives (the pericardial, pleural and peritoneal cavities) constitute 'The Mesothelium'. Initially they have a cuboidal form and the layer may appear pseudostratified (Fig. 1.1) Three events characterise their subsequent development:

1. The formation of a basal lamina that separates the mesothelium from the underlying mesenchyme
2. The appearance of intercellular junction
3. The change in cell form from cuboidal to squamous

The ordering and timing of these events appear to vary between species. In the mouse the cells become squamous and develop microvilli before contact regions appear (Suzuki and Nagano 1979), while in the rat junctional complexes are present while the cells are columnar (Gattone and Morse 1984).

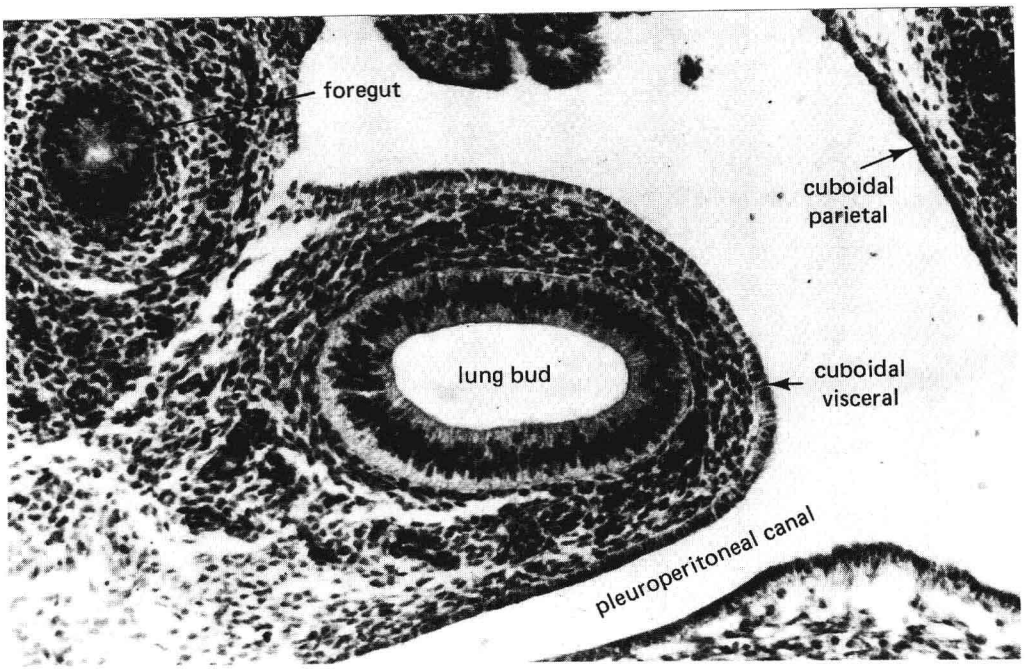


Fig. 1.1. A 7-mm human embryo; cuboidal mesothelium is shown lining the pleuroperitoneal canal. × 200

Structure of the Mesothelium

There appears to be no recognisable cytological difference between mesothelial cells lining the pericardial, pleural and peritoneal cavities. Comparative studies have failed to identify any feature that distinguishes between the mesothelia of animal species and man (Ferrans et al. 1980; Dobbie et al. 1981). Histochemical studies have not demonstrated evidence of a unique cytochemical profile in different mesothelia (Raftery 1973; Whitaker et al. 1980). However, on the basis of the activity of 16 enzymes and four other compounds, Whitaker et al. (1980) concluded that the similarity in cytochemical profile of mesothelial cells from different sites supports the concept of the mesothelium as an entity. In contrast, the quantity and quality of the submesothelial tissues varies between the three serous cavities, and also between species (Fig. 1.2–1.7).

The squamous nature of mesothelial cells seriously limits light microscope observations using conventional histological sections, and some workers have employed whole-mount preparations. Electron microscope techniques are free from these problems, and ultrastructural studies have confirmed light microscope descriptions and clarified areas of disagreement.

In surface view, the cells have a hexagonal profile, with some showing evidence of peripheral interdigitations, and others, regions of cell overlap. Tight and gap junctions are present between the bodies of adjacent cells (Fig. 1.8), but gap junctions of a different and probably more labile nature are found between cell processes (Simionescu and Simionescu 1977). The lateral

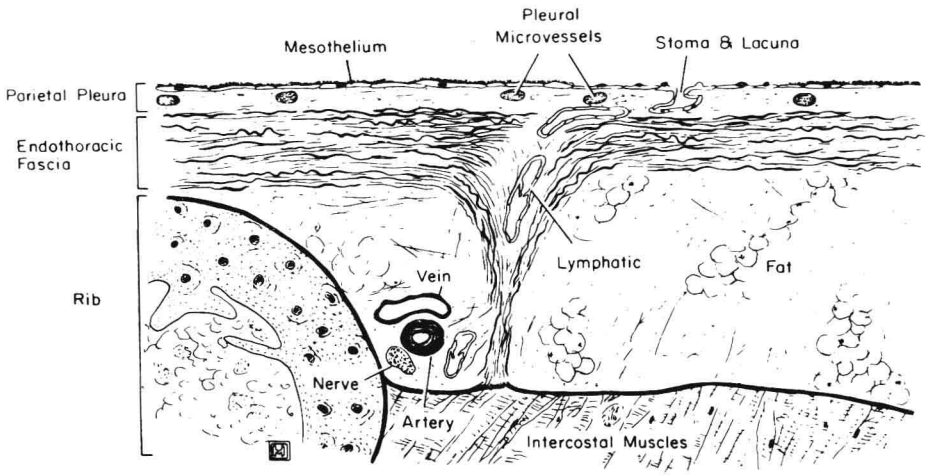
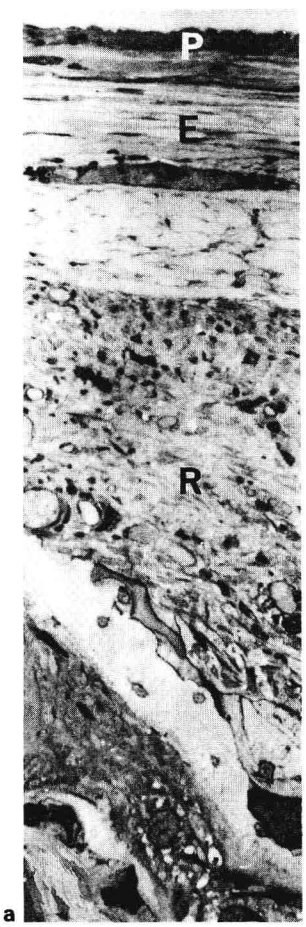


Fig. 1.2. The parietal pleura, consisting of a single layer of mesothelium and submesothelial connective tissue containing blood vessels, nerves and lymphatics. Beneath this layer is the endothoracic fascial layer which covers the ribs and intercostal tissues. (Albertine et al. 1982)



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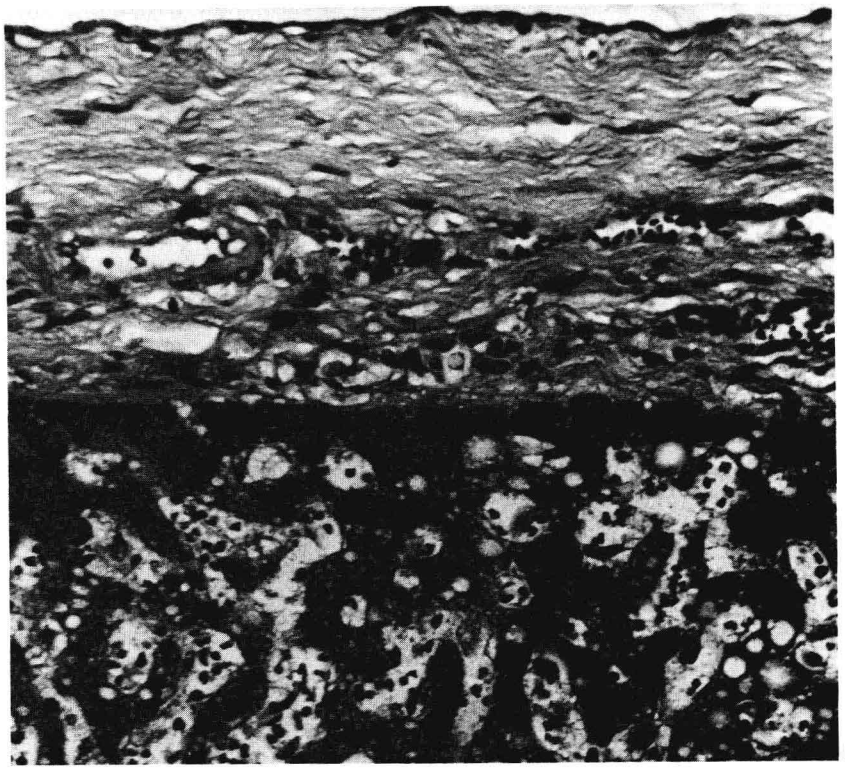

b

Fig. 1.3. a Light micrograph of the parietal pleura (*P*) and endothoracic fascia (*E*) overlying a rib (*R*) × 210. Albertine et al. 1982) **b** Light micrograph of the visceral peritoneum consisting of a single layer of mesothelial cells overlying the connective tissue which forms the liver capsule. × 337

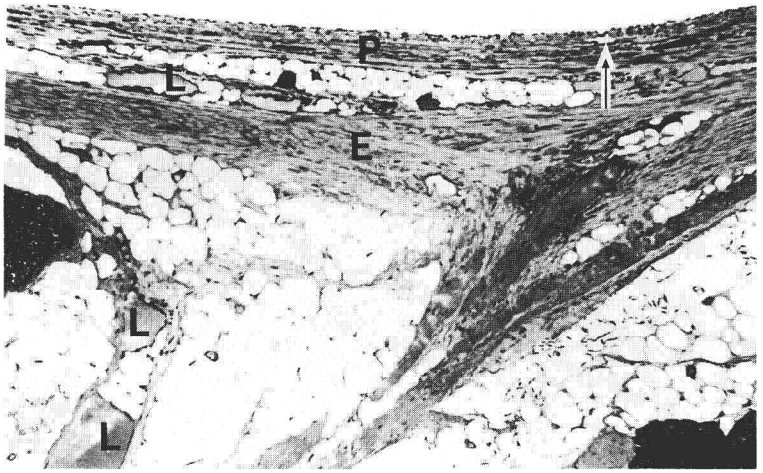

Fig. 1.4. Light micrograph of the parietal pleura (*P*) and endothoracic fascia (*E*) covering an intercostal space. A Lymphatic lacuna (*arrowed*) lies beneath the mesothelial cells. Collecting lymphatics (*L*) carry lymph away from the lymphatic lacunae. × 66 (Albertine et al. 1982)

intercellular spaces in the human pericardium are sometimes distended and lined with microvilli (Ishihara et al. 1980).

Typically, microvilli are found on the luminal cell surface (Fig. 1.9a, b), but their distribution is variable. In some instances the cell surface is covered with a homogeneous layer, but in others the microvilli tend to be concentrated at the cell periphery, leaving the supranuclear plasma membrane smooth. On the basis of the density, length and width of microvilli, Mariassy and Wheeldon (1983) identified five regions over the visceral pleura of the sheep. Isolated cilia have been described but their presence is an inconsistent finding. The nucleus has an irregular outline and lies in the central region of

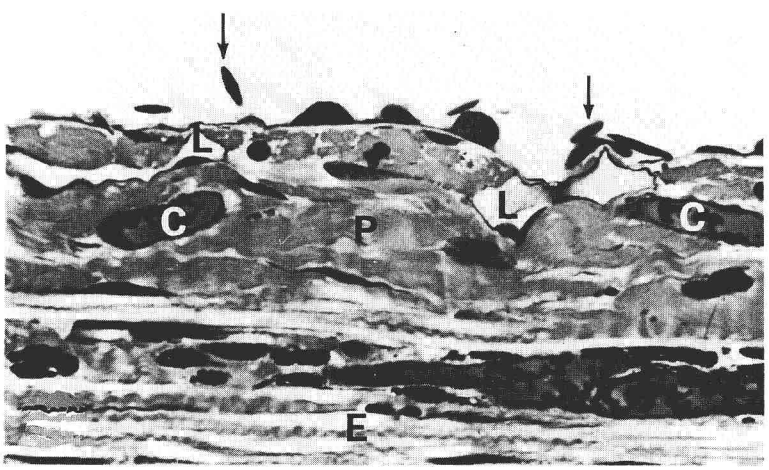

Fig. 1.5. High-power light micrograph of the parietal pleura (*P*) and endothoracic fascia (*E*) covering an intercostal space. There is nuclear bulging of the cells over the areas of lymphatic lacunae (*L*) in the parietal pleura. Blood capillaries (*C*) are seen in the submesothelial tissues. The *arrows* indicate chick red cells that were placed into the pleural space. × 660 (Albertine et al. 1982)

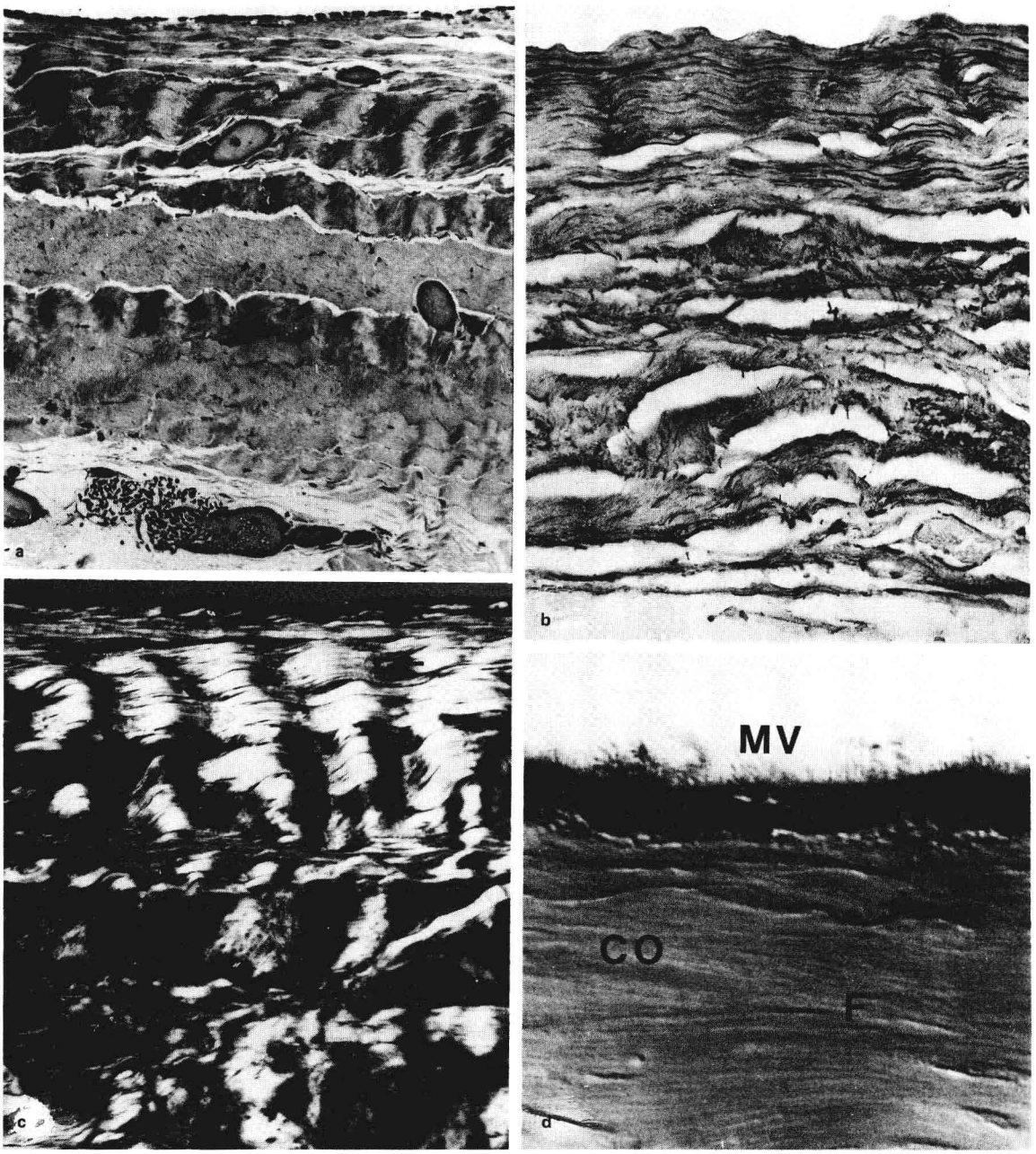

Fig. 1.6. a Light micrograph through the entire thickness of the parietal pericardium showing the mesothelial layer, several layers of collagen fibres, small thin-walled vessels and scattered connective tissue cells. Toluidine blue × 160. **b** Light micrograph similar to **a**, but stained by the elastic Van Gieson method. This demonstrates small elastic fibres, stained black, throughout the thickness of the pericardium. × 160. **c** Polarised light micrograph, similar to **a** showing birefringence of orientated collagen fibres which follow a wavy course. × 250. **d** High-power light micrograph of mesothelial cells showing surface microvilli (*MV*) and dense collagen (*CO*) in the submesothelial layer. Note the fibroblast-like cell (*F*) between the collagen fibres. × 1600 (Ishihara et al. 1980)