INTEGRATED OBSTETRICS AND GYNAECOLOGY FOR POSTGRADUATES

EDITED BY

SIR JOHN DEWHURST

THIRD EDITION

INTEGRATED OBSTETRICS AND GYNAECOLOGY FOR POSTGRADUATES

EDITED BY

SIR JOHN DEWHURST

MB, ChB, FRCS(Ed.), FRCOG

Professor of Obstetrics and Gynaecology
Institute of Obstetrics and Gynaecology at
Queen Charlotte's Hospital
for Women
University of London

THIRD EDITION

BLACKWELL SCIENTIFIC PUBLICATIONS
OXFORD LONDON EDINBURGH
BOSTON MELBOURNE

Editorial offices:
Osney Mead, Oxford, OX2 0EL
8 John Street, London, WC1N 2ES
9 Forrest Road, Edinburgh, EH1 2QH
52 Beacon Street, Boston, Massachusetts 02108, USA
99 Barry Street, Carlton, Victoria 3053, Australia

First published 1972
Second edition 1976
Third edition 1981

Spanish edition 1978

Printed and bound in
Great Britain by
William Clowes (Beccles) Limited
Beccles and London

DISTRIBUTORS

USA
Blackwell Mosby Book Distributors
11830 Westline Industrial Drive
St Louis, Missouri 63141

Canada
Blackwell Mosby Book Distributors
120 Melford Drive, Scarborough
Ontario, M1B 2X4

Australia
Blackwell Scientific Book Distributors
214 Berkeley Street, Carlton
Victoria 3053

British Library
Cataloguing in Publication Data

Integrated obstetrics and gynaecology for
postgraduates
1. Gynecology 2. Obstetrics
I. Dewhurst, *Sir* John
618 RG101

ISBN 0 632 00684 6

LIST OF CONTRIBUTORS

J.M.BEAZLEY MD, FRCOG
Professor of Obstetrics and Gynaecology, University of Liverpool.
Natural labour and its active management
Special circumstances affecting labour
Dystocia caused by the passages or passenger
Maternal injuries and complications

J.M.BRUDENELL MB, BS, FRCS, FRCOG
Consultant Obstetrician and Gynaecologist, King's College Hospital, London & Queen Victoria Hospital, East Grinstead
Diabetes, thyroid diseases and adrenal diseases complicating pregnancy
General surgical procedures, urinary tract injuries

G.V.P.CHAMBERLAIN MD, BS, FRCS, FRCOG
Consultant Obstetrician and Gynaecologist, Queen Charlotte's Hospital for Women, London
The fetus
Vital statistics in obstetrics
Resuscitation of the newborn

D.A.DAVEY PhD, MB, BS, MRCS, FRCOG
Professor of Obstetrics and Gynaecology, University of Cape Town, South Africa
Normal pregnancy: physiology and management
Dysfunctional uterine bleeding
The menopause and climacteric

SIR JOHN DEWHURST MB, ChB, FRCS(Ed.), FRCOG
Professor of Obstetrics and Gynaecology, Institute of Obstetrics and Gynaecology, Queen Charlotte's Hospital for Women, University of London
Normal and abnormal development of the genital organs
Gynaecological disorders in childhood and adolescence
The normal puerperium
Pre-eclampsia, eclampsia, hypertension and chronic renal disease
Miscellaneous disorders complicating pregnancy
Abnormalities of the puerperium
Obstetric operations and procedures
Infertility
Benign and premalignant lesions of the vulva, vagina and cervix
Cytogenetics for gynaecologists

R.M.FEROZE MD, BS, FRCS, FRCOG
Consultant Obstetrician and Gynaecologist, King's College Hospital, London
Tumours of the female genital tract
Tumours of the vulva and vagina
Benign tumours of the uterus
Malignant disease of the cervix
Malignant disease of the uterine body
Tumours of the ovary

E.D.MORRIS MD, BCh, FRCS, FRCOG
Consultant Obstetrician and Gynaecologist, Guy's Hospital, London & Queen Charlotte's Hospital for Women, London
Fertilization, implantation, placental function, early development
Malpositions of the occiput, malpresentations, multiple pregnancy, hydramnios, oligohydramnios and postmaturity
Contraception and sterilization

J.S.SCOTT MD, ChB, FRCS, FRCOG
Professor of Obstetrics and Gynaecology, University of Leeds
Abortion, ectopic pregnancy and trophoblastic growths
Antepartum haemorrhage
Prolapse and stress incontinence of urine

R.P.SHEARMAN MD, DGO, FRCOG
Professor of Obstetrics and Gynaecology, University of Sydney, Australia & Head, Division of Obstetrics and Gynaecology, Royal Prince Alfred Hospital, Sydney
Control of ovarian function
The intersexes
Primary amenorrhoea
The diagnosis and management of secondary amenorrhoea
Hirsutism and virilism
Endocrine changes during pregnancy

C.R.WHITFIELD MD, FRCOG, MRCP
Regius Professor of Midwifery, University of Glasgow & Honorary Consultant to the Queen Mother's Hospital and Western Infirmary, Glasgow
Heart disease in pregnancy
Blood disorders in pregnancy
Urinary tract disorders in pregnancy
Complications of the third stage of labour
Pelvic infection
Endometriosis

PREFACE TO THIRD EDITION

It is my privilege yet again to be writing a preface for a new edition of this book. Events in obstetrics and gynaecology have been changing rapidly since the last edition was published, necessitating a full revision. My colleagues and I have subjected the previous text to the closest scrutiny and a great deal of rewriting has been required. In doing this we have been conscious of the need to prune out old material so that the book would, if anything, be shorter not longer than formerly. We also had in mind the pressure which many postgraduate trainees are now under and we have attempted to simplify and explain recent advances and put them clearly into perspective and so assist in their easy assimilation. Furthermore, we have been aware of expense and have tried to keep the cost of the book within reasonable bounds by deleting unnecessary textual matter, reducing the size of some of the illustrations and eliminating others altogether. We hope that what we have to offer will be as popular as the first two editions have been.

The preparation of this volume has been accompanied by one great sadness, the death of Dr John Robertson, a contributor to the first and second editions. We mourn the untimely loss of such an able clinician and scientist as all who knew him or his work must. We have tried, however, to let some of his work live on by retaining those parts of his text which are still relevant to modern obstetrics and gynaecology so that he will, in one small sense, remain a contributor. The task of revision of the sections formerly written by Dr Robertson has been readily and ably undertaken by his good friend, Professor C.R.Whitfield, who I am delighted to welcome. Professor Whitfield has paid his tribute to his former colleague by this admirable and thoughtful revision of his work for which I am most grateful. May I also thank my contributors for undertaking the task of preparing this edition within a comparatively short period of time and for providing their scripts in time—or very nearly. My secretary, Mrs Hawkins, as always has tied up a lot of loose ends, dotted innumerable i's and crossed an infinite number of t's. May I record my gratitude to her also. Finally, may I thank my publishers for their willingness to help at all times, and may you, the reader, enjoy this book.

Sir John Dewhurst

PREFACE TO FIRST EDITION

Our purpose in writing this book has been to produce a comprehensive account of what the specialist in training in obstetrics and gynaecology must know. Unfortunately for him, he must now know a great deal, not only about his own subject, but about certain aspects of closely allied specialities such as endocrinology, biochemistry, cytogenetics, psychiatry, etc. Accordingly we have tried to offer the postgraduate student not only an advanced textbook in obstetrics and gynaecology but one which integrates the relevant aspects of other subjects which nowadays impinge more and more on the clinical field.

To achieve this aim within, we hope, a reasonable compass we have assumed some basic knowledge which the reader will have assimilated throughout his medical training, and we have taken matters on from there. Fundamental facts not in question are stated as briefly as is compatible with accuracy and clarity, and discussion is then devoted to more advanced aspects. We acknowledge that it is not possible even in this way to provide all the detail some readers may wish, so an appropriate bibliography is provided with each chapter. Wherever possible we have tried to give a positive opinion and our reasons for holding it, but to discuss nonetheless other important views; this we believe to be more helpful than a complete account of all possible opinions which may be held. We have chosen moreover to lay emphasis on fundamental aspects of the natural and the disease processes which are discussed; we believe concentration on these basic physiological and pathological features to be important to the proper training of a specialist. Clinical matters are, of course, dealt with in detail too, whenever theoretical discussion of them is rewarding. There are, however, some clinical aspects which cannot, at specialist level, be considered in theory with real benefit; examples of these are *how* to palpate a pregnant woman's abdomen and *how* to apply obstetric forceps. In general these matters are considered very briefly or perhaps not at all; this is not a book on *how* things are done, but on how correct treatment is chosen, what advantages one choice has over another, what complications are to be expected, etc. Practical matters, we believe, are better learnt in practice and with occasional reference to specialized textbooks devoted solely to them.

A word may be helpful about the manner in which the book is set out. We would willingly have followed the advice given to Alice when about to testify at the trial of the Knave of Hearts in Wonderland, 'Begin at the beginning, keep on until you come to the end and then stop'. But this advice is difficult to follow when attempting to find the beginning of complex subjects such as those to which this book is devoted. Does the beginning lie with fertilization; or with the events which lead up to it; or with the genital organs upon the correct function of which any pregnancy must depend; or does it lie somewhere else? And which direction must we follow then? The disorders of reproduction do not lie in a separate compartment from genital tract diseases, but each is clearly associated with the other for at least part of a woman's life. Although we have attempted to integrate obstetrics with gynaecology and with their associated specialities, some separation is essential in writing about them, and the plan we have followed is broadly this—we begin with the female child *in utero*, follow her through childhood to puberty, through adolescence to maturity, through pregnancy to motherhood, through her reproductive years to the climacteric and into old age. Some events have had to be taken out of order, however, although reiteration has been avoided by indicating to the reader where in the book are to be found other sections dealing with different aspects of any subject under consideration.

We hope that our efforts will provide a coherent, integrated account of the field we have attempted to cover which will be to the satisfaction of our readers.

ACKNOWLEDGEMENTS

In the presentation of this book, we have received assistance from numerous sources, and we wish to record our gratitude to all who have helped. We would specially like to indicate our indebtedness to those authors, publishers and editors listed below who have allowed us to reproduce material previously published elsewhere. To: Mr David Currie, Mr T. M. Coltart, Dr W. J. Garrett, Professor Sir Norman Jeffcoate, Dr Henry Roberts, Dr George Craig, Dr P. P. Franklyn, Professor W. J. Hamilton, Professor Llewellyn-Jones, Dr M. N. Grumbach, Dr J. B. Brown, Dr M. G. Coyle, Professor F. E. Hytten, Dr I. Leitch, Dr J. P. Gusdon Jr, Dr P. M. Elliott, Dr C. G. Paine, the late Dr S. Leon Israel, Dr E. C. Gillespie, Dr H. Steven, Professor R. W. Beard, Dr J. D. N. Nabarro, Dr N. W. Oakley, Dr R. C. Turner, Sir George Godber, Professor Harvey Carey, the late Professor J. P. Greenhill, Dr C. A. Salvatore, Dr J. A. Loraine, Dr E. T. Bell, Dr H. F. Traut, Dr A. Kuder, Dr A. L. Southam, Dr R. M. Richert, Dr A. M. Sutherland, Dr N. Vorys, Dr A. S. Neri, Dr Goerttler, Dr D. N. Danforth, Mr E. E. Philipp, Dr I. H. Thorneycroft, Dr D. R. Mishell Jr, Dr S. C. Stone, Dr K. M. Kharma, Dr R. M. Nakamura, Dr V. C. Stevens, Dr G. C. Liggins, Dr R. J. Fairclough, Dr S. A. Grieves, Dr J. Z. Kendall, Dr B. S. Knox, Dr D. Thompson, Dr W. G. Paterson, Dr G. E. Smart, Dr M. K. Macdonald, Dr J. S. Robson, Dr O. Ylikorkala, Dr T. H. Parmley, Mr G. D. Pinker, Dr M. Coppleston, Dr E. Pixley, Dr B. Reid, Dr L. Nilsson, Mr R. J. Beard, Dr B. H. Shearman, Dr H. Reyes, Dr Anne Anderson, Dr E. M. Alhava, Dr S. Meema, Dr R. Lindsay, Dr M. E. C. Paterson, Dr D. R. Meldrum, Dr I. V. Tataryn, Dr W. H. Utian, Dr S. Campbell, Dr M. I. Whitehead, Dr S. Chakravarti, Dr E. C. Jones and Dr G. Rybo, to Messrs: C. C. Thomas & Co, Baillière, Tindall and Cassell, Butterworth Medical Publications, Faber and Faber, Blackwell Scientific Publications, E. & S. Livingstone, The Surgical Publishing Co of Chicago, C. V. Mosby & Co, Gillmore and Lawrence, Harper & Rowe, Butterworth & Co., W. B. Saunders & Co., John Sherratt & Son, Controller of Her Majesty's Stationery Office, W. Heffer & Sons, Frontiers of Hormone Research, Williams and Wilkins Company, The Endocrine Society, Appleton, Century and Croft, M. T. P. Press Limited and W. Heinemann Medical Books; and to the Editors of: *Australia and New Zealand Journal of Obstetrics and Gynaecology, Hoeber Medical Journals, The Lancet, British Medical Journal, Journal of Obstetrics and Gynaecology of the British Commonwealth, Proceedings of the New York Academy of Sciences, Journal of Pathology and Bacteriology, Bulletin of The Johns Hopkins Hospital, American Journal of Obstetrics and Gynaecology, Journal of the International College of Surgeons, Proceedings of the Royal Medico-Chirurgical Society of Glasgow, Recent Progress in Hormone Research, Acta Obst. & Gyn. Scandinavica, British Journal of Hospital Medicine, Medical Journal of Obstetrics and Gynaecology, Annals of Clinical Research, the Irish Journal of Medical Sciences, The British Journal of Obstetrics and Gynaecology, Maturitas.*

We would like to offer our most grateful thanks also to: Mr Stuart Campbell, Dr Magnus Haines, Dr H. P. Ferreira, Dr J. Smitham, Dr Peter Renou, Dr P. N. Cowan, Dr J. Pryse-Davies, Mr A. Gillespie, Professor J. M. Beazley, Dr Mary Lucas, Miss Baker, Miss Lumby, Mrs Apsey, Miss Platt, Miss Collins, Miss Miller, Mrs G. Going, Mrs P. Hawkins, Miss A. Breeze and Miss Brodie, all of whom have given direct and most valuable assistance with the preparation of this book by supplying many of its illustrations or typing the manuscript.

It has been a great pleasure for us all to co-operate in this venture with Blackwell Scientific Publications to whom we are grateful for their help, understanding and forebearance.

CONTENTS

List of Contributors

Preface to Third Edition

Preface to First Edition

Acknowledgements *x*

1 Normal and Abnormal Development of the Genital Organs *1*

2 Gynaecological Disorders in Childhood and Adolescence *14*

3 Control of Ovarian Function *29*

4 The Intersexes *37*

5 Primary Amenorrhoea *49*

6 The Diagnosis and Management of Secondary Amenorrhoea *56*

7 Hirsutism and Virilism *67*

8 Fertilization, Implantation, Placental Function, Early Development *79*

9 Normal Pregnancy: physiology and management *103*

10 Endocrine Changes during Pregnancy *135*

11 The Fetus *146*

12 Natural Labour and its Active Management *180*

13 The Normal Puerperium *197*

14 Abortion, Ectopic Pregnancy and Trophoblastic Growths *203*

15 Antepartum Haemorrhage *248*

16 Pre-eclampsia, Eclampsia, Hypertension and Chronic Renal Disease *259*

17 Heart Disease in Pregnancy *279*

18 Blood Disorders in Pregnancy *291*

19 Urinary Tract Disorders in Pregnancy *319*

20 Diabetes, Thyroid Diseases and Adrenal Diseases Complicating Pregnancy *329*

21 Miscellaneous Disorders Complicating Pregnancy *354*

22 Malpositions of the Occiput, Malpresentations, Multiple Pregnancy, Hydramnios, Oligohydramnios and Postmaturity *373*

23 Special Circumstances Affecting Labour *409*

24 Dystocia Caused by the Passages or Passenger *423*

25 Complications of the Third Stage of Labour *437*

26 Abnormalities of the Puerperium *443*

27 Maternal Injuries and Complications *455*

28 Obstetric Operations and Procedures *468*

29 Vital Statistics in Obstetrics *488*

30 Contraception and Sterilization *504*

31 Pelvic Infection *526*

32 Endometriosis *536*

33 Infertility *550*

34 Dysfunctional Uterine Bleeding *565*

35 The Menopause and Climacteric *592*

36 Prolapse and Stress Incontinence of Urine *631*

37 Benign and Premalignant Lesions of the Vulva, Vagina and Cervix *654*

38 Tumours of the Female Genital Tract *670*

39 Tumours of the Vulva and Vagina *674*

40 Benign Tumours of the Uterus *696*

41 Malignant Disease of the Cervix *704*

42 Malignant Disease of the Uterine Body *731*

43 Tumours of the Ovary *745*

44 General Surgical Procedures, Urinary Tract Injuries *765*

45 Cytogenetics for Gynaecologists *778*

Index *788*

CHAPTER 1
NORMAL AND ABNORMAL DEVELOPMENT OF THE GENITAL ORGANS

This account of the development of the genital organs will begin, as in previous editions, with a consideration of why these organs develop as they do in the two sexes. There has been an important new development in our understanding of this process, although much remains uncertain. Wachtel (1979) has reviewed the matter admirably and in detail.

Sexual development depends initially on the arrangement of the sex chromosomes. Normal men have an XY sex chromosome arrangement and normal women an XX one (Fig. 1.1). Sometimes, however, individuals are born with additional sex chromosomes and are XXY, XYY, XXYY, XXX, XXXX, etc., and others with a single X only; still others have different arrangements which need not concern us here but which are dealt with in greater detail on page 778. Normally if a Y chromosome is present with one or more X chromosomes, testes will form in the early embryo and if two or more X chromosomes are present without a Y, ovaries form. If a single X chromosome is present alone, normal definitive gonadal tissue does not form and the gonads are represented by whitish streaks of tissue. It is likely that the effect of the Y chromosome in promoting testicular differentiation is by H–Y antigen which is thought to be the gene product of the male determining genes (see page 38 for further consideration).

The relationship between the gonad and the development of the other genital organs is, in summary, this. If testes form in the early embryo, that individual will develop male genital organs. If testes do not form, the individual will develop female genital organs whether ovaries are present or not. It may be concluded that the arrangement of the sex chromosomes normally determines the nature of the gonad, which in turn determines the differentiation of the other genital organs.

We will now turn our attention to how the genital organs develop.

THE DEVELOPMENT OF THE GENITAL ORGANS

Most embryological accounts agree on the principles of genital tract development as a whole, although different views are held on the development of the gonad and vagina.

The genital organs and those of the urinary tract arise in the intermediate mesoderm on either side

(a)

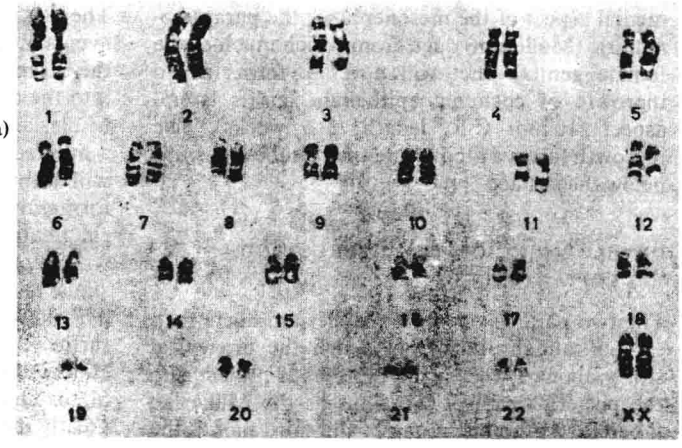
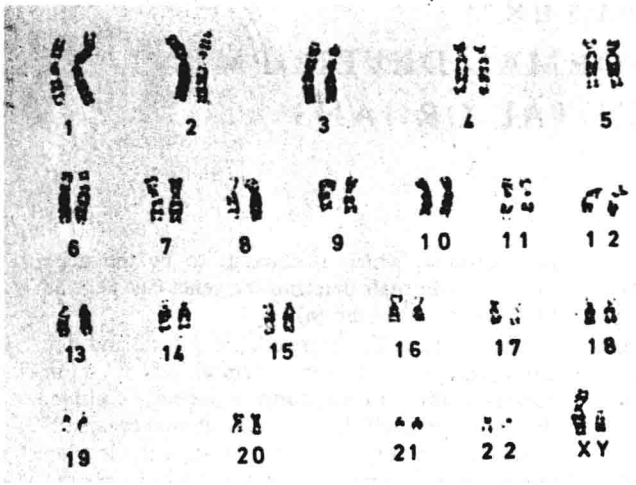


Fig. 1.1(a). Normal female karyotype showing individual G-banding pattern for each pair of chromosomes.



(b)

Fig. 1.1(b). Normal male karyotype showing individual G-banding pattern for each pair of chromosomes.

of the root of the mesentery, beneath the epithelium of the coelom. The pronephros, a few transient excretory tubules in the cervical region, appears first but quickly degenerates. The duct which begins in association with the pronephros persists and extends caudally to open at the cloaca, connecting as it does so with some of the tubules of the mesonephros shortly to appear. The duct is called the mesonephric (Wolffian) duct. The mesonephros itself, the second primitive kidney, develops as a swelling bulging into the dorsal wall of the coelom of the thoracic and upper lumbar regions. The mesonephros in the male persists in part as the excretory portion of the male genital system; in the female a few vestiges only survive (Fig. 1.2). The genital ridge in which the gonad of each sex is to develop is visible as a swelling on the medial aspect of the mesonephros; the paramesonephric (Müllerian) duct, from which much of the female genital tract will develop, forms as an ingrowth of coelomic epithelium on its lateral aspect (10 mm C.R. length; 5–6 weeks). The ingrowth forms a groove and then a tube and sinks below the surface.

DEVELOPMENT OF THE UTERUS AND FALLOPIAN TUBES

The two paramesonephric (Müllerian) ducts then extend caudally until they reach the urogenital sinus, about 9 weeks; the blind ends project into the posterior wall of the sinus as the Müllerian tubercle. At the beginning of the third month the Müllerian and Wolffian ducts and mesonephric tubules are all present and capable of development [Fig. 1.2(a)]. From this point onwards in the female there is degeneration of the Wolffian system and marked growth of the Müllerian system [Fig. 1.2(b)]. In the male the opposite occurs [Fig. 1.2(c)]. The lower ends of the Müllerian ducts come together in the mid-line and fuse and develop into the uterus and cervix; the cephalic ends of the duct remain separate to form the Fallopian tubes. The thick muscular walls of the uterus and cervix develop from proliferation of mesenchyme around the fused portions of the ducts.

DEVELOPMENT OF THE VAGINA

There is difference of opinion about the precise events in vaginal development. At the point where the paramesonephric ducts protrude their solid tips into the dorsal wall of the urogenital sinus as the Müllerian tubercle (30 mm stage; 9 weeks) there is a marked growth of tissue from which the vagina will ultimately form. Koff (1933) describes the formation of paired sinovaginal bulbs as posterior evaginations of the urogenital sinus; there is also stratification of the cells lining that part of the sinus, and this obliterates the Müllerian tubercle. The sinovaginal bulbs, which become solidified by further epithelial proliferation, fuse with the lower end of the Müllerian ducts to form the vaginal plate. This plate quickly grows in all dimensions, greatly increasing the distance between the cervix

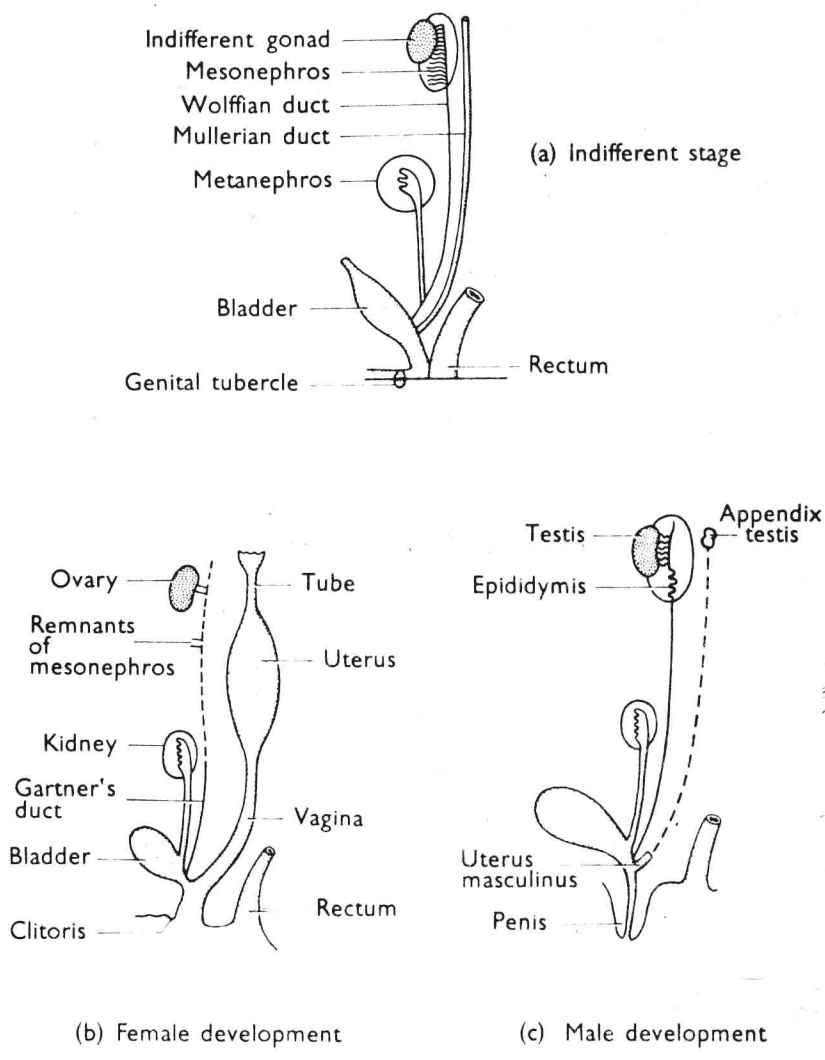


Fig. 1.2. Diagrammatic representation of genital tract development. (a) Indifferent stage. (b) Female development. (c) Male development. (By courtesy of Baillière, Tindall and Cassell.)

and the urogenital sinus. Later, the central cells of this plate break down to form the vaginal lumen.

According to Koff, approximately the upper four-fifths of the vagina is formed by the Müllerian ducts and the lower fifth from the urogenital sinus by the growth of the sinovaginal bulbs. He regards the hymen as being totally derived from the sinus epithelium. Vilas (1932) and Bulmer (1957) and others hold a different view. They believe that the sinus upgrowth extends up to the cervix, displacing the Müllerian component completely, the vagina being thus derived wholly from the endoderm of the urogenital sinus. It seems certain that some of the vagina is formed from the urogenital sinus, but it is not certain whether the Müllerian component is involved or not. See also Chapter 39 page 690.

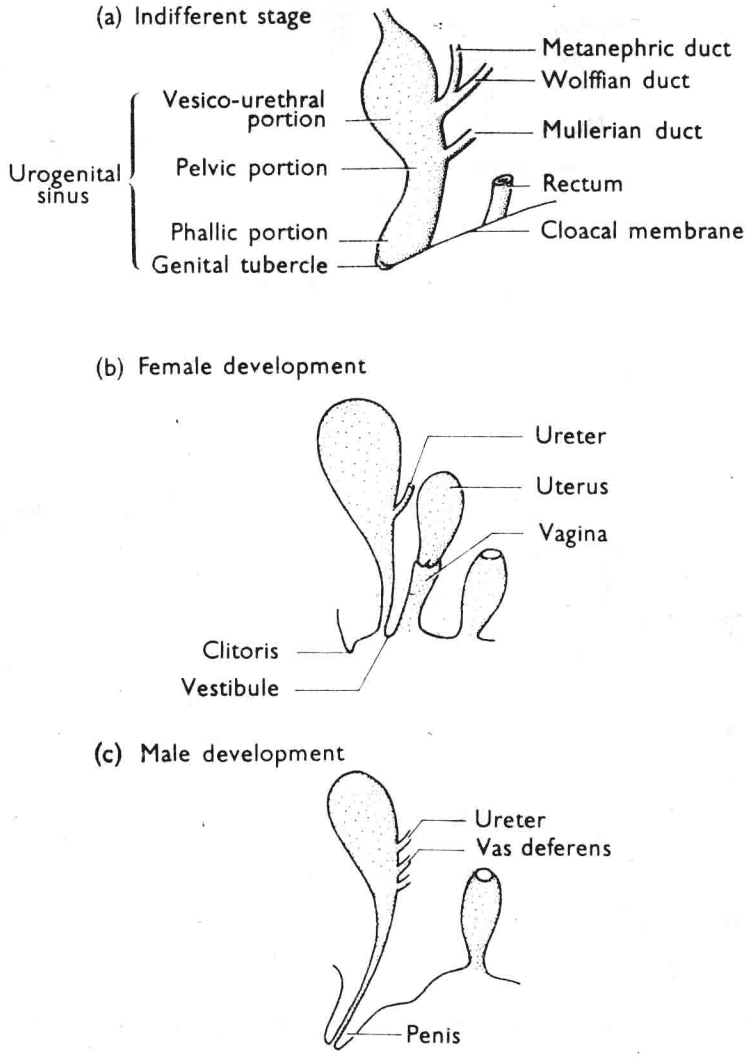


Fig. 1.3. Diagrammatic representation of lower genital tract development. (a) Indifferent stage. (b) Female development. (c) Male development. (By courtesy of Baillière, Tindall and Cassell.)

THE DEVELOPMENT OF THE EXTERNAL GENITALIA

The primitive cloaca becomes divided by a transverse septum into an anterior urogenital portion and a posterior rectal portion. The urogenital portion of the cloacal membrane breaks down shortly after division is complete (15 mm C.R. length). The urogenital sinus develops further into three portions (Fig. 1.3). There is an external, expanded, phallic part, a deeper, narrow, pelvic part between it and the region of the Müllerian tubercle, and a vesico-urethral part connected superiorly to the allantois. Externally in this region the genital tubercle forms a conical projection around the anterior part of the cloacal membrane.

Two pairs of swellings, a medial pair (the genital folds) and a lateral pair (genital swellings) are then formed by proliferation of mesoderm round the end of the urogenital sinus. Development up to this time (50 mm C.R. length; 10 weeks) is the same in the male and the female. Differentiation then occurs. The bladder and urethra form from the vesico-urethral portion of the urogenital sinus and the vestibule from the pelvic and phallic portions (Fig. 1.3). The genital tubercle enlarges only slightly and becomes the clitoris. The genital folds become the labia minora and the genital swellings enlarge to become the labia majora. In the male greater enlargement of the genital tubercle forms the penis. The genital folds fuse over a deep groove formed between them to become the penile part of the male urethra. The genital swellings enlarge, fuse and form the scrotum.

The final stage of the development of the clitoris or penis and the formation of the anterior surface of the bladder and the anterior abdominal wall up to the umbilicus is the result of growth of mesoderm extending ventrally round the body wall on each side to unite in the mid-line anteriorly.

DEVELOPMENT OF THE GONADS

The primitive gonad is first evident in embryos of 5.5–7.5 mm C.R. length (5 weeks). According to Gillman (1948) the gonad is of triple origin from the coelomic epithelium of the genital ridge, the underlying mesoderm and the primitive germ cells which come from an extragenital source (see below).

The gonad forms as a bulge on the medial aspect of the mesonephric ridge. Its histological appearances are alike in the early stages, whether it is to be testis or ovary. There is a proliferation of cells in and beneath the coelomic epithelium of the genital ridge. By 5 or 6 weeks these cells are seen spreading as ill-defined cords (sex cords) into the ridge, breaking up the mesenchyme into loose strands. Primitive germ cells are distinguishable as much larger structures, lying at first between the cords and then within them.

The differentiation of the testes is evident about 7 weeks by the disappearance of germ cells from the peripheral zone and gradual differentiation of remaining cells into fibroblasts and later into the tunica albuginea. The deeper parts of the sex cords give rise to the rete testis, the seminiferous and straight tubules. The first indication that the gonad will become an ovary is failure of these testicular changes to appear. The primitive ovary passes first into the stage of differentiation and growth, and later into that of follicle formation. The sex cords below the coelomic epithelium develop extensively, with many primitive germ cells evident in this active cellular zone (Fig. 1.4). The epithelial cells

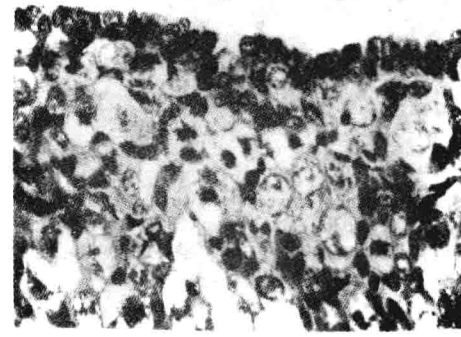


Fig. 1.4. Detail of immature ovary showing small epithelial cells (pregranulosa cells) and larger germ cells. (By courtesy of Dr J. Pryse-Davies.)

in this area are known as pregranulosa cells. The active growth phase then follows, involving the pregranulosa cells and the germ cells, which are now much reduced in size (14–16 weeks). This proliferation greatly enlarges the bulk of the gonad. The next stage (20 weeks onwards) shows the primitive germ cells (now known as oocytes) becoming surrounded by a ring of pregranulosa cells; stromal cells, developed from the ovarian mesenchyme, later surround the pregranulosa cells, now known as granulosa cells, and follicle formation is complete (Fig. 1.5). An interesting feature of the formation of follicles and the development of stroma is the disintegration of those oocytes which do not succeed in encircling themselves with a capsule of pregranulosa cells.

The interpretation of changes of this kind in early embryos is highly specialized, and other workers, although observing similar appearances, have interpreted them differently. Willis (1962) summarizes these different views.

It is now generally accepted that the germ cells arise in the endoderm before the formation of the mesoderm of the lateral plate and somite formation (Pinkerton *et al.* 1961). Pinkerton and his colleagues

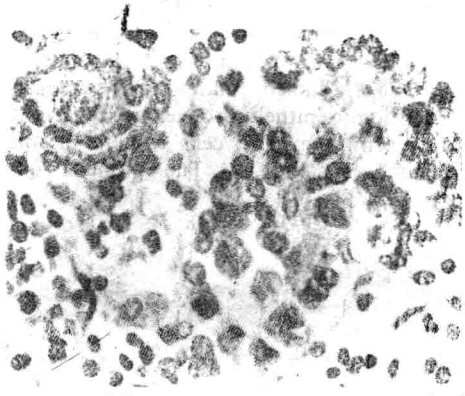


Fig. 1.5. A later ovary (31 weeks) showing a well-formed primary follicle (top left) and a germ cell (centre right) which is not yet completely surrounded by granulosa cells.

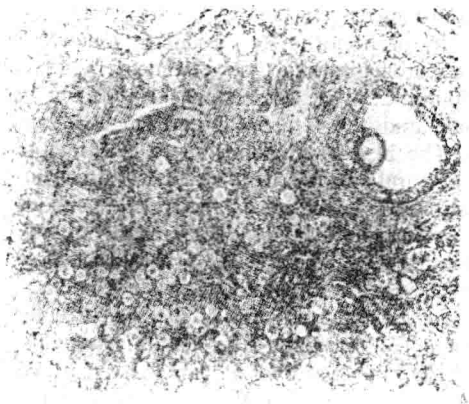


Fig. 1.6. Numerous primary follicles and one showing early development in the ovary of a child stillborn at 38 weeks

described germ cells as migrating along the endoderm of the yolk sac, into the gut, through the mesenchyme at the root of the mesentery and into the primitive gonad. Rapid proliferation of germ cells follows, until they become surrounded by granulosa cells as described above and become oocytes. Mitotic division, by which the germ cells have been increasing in numbers, then ceases and they enter the first stage of meiosis.

The number of oocytes is greatest sometime during pregnancy, and thereafter declines. Baker (1963) found that the total population of germ cells rose from some 600 000 at 2 months to a peak of almost 7 000 000 at 5 months. At birth the number had fallen to 2 000 000, of which half were atretic. After 28 weeks or so of intra-uterine life an increasing degree of follicle development is evident in the ovary. Follicles at various stages of development, and of various sizes, are seen (Pryse-Davies & Dewhurst 1971, de Sa 1975) (Figs. 1.6, 1.7). Simpson (1976) gives an excellent account of these events.

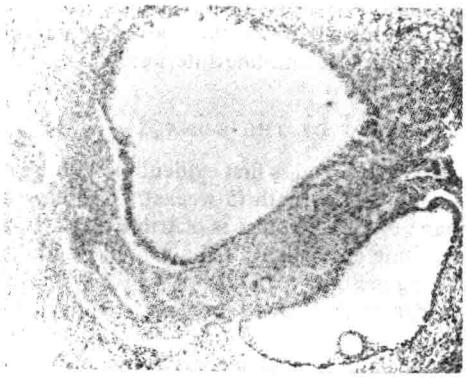


Fig. 1.7. Ovary from a child stillborn at 41 weeks showing a mature Graafian follicle, and a cystic follicle. (By courtesy of the Editor of *Journal of Pathology and Bacteriology*.)

GENITAL TRACT MALFORMATIONS

Numerous malformations of the genital tract have been described, some of little clinical significance, others of considerable importance.

Uterine anomalies

ABSENCE OF THE UTERUS

The uterus may be absent or of such rudimentary development as to be incapable of function of any kind. This type of anomaly is usually found when the vagina is absent also, the case presenting is one of primary amenorrhoea (see Chapter 5). Absence of the uterus may be associated with the development of the lower part of the vagina, which then

ends blindly. This combination of features should suggest a diagnosis of androgen insensitivity (testicular feminization) (see Chapter 4); however, similar development of the lower vagina only, and absence of the uterus, may occasionally be found in XX patients with ovaries. No treatment is of course possible for the uterine abnormality as such; it must be stressed however, that if the diagnosis is testicular feminization, testicular removal may be indicated on account of the increased risk of malignant change in the testes. Whether the patient is XY or XX, however, attention to psychological aspects of the case may be almost the most important facet of management.

FUSION ANOMALIES

Fusion anomalies of various kinds are not uncommon (Fig. 1.8) and may present clinically either in association with pregnancy or in other ways. The lesser degrees of fusion defects are quite common, the cornual parts of the uterus remaining separate, giving the organ a heart-shaped appearance. It is doubtful if such a minor degree of fusion defect *per se* gives rise to clinical symptoms or signs. The presence of a septum extending over some or all of the uterine cavity, however, is likely to give rise to clinical features. Such a septate or subseptate uterus may be of normal external appearance or of arcuate outline. Clinically, this state of affairs may come to light as a case of repeated unsuccessful pregnancy (see Chapter 4); a second likely method of presentation is as repeated transverse lie of the fetus in late pregnancy, since it tends to lie with the head in one cornu and the breech in the other (see Chapter 22).

In more extreme forms of failure of fusion the clinical features may be less, rather than more, marked. Two almost separate uterine bodies with one cervix are probably less likely to be associated

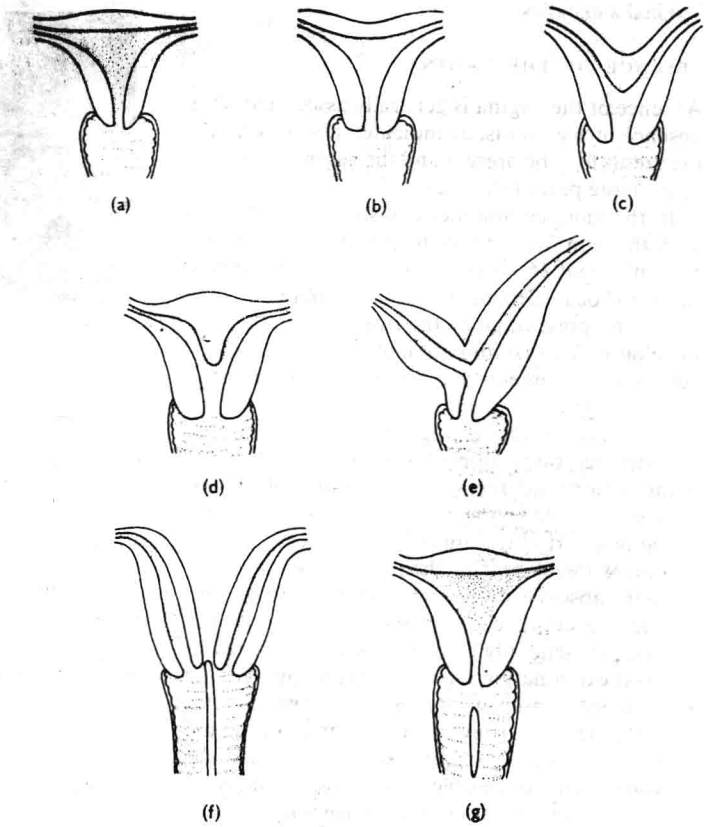


Fig. 1.8. Various fusion abnormalities of the uterus and vagina. (a) Normal appearance. (b) Arcuate fundus with little effect on the shape of the cavity. (c) Bicornuate uterus. (d) Subseptate uterus with normal outline. (e) Rudimentary horn. (f) Uterus didelphys. (g) Normal uterus with partial vaginal septum.

with repeated abnormal lies than the lesser degrees of fusion defect mentioned above. Complete duplication of the uterus and cervix (uterus didelphys) if associated with any clinical fault at all might present as obstruction to descent of the head in late pregnancy or labour by the non-pregnant horn.

Rudimentary development of one horn may give rise to a very serious situation if a pregnancy is implanted there. Rupture of the horn with profound bleeding may occur as the pregnancy increases in size. The clinical picture will, in some ways, resemble that of a ruptured ectopic pregnancy, with the difference that the amenorrhoea would probably be measured in months rather than weeks; shock may be profound. A poorly developed or rudimentary horn may give rise to dysmenorrhoea and pelvic pain if there is any obstruction to communication between the horn and the main uterine cavity or the vagina. Surgical removal would then be indicated.

Vaginal anomalies

ABSENCE OF THE VAGINA

Absence of the vagina is generally associated with absence of the uterus, as indicated above. Rarely, the uterus may be present and the vagina, or at any rate a large part of it, absent.

In the more common circumstances of absence of both vagina and uterus the patient will probably present about 16 years or so of age with primary amenorrhoea. Secondary sexual characteristics should be present, since the ovaries are normally developed. This combination of normal secondary sexual development and primary amenorrhoea should suggest an anatomical cause, such as an imperforate or absent vagina, for the failure to menstruate. Inspection of the vulva, abdominal examination and rectal examination will be required to exclude the presence of any retained blood in a part of the upper genital tract.

Vulval development should be normal apart from the absence of the vaginal introitus (Fig. 1.9).

The presumptive diagnosis of absence of the vagina can generally be made without difficulty at the first examination. A very short vagina arising in androgen insensitivity may be mistaken for simple absence, so in every case of apparent vaginal absence a buccal smear, at least, should be performed and, if possible, a chromosome analysis. If the buccal smear is chromatin negative and the chromosome analysis confirms XY sex chromosomes, the case takes on an entirely different aspect (see Chapter 4).

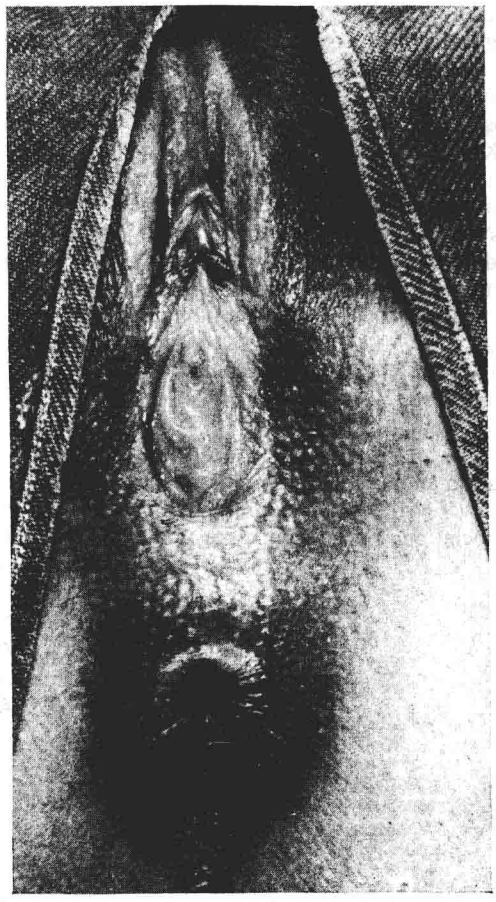


Fig. 1.9. Vulval appearances in a case of absence of the vagina.

An intravenous pyelogram is desirable in view of the frequent association of the renal tract anomalies which may have a bearing on treatment (Fig. 1.10). If there is any suggestion that there is a functioning uterus present, laparoscopy is indicated to confirm or refute this; indeed, laparoscopy may be employed in any apparent case of vaginal absence to avoid the possibility of error; the intravenous pyelogram should first be performed since there would be a real risk of injury of a pelvic kidney with the laparoscope if the organ were in this position.