



# FOETAL AND NEONATAL PATHOLOGY

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*TO MY WIFE ELLEN*

## PREFACE TO SECOND EDITION

In the eleven years since the first edition more publications bearing on the pathology of the foetus and neonate have probably appeared than existed prior to 1952. The work has, therefore, been completely revised and almost entirely rewritten, though the general arrangement and the basic approach have remained substantially unaltered. Every effort has been made to incorporate the contributions of workers in many lands. Even when it has not been practical to trace the evolution of present day concepts and do justice to their originators, it is necessary to indicate contemporary views, and then the more valuable and accessible references have been selected. Much of the earlier, valuable and basic work must still be recorded, but in some chapters over three-quarters of the references are to contributions and reviews published in the last decade. The author has tried, especially on difficult and uncertain issues, to indicate a personal approach, but considers that, during this formative and growing period of the subject, the text must be closely supported by numerous references. The titles of the papers are only given for the more useful review articles; the text itself, and not the bibliography, tries to indicate the references for further reading on specific subjects.

The belief that pathology is only morbid anatomy dies slowly, and in some centres pathology is slowly dying because it remains only morbid anatomy. The author, working primarily in general pathology and in a large hospital and reference laboratory, is aware that he has advanced unwisely into many fields where his lack of direct and expert knowledge is very apparent. He has been concerned to find a dynamic basis for many disease conditions and to emphasize the frequent limitations of the morphological approach as well as its value. This eclectic approach has doubtless resulted in errors of fact and emphasis, but the pathologist must range widely in his attempt to understand the border between health and disease and the basis of disease processes.

The first edition was based on a relatively unselected series of post-mortem examinations. Especially since 1954, when the author became responsible for all histopathological examinations in Northern Ireland outside the hospitals of the medical school, material has of necessity been selected. When data from the older series still have illustrative value they are retained. The problems of foetal and neonatal pathology as defined by that survey remain and disappointingly few have been solved. Some change in their relative importance has occurred, but this cannot be quantitatively established.

I am indebted to my colleagues in the Belfast Medical School, especially to those mentioned in the first edition, and to colleagues throughout Northern Ireland who have supplied me with material. Portions of the text have been modified from lectures given in South America in 1960 as advisory specialist to Uruguay and guest lecturer in the Argentine and Brazil for the British Council, and I have benefited from discussions with well informed and analytical minds there, and especially from contacts with Dr. Alberto Matteo of Montevideo. My laboratory and secretarial staff have supported me in

## PREFACE TO SECOND EDITION

the labour of this revision. Mr. John Orchin, F.I.M.L.T., has contributed both by histological preparation and by photography. In the last few years I have had the valued services of Mr. J. A. Robin for photography. Miss O. McCormick has cheerfully carried the burden of typing and retyping and Miss McKelvey has helped with many details of organization. Miss Webster and the staff of the Medical Library of Queen's University have been more than helpful at all times. Mr. G. A. Smith, M.M.A.A., has been responsible for further diagrams and pen drawings. Above all I owe a great debt to my wife for accepting the disorganization of home and family life entailed in the rewriting of this book.

Again, the publishers have extended to me every kindness, and have facilitated my efforts in every way.



## PREFACE TO FIRST EDITION

This work is an attempt to provide a basis for the study of disease in the foetus and newborn infant. An improvement in the general standard of midwifery has reduced deaths from physical trauma. Infections, acquired during and after birth, are becoming less frequent owing to better hygiene in the labour ward and nursery, and those which occur are sometimes controlled by the use of the new antibiotic drugs. If further advances are to be made a wider appreciation of the disturbances peculiar to foetal and neonatal life is increasingly necessary. The present study is arbitrarily divided into the disturbances arising during intra-uterine life, those due to the failure of the foetus to adapt its vital functions to the new conditions imposed by the transition to extra-uterine life, and those produced by infections in both intra-uterine and extra-uterine life. The varied nature of these disturbances and the arrangement adapted for their discussion are indicated in separate introductions to each of these three divisions. Disturbances in the period after birth are often related to events occurring during birth, and disturbances at both periods often depend on events occurring earlier and during intra-uterine life. This interdependence of ante-natal, intra-natal and post-natal events may give some unity to the pathology of foetal and neonatal life and may justify its separate discussion. The subject should not be separated from general pathology, but special study is necessary and has been based on a review of autopsies on 530 stillborn infants and 802 infants dying in their first month of life from the Royal Maternity Hospital and from the Jubilee Maternity Hospital in Belfast. The data derived from this relatively unselected material have been presented in various tables and provide some numerical background for the discussion of the literature. Throughout this study the limitations of existing knowledge and methods have always been very apparent, and an attempt will be made to distinguish between what is relatively well established and what is unknown and in need of further investigation.

It is unlikely that a work concerned with so many different and often separate fields of study has been written without ignoring or misinterpreting the observations and viewpoints of some who have laboured hard to advance existing knowledge, and some observations of great value have probably been omitted. It is hoped that those concerned will forgive these failings and help to make it possible to correct them later. When there have been several references of nearly equal value those in books and journals of recent date and likely to be found in hospitals and in smaller libraries have usually been selected. It is hoped that a greater mutual awareness of the contributions made in different parts of the English-speaking world will be encouraged by the frequent selection of both a British and an American study on the same subject. Papers in languages other than English have only been cited when they are of special value or the information is not otherwise available. Authors' names in capital letters along with the title of the paper indicate the more valuable references and reviews and it may be useful to consult these first.

## PREFACE TO FIRST EDITION

It is impossible to acknowledge by name all who inspired and assisted me in this work. I particularly wish to thank Professor J. H. Biggart who inspired this book seven years ago and encouraged and helped me in every way during the collection of material and during the prolonged labour of its actual writing. While I must accept responsibility for the opinions expressed I have been much guided by his suggestions and by his advice. The medical staffs of the maternity hospitals of the Belfast Medical School have taught me much and have been patient with me during many clinico-pathological conferences. Professor F. M. B. Allen and Professor C. H. G. Macafee have been good enough to read and comment on portions of the book in manuscript. The Rockefeller Foundation of New York made it possible for me to spend a year studying foetal and neonatal pathology under Dr. Sidney Farber at the Children's Hospital in Boston. The mental stimulus and the many facilities and kindnesses received there did much to enlarge my knowledge and appreciation of the subject. I am also much indebted to workers in other centres in North America who discussed their work and shared their ideas with me.

The book owes much to a research grant made to me by the Northern Ireland Hospitals Authority. This made it possible to employ secretarial assistance to collate and organize the data on which it is based. A research grant from the Medical Research Council of Great Britain for apparatus for the study of lung structure was responsible for some understanding of lung development and for a further development of the method used for the preparation of the casts of the ultimate air space of the developing lung illustrated in Figs. 18 and 20.

I am much indebted to Mr. D. McA. Mehaffey, A.R.P.S., for the photographs, and to Mr. G. A. Smith, M.M.A.A., artist to the Royal Victoria Hospital Group, for the care and thought he has given to the diagrams and pen drawings. The technical assistance of Messrs. J. Davidson and R. Russell over many years is appreciated. My secretary, Mrs. R. M. Price, has lightened the burden of preparation by the accuracy with which she has typed repeated drafts of the manuscript and by the meticulous care she has taken in the collation of data and in the keeping of records.

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# CONTENTS

<i>Preface to Second Edition</i> .. .. .	xi
<i>Preface to First Edition</i> .. .. .	xiii

## Part I—DISTURBANCES OF PRE-NATAL LIFE

### Chapter

1. ENVIRONMENTAL AND HEREDITARY INFLUENCES .. .. .	3
External environment .. .. .	3
Internal environment .. .. .	4
Heredity .. .. .	9
2. CONGENITAL ABNORMALITIES .. .. .	14
Incidence .. .. .	15
Abnormalities with an established hereditary basis .. .. .	18
Deformities due to physical intra-uterine moulding strains .. .. .	19
The controversy on environment versus heredity .. .. .	19
The contribution of chromosomal abnormality and of gene mutation .. .. .	28
Conclusion.. .. .	29
3. THE FOETAL CIRCULATION, THE PLACENTA AND THE FOETAL MEMBRANES .. .. .	34
The foetal vascular system .. .. .	34
The foetal part of the placenta .. .. .	42
The maternal part of the placenta .. .. .	55
The placenta as a whole—senescent and pathological changes .. .. .	59
Placental efficiency and reserve .. .. .	71
The amnion and the chorion .. .. .	74
Abnormalities of the umbilical cord .. .. .	77
4. FOETAL NUTRITION AND GROWTH .. .. .	83
The sharing of available nutrient between mother and foetus .. .. .	83
Assessment of intra-uterine nutrition .. .. .	87
Validity for man of animal observations .. .. .	90
Some results of maternal nutritional deficiency .. .. .	91
Placental transfer and foetal nutrition .. .. .	95
Conclusion.. .. .	96
5. PREMATUREITY AND POSTMATURITY AND LARGE BABIES .. .. .	99
Assessment of the maturity of the infant .. .. .	99
Handicaps imposed by premature birth .. .. .	106
Immaturity and retrolental fibroplasia .. .. .	111
The incidence of prematurity .. .. .	112
Aetiology .. .. .	112
The fate of the premature infant .. .. .	113
Postmaturity .. .. .	119
Large babies .. .. .	122

## CONTENTS

6. STILLBIRTHS AND FOETAL DEATHS	129
Abortion, stillbirth and foetal death	129
Methods of classification and comparison of results	131
Factors influencing the general incidence of stillbirth	139
The pathological study of stillborn infants	141
7. MULTIPLE BIRTHS	145
Like and unlike twins	145
The placenta and foetal membranes in twins	147
Asymmetry, double monsters and teratomas	150
Incidence of multiple births and influence of environment and heredity	158
Triplets, quadruplets and quintuplets	159
The hazards of plural births	159
8. CONGENITAL TUMOURS	163
Hamartomas, heterotopia and simple tumours	163
Embryomas and teratomas	168
Malignant tumours	169
Congenital leukaemia	171
Transfer of malignant disease from the mother	172
Congenital tumours and carcinogenesis	172
 <b>Part II—ADAPTATION TO EXTRA-UTERINE EXISTENCE</b>	
9. ADAPTATION OF THE NORMAL FOETUS TO EXTRA-UTERINE RESPIRATION	179
Preparations for the initiation of extra-uterine respiration	179
Changes in the circulatory system associated with extra-uterine respiration	189
The initiation of extra-uterine respiration	190
The maintenance of extra-uterine respiration	194
The anatomical basis of imperfect pulmonary respiration	195
Pre-natal or extrinsic anoxia and adaptation to extra-uterine respiration	198
10. LESIONS WITHIN THE INFANT INFLUENCING ADAPTATION TO EXTRA-UTERINE RESPIRATION	211
Lesions involving the air passages and lungs	211
Disturbances involving the heart and blood vessels	219
Disturbances involving the central nervous system	236
11. THE BLOOD CONSTITUENTS AND ADAPTATION TO EXTRA-UTERINE LIFE	250
Disturbances involving the red blood cells and their formative tissue	250
The metabolism of the bile pigments	260
Thrombosis and embolism	264
Bleeding disturbances	269

## CONTENTS

12. ADAPTATION TO EXTRA-UTERINE ALIMENTATION .. .. .	278
Disturbances of the movement of the intestinal contents ..	278
Disturbances of digestion .. .. .	303
Absorption from the intestine .. .. .	316
13. THE ESTABLISHMENT OF POST-NATAL METABOLISM .. .. .	324
Metabolism of specific substances .. .. .	325
Energy metabolism and body temperature .. .. .	342
The role of the endocrine glands .. .. .	344
Toxic agents and post-natal metabolism .. .. .	356
14. POST-NATAL EXCRETION AND ITS CONTRIBUTION TO THE INTERNAL ENVIRONMENT .. .. .	364
Biochemical factors influencing excretion .. .. .	364
Excretory disturbances primarily of renal origin .. .. .	366
The urinary passages and disturbances of excretion .. .. .	374
15. CONDITIONS INTERFERING WITH NORMAL POST-NATAL DEVELOPMENT AND GROWTH .. .. .	380
Lesions anatomically limited to the central nervous system ..	380
Lesions of the nervous system associated with defects of adjacent structures .. .. .	389
Lesions of the skeleton and supporting tissues .. .. .	399
Lesions of the integument .. .. .	410
Lesions of the eye .. .. .	413
Abnormalities of sex differentiation .. .. .	414
Disturbances affecting multiple tissues and organs .. .. .	415
 <b>Part III—INFECTIONS IN FOETAL AND NEONATAL LIFE</b>	
16. DEFENCE MECHANISMS IN THE FOETUS AND NEWBORN INFANT	425
The integrity and protection of exposed surfaces .. .. .	425
Humoral substances and infections .. .. .	427
Cellular reactions in infection .. .. .	434
17. MICROBES OF THE INTRA-UTERINE AND POST-NATAL ENVIRONMENT	440
Microbic environment before the membranes rupture .. .. .	440
Microbic environment after the rupture of the membranes ..	442
Acquisition of the post-natal flora .. .. .	444
18. PATHOLOGY OF ACUTE INFECTIONS ACQUIRED IN UTERO .. .. .	451
Protozoal and bacterial infections with unruptured membranes	451
Virus infections with unruptured membranes .. .. .	455
Infections with membranes ruptured: Syndrome of infection of the amnion .. .. .	457
19. THE PATHOLOGY OF ACUTE INFECTIONS ACQUIRED AFTER BIRTH	469
Predominant involvement of the respiratory system .. .. .	471
Predominant involvement of the alimentary canal .. .. .	479
Predominant involvement of the nervous system .. .. .	487
Wound and skin infections .. .. .	490

## CONTENTS

Infection of the urinary system .. .. .	494
Septicaemia and blood disseminated sepsis .. .. .	494
Disseminated virus infections .. .. .	498
<b>20. CHRONIC AND GENERALIZED SPECIFIC INFECTIONS IN FOETUS AND</b>	
NEONATE .. .. .	505
Syphilis .. .. .	505
Tuberculosis .. .. .	512
Toxoplasmosis .. .. .	513
Torulosis, coccidioidomycosis and histoplasmosis .. .. .	516
<b>INDEX .. .. .</b>	<b>521</b>

## PART I

### DISTURBANCES OF PRE-NATAL LIFE

To understand disease in the human infant at birth and in the days immediately after birth it is necessary to know something of life and development during intra-uterine existence and of the adaptations made in preparation for extra-uterine life. A few facts from this pre-natal period are well established, but they do not yet form a complete picture. Problems relating to the production of form through chemical processes and the interplay of inheritance and environment are of special importance during this period. It is not possible to discuss in any detail such major problems of biology, but it is proposed to consider briefly the environment, both external and internal of the embryo, and its close dependence on the relatively fixed internal environment of the mother. It will then be possible to emphasize some of the hereditary influences most important at this period of life. The study of the aetiology of foetal abnormalities should illustrate further the interplay of hereditary and environmental factors, and also the difficulty of applying the few facts yet known about either to any specific problem. Congenital abnormalities and their combinations and variations are almost limitless. The separate anomalies will be discussed only as they become important by interfering with foetal life or with the full attainment of some extra-uterine function.

Normal development and growth is dependent on the nutrition received through the placenta. Changes in the placenta and in the foetal and maternal circulations which subserve it must be considered and related to the requirements of the foetus. The controversial, and often uncritical, observations on the influence of maternal nutrition on the human foetus will be presented and considered along with experimental studies in animals and with what little is known of the partition of nutrient substances between foetus and mother. The observations available on premature birth, on the birth of abnormally large infants and on the intra-uterine death of the foetus cannot be satisfactorily integrated with the few facts yet known of normal pre-natal life. These practical problems demand some attention from the pathologist, but they must be discussed in some isolation from other aspects of intra-uterine life. It will also be convenient to discuss in some similar isolation plural births and to refer briefly to congenital tumours.





## CHAPTER 1

### ENVIRONMENTAL AND HEREDITARY INFLUENCES

#### EXTERNAL ENVIRONMENT

For a few days before and during implantation the external environment of the human ovum is the fluid in the Fallopian tubes and uterine cavity, and this is provided by glandular secretions, by transudates and by tissue detritus of the endometrium. These materials also provide nutrition, but this histotrophic nutrition is of very little significance for man and other species where there is invasion of the uterine mucosa and especially of maternal blood vessels by the tissues of the foetal trophoblast. Events before and immediately after fertilization are illustrated and described by Shettles (1960). It is only about the twentieth day after fertilization that the heart starts to beat and a foetal circulation is established. Until then the embedded chorionic vesicle with a diameter of 7 mm must depend on diffusion for transfer of metabolites. With the development of a foetal vascular system, a placenta and protective membranes, nutrition is derived directly from the constituents of the mother's blood (haemotrophic nutrition). The free environment of the human embryo is also ended and its external world is its 'private pool' of amniotic fluid.

The aquatic environment provided by the amniotic fluid is most important for the higher mammalian embryo. Only a fluid environment could adequately support during development its soft and delicate external form and its large and poorly supported nervous system. Especially during the early and critical months of development it prevents easily damaged foetal tissues pressing against one another, against the wall of the uterus, or, indirectly, against other maternal structures. Certain deformities, such as many examples of club feet, probably result from pressure on foetal tissues (page 19). They show how easily foetal tissues may be moulded by pressure, and the ease with which these deformities may be corrected immediately after birth suggests that they probably often arise in the last weeks of foetal life as the proportion of fluid to foetus declines greatly. Muscle movements and probably other mechanisms, which facilitate the return of venous blood in post-natal life, are very intermittent or absent in the foetus in utero. Local increases in foetal venous pressure, resulting from the influence of gravity, might be sufficient to cause embarrassment to the circulation in parts of the foetus which were for long periods in a dependent position. The amniotic fluid has almost the same specific gravity as the blood. It exerts an external pressure on the foetal body, which is opposite to and capable of neutralizing the action of gravity on the blood lying in the venous channels. Extensive oedema of dependent parts of the foetus is thus avoided. The amniotic fluid and the various maternal tissues surrounding the foetus also effectively prevent changes of body temperature, and the foetus benefits from the stability of the highly developed temperature-regulating centre of its mother.