

Pathology of the Lung

H. Spencer

Fourth edition

Volume 1

PATHOLOGY^{v.1} OF THE LUNG

Fourth Edition

(IN TWO VOLUMES)

H. SPENCER

M.D.(Lond.), Ph.D., F.R.C.S.Eng., F.R.C.P., F.R.C.Path.

*meritus Professor of Morbid Anatomy in the University of London at St Thomas's Hospital Medical School
and Honorary Consultant Pathologist to St Thomas' Hospital London*

Now

Visiting Professor of Pathology, St Mary's Hospital Medical School, London

Volume 1



PERGAMON PRESS

OXFORD · NEW YORK · TORONTO · SYDNEY · PARIS · FRANKFURT

U.K.	Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 0BW, England
U.S.A.	Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, New York 10523, U.S.A.
CANADA	Pergamon Press Canada Ltd., Suite 104, 150 Consumers Road, Willowdale, Ontario M2J 1P9, Canada
AUSTRALIA	Pergamon Press (Aust.) Pty. Ltd., P.O. Box 544, Potts Point, N.S.W. 2011, Australia
FRANCE	Pergamon Press SARL, 24 rue des Ecoles, 75240 Paris, Cedex 05, France
FEDERAL REPUBLIC OF GERMANY	Pergamon Press GmbH, Hammerweg 6, D-6242 Kronberg-Taunus, Federal Republic of Germany

Copyright © 1985 Pergamon Press Ltd.

All Rights Reserved. No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means: electronic, electrostatic, magnetic tape, mechanical, photocopying, recording or otherwise, without permission in writing from the publishers.

First edition 1962
 Reprinted 1963
 Second edition 1968
 Reprinted 1969, 1973, 1975
 Third edition 1977
 Reprinted 1977, 1978
 Fourth edition 1985

Library of Congress Cataloging in Publication Data

Spencer, Herbert, 1915-
 Pathology of the lung.
 Bibliography: p. 1109
 Includes index.
 1. Lungs—Diseases. I. Title. [DNLM: 1. Lung Diseases. WF 600 S745p]
 RC756.S65 1984 616.2'407 84-11167

British Library Cataloguing in Publication Data

Spencer, H.
 Pathology of the lung.—4th ed.
 1. Lungs—Diseases
 I. Title
 616.2'407 RC756

ISBN 0-08-030772-8

Printed in Great Britain by A. Wheaton & Co. Ltd., Exeter

Preface to the Fourth Edition

"At first glance the lungs may seem uncomplicated, but many wise men have gone astray in their labyrinths." These words were written by the late Dr A. A. Liebow in his original foreword to the first edition of this book and they remain as true today. The author would like to pay tribute to the memory of Dr Liebow whose many original contributions to lung pathology will serve as his memorial. Also the author owed much to Dr Liebow for his help and encouragement over many years.

Pathology, in common with all branches of science, is for ever changing as new concepts of disease and new techniques are developed and applied. From being largely concerned with descriptions of morphological changes in diseased organs, it is becoming increasingly concerned with trying to understand how such changes occur. The development of immunology, molecular biology, enzyme chemistry and the application of newer physical methods of examination such as electron microscopy and dust particle analysis are rapidly changing some of the older concepts of disease. Nevertheless, the value of careful and thoughtful macroscopic and microscopic examination still remain the basic techniques in pathology. Some of the results of the application of the newer techniques are included in this text.

In this fourth edition the subject matter in every chapter has been re-examined, altered, elaborated or deleted, and several newly recognized diseases have been included. Pathology, the study of disease, should not be limited to a narrow description of structural changes, but should of necessity include consideration of all relevant matter concerned with the condition. Although the main emphasis is still placed upon the structural changes, many such changes result from disordered physiology and the physiology of the lungs need ever to be considered.

In earlier editions pulmonary tuberculosis was not included, as its pathology had been so thoroughly and well described in earlier years when it was still a major scourge in developed nations. The recession of its former importance in such countries, however, has tended to obscure the fact that it still remains one of the foremost diseases when the world is considered as a whole. For this reason an outline of the pathology of pulmonary tuberculosis has now been included. The bacterial pneumonias now include pneumonias caused by the *Legionella* group of micro-organisms.

The realization of the importance of immunology as a factor in many pulmonary diseases such as interstitial alveolar fibrosis and the angeitic disorders is better realized. Also the relationship of lymphomatous conditions to disordered immunological states is still but dimly appreciated. The importance of natural or induced immunodepression as a cause of opportunist fungal, parasitic and viral diseases has led to a great increase in such diseases. Neoplastic disorders such as Kaposi sarcoma spreading to the lungs, which formerly was only seen in African children, is now seen in immunodepressant states in adults.

About sixty new illustrations have been added to illustrate both new diseases and to improve upon earlier pictures.

The author would again like to acknowledge the continuing help with both material and illustrations that he has received from many pathologists and friends throughout the world without which this book

would not have been possible. He would also like to thank Professor K. Porter for providing both the opportunity and facilities to enable him to continue working after retirement at St Mary's Hospital Medical School, thus enabling this edition to be completed. Yet again without the continuing support and encouragement of my wife this fourth edition would never have been attempted, and the unfailing courtesy and help of my publishers has again made the task so much easier.

London, 1984

H. SPENCER

Contents

Volume 1

PREFACE TO THE FOURTH EDITION

xiii

1. Embryology of the Lung

1

Intrauterine Development

1

Extrauterine Air-passage Growth

10

Development of the Pulmonary Vessels

13

2. The Anatomy of the Lung

17

General

17

Gross Anatomy

18

Microscopical Anatomy of the Air Passages

23

The Pulmonary Vascular System

53

The Pulmonary and Bronchial Venous System

63

The Pulmonary Nervous Supply

68

Anatomical Differences between the Adult and the Neonatal Lung

76

Visceral Pleura

76

3. Congenital Abnormalities of the Lung, Pulmonary Vessels and Lymphatics

79

Genetically Based Lung Abnormalities

79

Defects of Lung Organogenesis of Probable Non-genetic Origin

79

Primary Agenesis (Aplasia) and Hypoplasia of the Lung

80

Congenital Bronchopulmonary Foregut Malformations (Accessory Bronchi), Accessory Lungs, and Sequestered Lungs

86

Lung Cysts

98

Congenital Cysts including Congenital Adenomatoid Malformation

99

Congenital Abnormalities of the Pulmonary Artery

108

Congenital Abnormalities of the Pulmonary Veins

117

Congenital Pulmonary Lymphangiectasis

125

Congenital Tracheobronchomegaly

120

4. Diseases of the Bronchial Tree

131

Acute Bronchitis (Large Bronchi)

132

Acute Bronchiolitis

133

Chronic Bronchitis and Bronchiolitis

135

Bronchiectasis, General features

147

Infective Bronchiectasis

150

Collapse (Atelactic) Bronchiectasis

152

Congenital Bronchiectasis and Saccular Bronchiectasis

154

5. The Bacterial Pneumonias	167
<i>Pneumococcal Pneumonia (Lobar Pneumonia)</i>	169
<i>Pneumococcal Bronchopneumonia</i>	175
<i>Staphylococcal Pneumonia</i>	176
<i>Streptococcus pyogenes</i> (β -Haemolytic <i>Streptococcal Pneumonia</i>)	181
<i>Klebsiella Pneumonia</i>	183
<i>Aspiration Pneumonia</i>	187
<i>Haemophilus influenzae Pneumonia</i>	190
<i>Pseudomonas and B. proteus Pneumonia</i>	192
<i>Fulminating Interstitial Pneumonia in Infancy (Cot Deaths)</i>	194
<i>Neonatal Pneumonia</i>	194
<i>Plague Pneumonia</i>	196
<i>Anthrax Pneumonia</i>	201
<i>Tularaemic Pneumonia</i>	203
<i>Brucellosis Pneumonia</i>	206
<i>E. coli Pneumonia</i>	206
<i>Meningococcal Pneumonia</i>	207
<i>Legionnaires' Disease</i>	207
<i>Atypical Legionella Pneumonias</i>	212
6. Pneumonias Due to Rickettsiae, Chlamydiae, Viruses and Mycoplasma	213
<i>Rickettsial Pneumonias</i>	213
<i>Q Fever</i>	213
<i>Psittacosis (Ornithosis)</i>	217
<i>Psittacosis-like Disease due to Other Species of Chlamydia (Bedsoniae)</i>	221
<i>Virus and Mycoplasma Pneumonias</i>	222
<i>Influenzal Pneumonitis</i>	223
<i>Measles and Giant-cell Pneumonia</i>	230
<i>Cytomegalovirus Pneumonitis</i>	236
<i>Adenovirus Infections in the Lung</i>	241
<i>Varicella (Chicken Pox) Pneumonitis</i>	244
<i>Other Virus Diseases of the Lung</i>	246
<i>Congenital Rubella Pneumonia</i>	252
<i>Mycoplasma Pneumonia</i>	253
<i>Rabies following Inhalation of the Virus</i>	258
<i>Whooping-cough (Pertussis) Pneumonia</i>	258
7. Chronic Infective Pneumonias	261
<i>Pulmonary Botryomycosis</i>	267
<i>Pulmonary Tuberculosis</i>	268
<i>Pulmonary Atypical Mycobacteriosis</i>	276
<i>Congenital Pulmonary Syphilis</i>	278
<i>Acquired Pulmonary Syphilis</i>	280
<i>Syphilitic Pulmonary Arteritis</i>	283
<i>Pulmonary Actinomycosis</i>	284
<i>Pulmonary Nocardiosis</i>	287
<i>Glanders and Melioidosis</i>	291
8. The Pulmonary Mycotic Diseases	295
<i>Pulmonary Phycomycosis (Zygomycosis)</i>	297
<i>Coccidioidomycosis</i>	299
<i>Pulmonary Aspergillosis</i>	307
<i>Pulmonary Blastomycosis</i>	318
<i>Paracoccidioidomycosis</i>	322

<i>Cryptococcosis</i>	327
<i>Histoplasmosis</i>	332
<i>Pulmonary Candidiasis</i>	342
<i>Pulmonary Torulopsis</i>	346
<i>Pulmonary Sporotrichosis</i>	347
<i>Geotrichosis</i>	349
<i>Adiaspiromycosis</i>	350
<i>Pulmonary Petriellidosis</i>	351
9. Lung Abscesses	355
<i>Inhalational Lung Abscess</i>	355
<i>Lung Abscesses due to Bronchial Obstruction</i>	360
<i>Synpneumonic Lung Abscesses</i>	361
<i>Pyæmic Lung Abscesses and Septic Infarcts</i>	362
<i>Traumatic Lung Abscesses</i>	362
<i>Transdiaphragmatic Spread of Infection</i>	365
<i>Lung Abscesses due to Infected Hydatid Cysts</i>	365
10. Pulmonary Parasitic Diseases	367
<i>Amoebic Lung Abscesses</i>	368
<i>Pneumocystis Pneumonia</i>	372
<i>Toxoplasmosis of the Lung</i>	379
<i>Pulmonary Kala-azar</i>	381
<i>Pulmonary Schistosomiasis</i>	382
<i>Paragonimiasis</i>	389
<i>Pulmonary Opisthorciasis</i>	393
<i>Hydatid Disease of the Lung</i>	394
<i>Pulmonary Strongyloidosis</i>	401
<i>Hookworm Diseases (Pulmonary Manifestations)</i>	402
<i>Pulmonary Ascariasis</i>	403
<i>Pulmonary Filariasis (Tropical Eosinophilic Lung)</i>	405
<i>Pulmonary Dirofilariasis</i>	409
<i>Pulmonary Pentastomiasis</i>	410
<i>Pulmonary Acariasis</i>	412
11. The Pneumoconioses and Other Occupational Lung Diseases	413
<i>Pneumoconioses, general features</i>	413
<i>Silicosis</i>	423
<i>Coal-workers' Pneumoconiosis</i>	440
<i>Carbon-electrode-maker's Pneumoconiosis</i>	456
<i>Anthracosis</i>	456
<i>Graphite Lung</i>	457
<i>Talcosis</i>	458
<i>Siderotic Lung Diseases</i>	461
<i>Haematite-miner's Lung</i>	462
<i>Silver-polisher's Lung</i>	468
<i>Asbestosis</i>	468
<i>Kaolin Pneumoconiosis</i>	476
<i>Fuller's Earth Lung</i>	477
<i>Fibre-glass Lung</i>	479
<i>Aluminium Lung</i>	480
<i>Hard-metal Lung Disease</i>	481
<i>Titanium Lung</i>	482
<i>Barium Lung (Baritosis)</i>	482
<i>Stannosis</i>	484

<i>Occupational Lung Disease due to Fumes, Fine Dusts and Sprays, General Features</i>	484
<i>Bauxite Lung</i>	484
<i>Silica Fume Pneumonitis</i>	487
<i>Beryllium Pneumonitis</i>	487
<i>Arc-welder's Lung</i>	492
<i>Cadmium Pneumonitis</i>	493
<i>Mercury Pneumonitis</i>	494
<i>Thesaurosis</i>	494
<i>Vegetable and Protein Dust Diseases, General Features</i>	495
<i>Farmer's Lung</i>	497
<i>Bagassosis</i>	501
<i>Byssinosis</i>	503
<i>Capsicum Lung</i>	506
<i>Maple-bark-stripper's Lung</i>	507
<i>Mushroom-picker's Lung</i>	508
<i>Sequoiosis</i>	508
<i>Pigeon-breeder's and Budgerigar-fancier's Lung</i>	508
<i>Pituitary Snuff Lung</i>	510
12. Radiation Injuries to the Lung and Lipoid Pneumonia	511
<i>Radiation Fibrosis of the Lung</i>	511
<i>Inhalation Lipoid Pneumonia including Liquid Paraffin Granuloma</i>	517
<i>Kerosene Inhalation</i>	525
13. Collapse, Bronchial Obstruction and Its Sequelae, Shock Lung and Foreign Bodies in the Lung	527
<i>Collapse of the Lung</i>	527
<i>Neonatal Collapse (Atelectasis)</i>	532
<i>Obstructive Pneumonitis (Chronic Absorption Collapse)</i>	544
<i>Foreign Bodies</i>	550
<i>Collapse due to Lymphadenitis (Middle Lobe Syndrome)</i>	551
<i>Bronchopulmonary Lithiasis</i>	552
<i>Shock Lung</i>	552
14. Emphysema	557
<i>Pathogenesis</i>	559
<i>Varieties of Emphysema</i>	566
<i>Interstitial Emphysema</i>	592
<i>Apical Lung Scars</i>	593
Volume 2	
15. Pulmonary Thrombosis, Fibrin Thrombosis, Pulmonary Embolism and Infarction	595
<i>Pulmonary Thrombosis</i>	595
<i>Fibrin Thrombosis of Pulmonary Vessels</i>	598
<i>Pulmonary Embolism</i>	599
<i>Emboli of Extravascular Origin</i>	606
<i>Pulmonary Infarction</i>	624

16. Chronic Pulmonary Hypertension	631
<i>General Features and Physiology of the Pulmonary Circulation</i>	631
<i>Chronic Pulmonary Hypertension</i>	639
<i>General Causes of Chronic Pulmonary Hypertension</i>	640
<i>Primary (Idiopathic) Pulmonary Hypertension (PPH)</i>	658
<i>Hyperkinetic Pulmonary Hypertension</i>	660
<i>Chronic Passive Pulmonary Hypertension (Post-capillary Resistance Group)</i>	666
<i>Chronic Left Ventricular Failure</i>	667
<i>Mitral Stenosis</i>	667
<i>Rare Causes of Chronic Passive Pulmonary Hypertension</i>	682
<i>Chronic Pulmonary Hypertension associated with Chronic Cirrhosis of the Liver</i>	690
<i>Mechanical Obstructive Pulmonary Hypertension</i>	691
<i>Embolic Obstruction of the Pulmonary Vasculature</i>	691
<i>Thrombosis of the Small Pulmonary Arteries and Capillaries</i>	696
<i>Primary Non-vascular Lung Disease Causing Secondary Chronic Obstruction of the Pulmonary Arteries and Capillaries</i>	696
<i>Hypoxic and Idiopathic Causes of Chronic Pulmonary Hypertension</i>	696
<i>Emphysema</i>	696
<i>High-altitude Pulmonary Hypertension</i>	696
<i>Pulmonary Hypertension due to Kyphoscoliosis</i>	699
<i>Pulmonary Hypertension due to "Pickwickian" Syndrome</i>	700
<i>Pulmonary Hypertension due to Progressive Systemic Sclerosis (PSC)</i>	700
<i>Pulmonary Hypertension due to Idiopathic Pulmonary Haemosiderosis</i>	702
<i>Aneurysms of the Pulmonary Artery</i>	702
17. Pulmonary Oedema and Its Complications and the Effects of Some Toxic Gases and Substances on the Lung	705
<i>Pulmonary Oedema</i>	705
<i>Acute Pulmonary Oedema due to Chemical Agents</i>	717
<i>Paraquat Lung</i>	719
<i>"Uraemic" Lung (Fibrinous Pulmonary Oedema)</i>	721
<i>Alveolar Lipoproteinosis (Alveolar Proteinosis)</i>	726
18. Degenerative and Metabolic Disorders of the Lung	733
<i>Amyloidosis of the Lung</i>	733
<i>Pulmonary Corpora Amylacea</i>	739
<i>Pulmonary Alveolar Microlithiasis</i>	740
<i>Alveolar Calcification in the Lung</i>	744
<i>Pulmonary Ossification</i>	747
<i>The Pulmonary Lipoidoses</i>	750
<i>von Gierke's Disease</i>	753
<i>Cystine Storage Disease (Lignac-Fanconi Disease)</i>	753
19. Pulmonary Diseases of Uncertain Aetiology	755
<i>Rheumatic Pneumonitis</i>	755
<i>Bronchial Asthma</i>	758
<i>Chronic Asthma</i>	764
<i>Eosinophilic Pneumonia and the Pathergic Angeitides</i>	764
<i>Eosinophilic Pneumonia and Bronchocentric Granulomatosis</i>	765
<i>Pulmonary Allergic Granulomas</i>	771
<i>Generalized (Classical) Wegener's Granulomatosis</i>	773
<i>Localized Wegener's Granulomatosis</i>	780
<i>Benign Lymphocytic Angeitis (BLA)</i>	781
<i>Sarcoidall Angeitis</i>	782

<i>Lymphomatoid Granulomatosis</i>	783
<i>Goodpasture's Syndrome</i>	787
<i>Idiopathic Interstitial Fibrosis of the Lung (IIFL)</i>	788
<i>Lung Changes in Progressive Systemic Sclerosis (PSC)</i>	802
<i>Pulmonary Changes in Rheumatoid Disease</i>	807
<i>Pulmonary Changes in Diffuse Lupus Erythematosus (DLE) and Dermatomyositis (Polymyositis)</i>	814
<i>Toxic Oil Syndrome</i>	815
<i>Pulmonary Changes in Sjögren's Syndrome</i>	816
<i>Idiopathic Pulmonary Haemosiderosis</i>	817
<i>Relapsing Polychondritis</i>	821
<i>Pulmonary Sarcoidosis</i>	824
<i>Desquamative Interstitial Pneumonia (DIP)</i>	832
<i>Malakoplakia of the Lung</i>	835
20. Carcinoma of the Lung	837
<i>Incidence Rates</i>	837
<i>Aetiological Factors</i>	842
<i>Atypical Hyperplasias and Pre-carcinomatous Conditions in the Lung</i>	855
<i>General Features and Histological Varieties of Lung Cancer</i>	866
<i>Histological Types of Lung Cancer</i>	870
<i>Squamous Cell Carcinoma</i>	872
<i>Small round and Oat-celled Carcinoma</i>	877
<i>Adenocarcinoma</i>	884
<i>Large Cell Cancer (Giant-celled lung cancer)</i>	900
<i>Carcino-Sarcoma of the Lung</i>	904
<i>Basal-celled Carcinoma of the Bronchus</i>	907
<i>The Staging of Lung Cancers</i>	907
<i>The Blood-supply of Lung Cancers</i>	914
<i>The Spread of Lung Cancer</i>	915
<i>Cytological and Other Laboratory Procedures in the Diagnosis of Lung Cancer</i>	927
21. Rare Pulmonary Tumours	933
<i>Bronchial Carcinoid</i>	934
<i>Neurofibroma and Neurofibrosarcoma of the Lung</i>	946
<i>Myoblastoma of the Bronchus</i>	948
<i>Malignant Melanoma of the Bronchus</i>	951
<i>Pulmonary Chemodectoma</i>	953
<i>Benign "Clear-cell" Tumour of the Lung</i>	955
<i>Papilloma of the Bronchus</i>	956
<i>Monomorphic Bronchial Cystadenoma and coincident Bronchial Papilloma and Cystadenoma</i>	961
<i>Pleomorphic Bronchial Gland Adenomas</i>	962
<i>Bronchial Oncocytomatous Adenomas</i>	962
<i>Bronchial Mucoepidermoid Adenoma</i>	962
<i>Adenoid Cystic Carcinoma of the Bronchus</i>	968
<i>Mucinous Multilocular Cyst Adenoma (Carcinoma of the Lung)</i>	970
<i>Chondroma of the Bronchus</i>	970
<i>Lipomas of Bronchus and Lung</i>	972
<i>Pulmonary Fibroma and Myxoma</i>	976
<i>Pulmonary Fibroleiomyomas</i>	978
<i>Pulmonary Sarcoma</i>	980
<i>Pulmonary Rhabdomyosarcomas</i>	985
<i>Embryonal Pulmonary Sarcoma</i>	987
<i>Intravascular and Sclerosing Bronchiolar-Alveolar Tumour (IVSBAT)</i>	987
<i>Tumours of Vascular Origin</i>	990
<i>Benign and Malignant Tumours of the Pleura</i>	1000
<i>Benign Local Pleural Fibroma</i>	1002

CONTENTS

xi

<i>Malignant Pleural Tumours (Mesothelioma)</i>	1006
<i>Squamous-celled Pleural Carcinoma</i>	1010
<i>Endometriosis of Pleura and Lung</i>	1011
<i>Pulmonary Plasma Cell Granulomas—Pulmonary Histiocytic Tumours</i>	1012
<i>Sclerosing Angioma of the Lung (Sclerosing Granuloma)</i>	1017
22. Pulmonary Reticuloses	1021
<i>Pulmonary Lymphoid Hyperplasia</i>	1021
<i>Hodgkin's Disease</i>	1022
<i>Pre-lymphomatous States including Pseudo-lymphoma, Lymphocytic Interstitial Pneumonia (LIP) and Waldenström's Macroglobulinaemia</i>	1025
<i>Sjögren's Syndrome and its Relationship to Pulmonary Pre-lymphomatous and Lymphomatous states</i>	1032
<i>Waldenström's Macroglobulinaemia</i>	1032
<i>Pulmonary Lymphomas (Lymphosarcoma and Histiocytic (Reticulum)-celled Sarcoma)</i>	1033
<i>Plasmacytoma of the Lung</i>	1037
<i>Leukaemic Lung</i>	1039
<i>Lung Reactions to Cytotoxic (Radiomimetic) Drugs used in Leukaemia</i>	1042
<i>Giant Intrathoracic Lymph Nodes</i>	1044
<i>Histiocytosis X Disease (Histiocytic Reticuloses)</i>	1046
23. Hamartomas, Blastoma and Teratoma of the Lung	1061
<i>Pulmonary Hamartoma and Blastoma (Embryoma)</i>	1061
<i>Local Pulmonary Hamartomas</i>	1061
<i>A Single or Multiple Focal Overgrowth of Myomatous Tissue</i>	1067
<i>Pulmonary Lymphangioleiomyomatosis</i>	1069
<i>Tuberose Sclerosis</i>	1073
<i>Pulmonary Changes in Generalized Neurofibromatosis</i>	1075
<i>Pulmonary Blastoma (Embryoma)</i>	1075
<i>Intrapulmonary Teratomas</i>	1079
24. Secondary Tumours in the Lung	1085
AN APPENDIX OF TECHNICAL METHODS USED IN THE STUDY OF LUNG PATHOLOGY	1097
REFERENCES	1109
INDEX	1163

CHAPTER 1

Embryology of the Lung

A KNOWLEDGE of the development of the lung and of its vascular supply and drainage is essential if the many congenital abnormalities occurring in the organ are to be understood.

Intrauterine Development

The respiratory anlage or laryngo-tracheal groove first appears as a median, ventral groove in the floor of the gut caudal to the pharyngeal pouches at about the 3.0 mm (20 somite stage), 24 days after ovulation. At this stage of growth the oesophagus and stomach have not yet differentiated and the laryngo-tracheal depression lies just proximal to the liver diverticulum.

As development proceeds the larynx and trachea grow as a ventral diverticulum in a caudal direction, separated from the foregut by a spur of entoderm and later by mesenchyme which grows between the two structures. The ingrowth of the mesenchyme, which surrounds the foregut, commences at the distal end of the tracheal bud and spreads cranially to where the two structures join at the distal part of the pharynx.

The caudal end of the trachea divides into two bronchial buds at about the 5.0 mm (4th week) stage and each of these proceeds to form the main (primary) bronchi. The further growth of the bronchi is asymmetric, the right being the larger as it grows caudally and dorsally, whilst the left assumes a more horizontal position. Each main bronchus and its branches end in flask-shaped swellings. The right bronchus first buds a ventral branch, which is soon followed by a lateral division situated more proximally, which is destined to become the eparterial bronchus.

By the 8–10 mm (32–35 days) stage, the buds of the lobar (secondary) bronchi have appeared, and each bud with its surrounding mesenchyme will later form a lobe of the lung. A further burst of rapid growth during the 9–11 mm (35–45 days) stage leads to the formation of the segmental and subsegmental bronchial buds (Boyden, 1955a). At this stage the developing lung buds have become well separated ventrally from the elongating oesophagus due to the ingrowth of investing mesenchyme. From this time onwards the lungs gradually grow and assume their adult form, but the main bronchi supplying the lower lobes remain the axial continuations of the original main bronchi. All the bronchi are branches of the primary bronchus up to the 50 mm (12 weeks) stage (Fig. 1.1). The further development of the segmental and subsegmental bronchi was described by Bucher and Reid (1961a) and the ensuing account is based largely on their observations. They found that the period of greatest growth in the subsegmental bronchi took place during the 50–120 mm (12th–16th weeks) stage when about 70 per cent of the full-term bronchial tree was formed. They counted the number of epithelialized branches arising in each of the eighteen segmental bronchi counting distally, but selected for detailed examination certain of the largest axial bronchi. Some of the bronchi selected for such examination were found initially to run outwards to the pleural surface whereupon they bent at right angles to continue their further course and branching, lying subjacent and parallel to the pleural surface. In the upper right and left anterior axillary segmental bronchi they found on average 17 and 18 branches respectively. In the medial bronchus

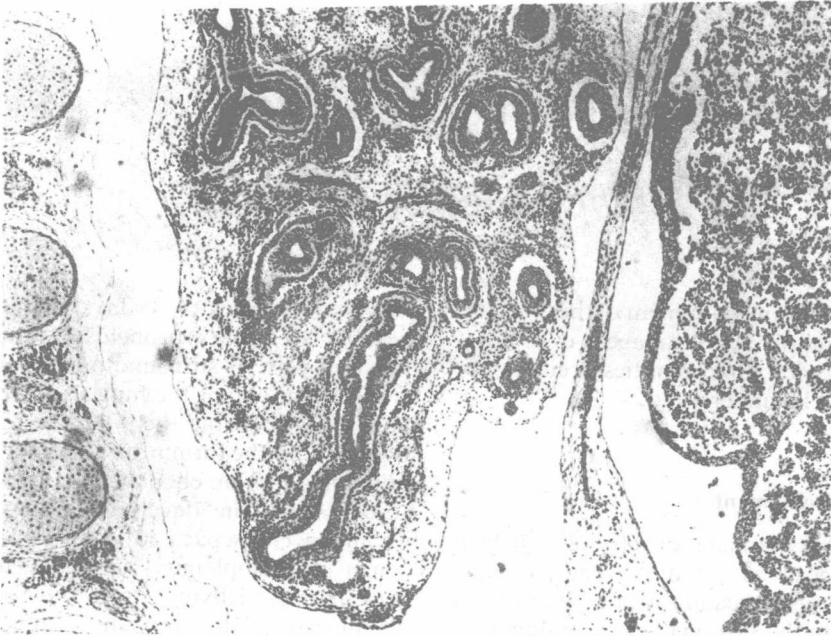


FIG. 1.1. Developing lung 20 mm stage showing bronchial tubes but as yet no attempt to form alveolar tissue. $\times 40$.

supplying the right middle lobe they found an average of 23 branches and in the left lingula bronchus 22 branches. In the anterior basal bronchi in both lower lobes there were on average 19 branches, and 21 along the posterior basal bronchi. The number of branches arising from the middle lobe bronchi was in close agreement with the figure quoted by Boyden and Tompsett (1962) in a full-term infant, thus proving that little further development of the bronchi occurs after the end of the 16th week of foetal life.

Boyden (1955a) had earlier found that up to about the 56 mm (12th week) stage, one to five more post-segmental branches were present on average along the axial bronchi in the right than the left lung, but after about the 70 mm (14th week) stage little difference in growth rate occurred. This finding was confirmed by Bucher and Reid (1961a). Although the burst of bronchial growth activity that occurs during the 40–120 mm (10–16 weeks) stage involves all segments of the lungs, the growth rate may not be uniform, and is normally greatest in the lower

lobe basal segments as the general growth of both lungs proceeds more in a caudal than cephalic direction. This tendency to greater continued growth in the caudal parts of the lungs results in a greater number of branches along the segmental bronchi in the lower lobes in full-term infants.

By 16 weeks the number of bronchial generations in the lower lobes may exceed the number found in the adult lung. This excess of distal air passages later becomes transformed into alveolated tissues.

Until the 150 mm (18th week) stage the lung consists only of branching bronchi surrounded by mesenchyme and it shows no differentiation into alveolar tissue before about the 180 mm (20 weeks) stage (Fig. 1.2).

After the 180 mm (20th week) stage the number of fully epithelialized segmental bronchial branches may appear to decrease as some of the most distal air passages begin to partly lose their light visible epithelium following capillary ingrowth and conversion of the tubes into partly epithelialized, partly alveolated respiratory

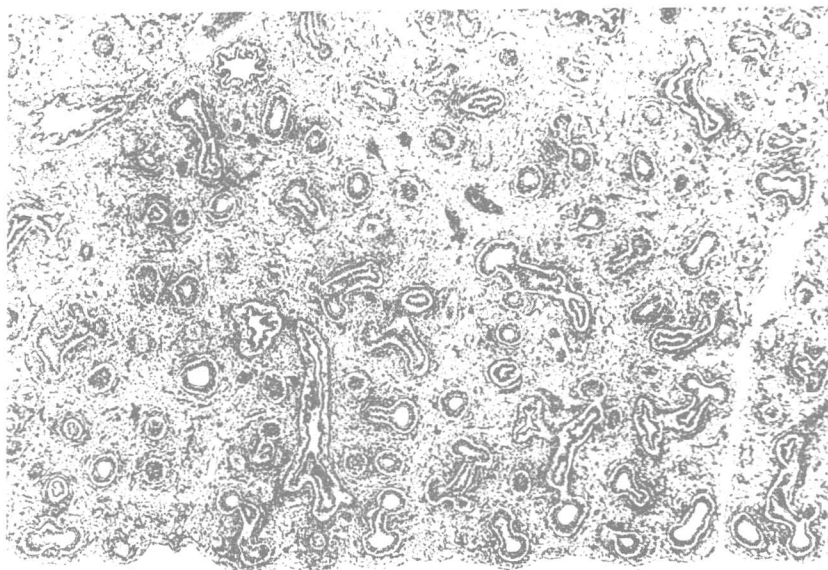


FIG. 1.2. A slightly later stage of pulmonary development 60 mm stage showing more extensive branching of the bronchial tubes but still no attempt to form alveoli. $\times 40$.

bronchioles. During the 180–300 mm (20–24th weeks) stage the most distal air passages end in clumps of cells which begin to cannulate to form alveoli (Fig. 1.4). After the 300 mm (24 weeks) stage the terminal bronchioles develop up to four generations of smooth non-alveolated bronchioles destined later to become respiratory bronchioles. Each generation of these future respiratory bronchioles gives rise to two or three branches. The most distal generation of respiratory bronchioles terminate in two clusters of very thin-walled saccules which are the precursors and immature forms of future alveoli (Boyden, 1972). The distal generations of respiratory bronchioles are themselves lined by flattened epithelium and were referred to by Boyden (1967) as transitional ducts. The alveolar saccules at the time of birth further subdivide into four lobules and immature shallow depressions appear in their walls which are very primitive alveoli. The knob-like clumps of cells forming the saccules resemble acini as they cannulate, and were referred to as pneumoneres by Farber and

Wilson (1933). Although the saccules are very immature respiratory structures they suffice for adequate gas exchange in many prematurely born infants.

Coincident with the first appearance of the alveoli the lung septa begin to appear (Reid and Rubino, 1959). The septa are best developed beneath the sharp margins and apices of the lungs but do not isolate one portion of lung from another as they are only incomplete septa. As Boyden (1955b) and Reid (1954) showed, the pleural fissures between lobes are very variable and are often incomplete, often failing to extend to the hilum. Communication between lobes may therefore occur and may account for translobar spread of pneumonia in adult life. A distinct sheath forms around the larger bronchi and vessels central to the lobules.

The development of the lung saccules (acini) is accompanied by considerable vascular proliferation throughout the growing lung and the newly formed alveoli are invaded by capillaries. The developing alveolar epithelial lining attenu-

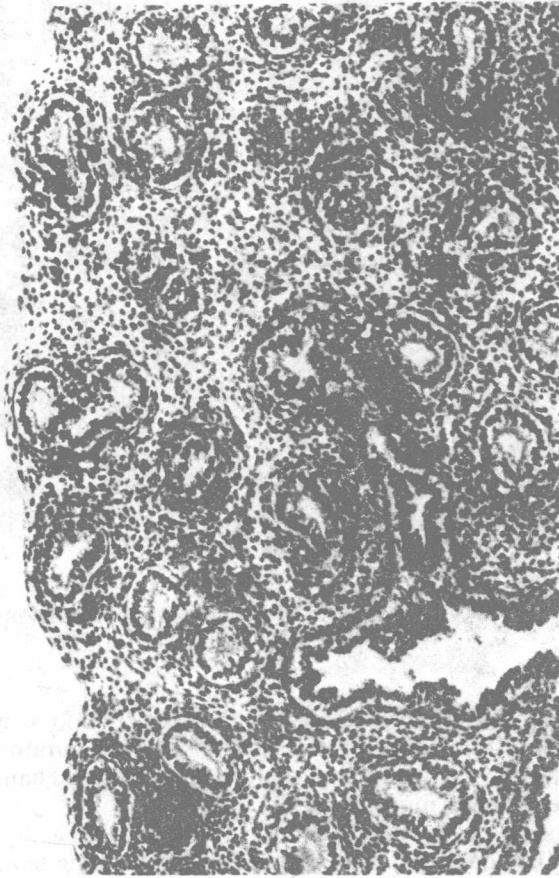


FIG. 1.3. Developing lung from a 10 cm long foetus (14 weeks old). $\times 100$.

ates and appears to be partly disrupted by the underlying capillaries (Fig. 1.5). This appearance led to the erroneous conclusion reached by Barnard and Day (1937) that there was no continuous alveolar epithelial lining. The further intrauterine development of the lung leads to further attenuation of the alveolar epithelium until at full-term only a few alveolar epithelial cell nuclei are still visible lying in spaces between the alveolar capillaries. After birth the respiratory movements lead to still further thinning of the cytoplasm of the alveolar epithelium which assumes its post-natal inconspicuous appearance. The existence of such alveolar epithelial

cells in normal postnatal lung was finally proved by Low (1953) following the introduction of the electron microscope. The mode of growth of alveoli both *in utero* and after birth is uncertain. Loosli and Potter (1951) considered they grew as a result of septal division within existing saccules. Macklin (1936b), however, regarded alveoli as being analogous to interstitial emphysematous spaces in which the lung mesenchyme split and allowed the capillaries to come into intimate contact with fluid and later air contained in the alveolar spaces.

In the adult lung the number of segmental bronchial branches along axial bronchi may

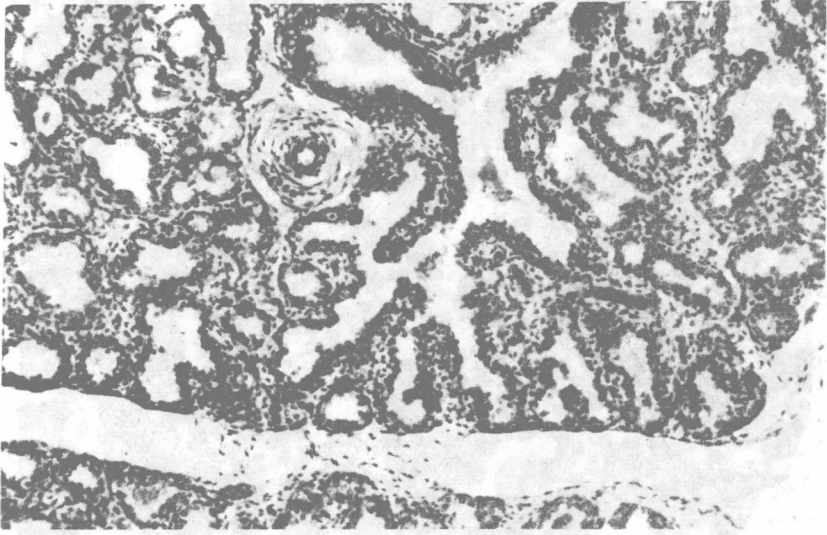


FIG. 1.4. Foetal lung between 22 and 25 weeks of age. Note the development of rudimentary alveolar ducts and the beginning of alveolar development. $\times 100$ H and E.

again increase compared with the number found in the full-term infant. This has been attributed by both Engel (1947) and Bucher and Reid (1961a) to conversion once again of respiratory bronchioles into fully epithelialized terminal bronchioles during childhood. This process was observed by Willson (1928) to occur in mice, and by Bremer (1935) in cats. Boyden (1965), as stated previously, however, believed the reverse process occurs, namely that terminal bronchioles are converted into respiratory bronchioles. The further course of post-natal lung growth is considered separately. The mode of bronchial division is still disputed, some regarding all growth as proceeding from the growing tip, others considering that lateral branching takes place proximal to the tip. According to Arey (1946), both methods occur. The failure of bronchial growth is responsible for the absence of lobes, segments or smaller volumes of lung in the future organ, and its cessation at an early stage can be responsible for the later development of congenital bronchiectasis.

The evolution of the asymmetric adult bronchial pattern has excited much interest, but is probably caused by the laevo-rotation of the

heart, and the persistence of the left dorsal aorta and fourth left aortic arch to form the arch of the aorta. In aquatic mammals with a central heart, such as the cetacea and pinnipedia, the lungs exhibit a symmetrical pattern and in hippopotami both lungs possess eparterial bronchi. Aeby (1880) considered that the left eparterial bronchus had become suppressed in man, but according to the **migration theory**, first propounded by Willach (1888), the bronchi were originally arranged symmetrically but migrated from their primary sites of origin from main bronchi to become attached to branch bronchi. Huntington (1920) strongly refutes this latter view, adding "comparative anatomy if correctly interpreted absolutely negatives the migratory theory, and teaches that a branch budding from any point of the bronchial tree develops at the site of its first inception".

The **selection theory** of bronchial development maintains that the eventual size of the lung, and therefore the growth of the bronchi, is ultimately dependent on the amount of coelomic space available to accommodate it. The later cessation of branching along the axial segmental bronchi in the lower lobes, referred to above, is probably due