

OBSTETRICAL AND GYNAECOLOGICAL PATHOLOGY

For Postgraduate Students

BY

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PATHOLOGY



TLAZOLTEOTL, AZTEC GODDESS OF CHILDBIRTH

Statuette (8½ in. high) in aplite speckled with garnets. From the collection of Mr Robert Woods Bliss, Washington, D.C., U.S.A.; photograph by the Arts Council of Great Britain. (With thanks and acknowledgments to Mr Bliss and the Arts Council.)

TO

SIR ARTHUR GEMMELL

WITH AFFECTION AND RESPECT

FOREWORD

DR REWELL has written this book from his own experiences at the Liverpool Maternity Hospital, the Women's Hospital, Liverpool, and also as Professor under the Colombo Plan at the Government Hospital for Women and Children, Madras, India.

He has assumed that the reader has the basic knowledge of Obstetrical and Gynaecological Pathology required for a qualifying degree. So he has set out to supply the wider knowledge which is necessary for a higher qualification such as the Membership of the Royal College of Obstetricians and Gynaecologists.

This is essentially a book of personal experiences and views yet, in the main, it expresses generally accepted opinions. I wish it every success.

ARTHUR A. GEMMELL.

LIVERPOOL, 1960.

PREFACE

THIS book is intended for the postgraduate student studying gynaecology and obstetrics as a clinical subject and reading for a 'higher' examination. With the increased complexity of medicine the number of specialists has increased greatly, both in developed and underdeveloped countries. Despite the great back-log of poverty and ignorance that have to be dispelled in the latter, those responsible for the organisation of medicine realise that a thinly spread general medical service is no longer adequate. To maintain the standards of general medicine they must create and support a cadre, however small, of trained specialists who can practise their subject, teach it at postgraduate level and enlarge its boundaries. Such specialists in underdeveloped countries have a big job in front of them. They must practise, teach and investigate, but must also carry over into their own work what is useful to them in medicine as practised in more developed countries, sorting out the fundamentals of universal validity and building up a body of knowledge of disease among their own people which is more directly applicable to the troubles they endure, yet integrated closely with developments in world medicine, taking advantage of its advances and contributing to them at the same time. All this is in addition to and distinct from conquest of the 'tropical' diseases, which can now be organised on an international scale. The materials for such an edifice as yet exist in only a few places, but in the following pages a definite attempt will be made to show at least how they may be gathered in one small corner of medical science, although the emphasis has perforce to remain on problems as seen in Britain.

This does not pretend to be a practical manual and can give the reader only a theoretical basis for his clinical work. It is hoped that he may be encouraged by its aid to proceed to more practical work in pathology, the only way, of course, by which to learn the subject properly. It may perhaps give some assistance to the pathologist or surgeon with general experience in pathology, but limited experience in its special field. It will be obvious that it has been written by a morbid anatomist. Important subjects such as endocrine physiology, iso-immunisation, or anaemia will be dealt with briefly, but no apology is offered for this brevity.

Adequate theoretical discussion demands a treatise for each; excellent ones exist and some will be quoted. Morbid anatomy, however, remains the province of the hospital pathologist and also the basis of much of the work of the clinician in gynaecology. Students still find many difficulties in the subject, while the pathologist in a special centre sees much more of the material than any individual clinician and so is better equipped to make a theoretical synthesis. Much basic knowledge on the part of the reader has been assumed. Thus no complete description in detail of the histology of the endometrial cycle has been given, although attention is given to points in dispute, as well as to those which experience has shown to cause difficulty to postgraduate students.

The personal statistics and illustrations are based on material seen at the Women's and Maternity Hospitals, Liverpool, from the beginning of 1950 until the end of 1959. Although I am responsible for the majority of the histological diagnoses, some were made by my colleague Dr J. S. Elwood. Many of the ideas put forward have been formulated originally by my Registrars, notably Dr M. K. Alexander, Dr R. P. Towers and Dr D. J. B. Ashley, and especially Dr Allan Rowson, who has trained in gynaecology and who has prepared many of the statistics. For the years 1956 and 1957 I was in Madras, South India, under the Colombo Plan as Professor of Pathology at the Institute of Obstetrics and Gynaecology at Egmore, recently upgraded by the Central Government as a national centre for postgraduate training, although similar work had been going on there for many years. Pathology had been carried on for several years in the hospital to which the Institute is attached by Dr B. M. V. Shetty, and he has succeeded me as Professor there; many of his diagnoses and ideas are inevitably included here. While I was in India my place in Liverpool was taken by Dr Hilda Harris and many of her diagnoses are also included in the statistics.

Fairly full references have been given. It appears to me to be only honest to acknowledge the source of ideas that have proved useful in practice, and only fair to give the student a key by which to obtain these ideas in their pure form without the distortion that the most conscientious summary must impose on them. Even where a fact or concept is well known or discovered independently by the author a reference may be useful, as it emphasises that the work is accepted by others, gives a fuller discussion and describes earlier work in the same field. Apology is made in advance both for omission of important work and for the errors inevitable in

transcription. New discoveries published after the end of 1959 are not included. Preference has been given to articles published in English and in journals which are easily available, even where this meant omitting an important early discussion and quoting a relatively slight paper which does, however, give the key to earlier work. Really important sources of information are distinguished in the text. For very recent work some journals more difficult of access must be quoted, and also when dealing with points in dispute. Thus in any discussion of the histogenesis of tumours it is inevitable that much early German work should be mentioned. I read French with some ease and German with considerable difficulty, and can but trust that my interpretation of German texts is correct. At any rate, an attempt has been made to read all that are quoted; some that appeared important have been omitted because I was unable to understand them. Fortunately much work from Asia, Eastern Europe and South America is published in English, French or German, while there are several sources of abstracts in English of papers in languages other than these. Much help has been given to me in obtaining books and periodicals by the library staff of the Royal Society of Medicine, London, and of the Cohen Library of the University of Liverpool, of the Liverpool School of Tropical Medicine and especially by Mr and Mrs W. A. Lee of the Liverpool Medical Institution.

The typescript has been prepared by Mrs J. Atkinson.

High-quality block-making is expensive and adds greatly to the cost of a book, so the number of illustrations has been kept down to what appeared essential. The practising surgeon soon learns to recognise gross morbid appearances, so most of the blocks are of photomicrographs as he is less likely to be familiar with this aspect. It is for this reason that many arrows to features of importance have been superimposed; they may appear unnecessary to the trained histologist. Figures 80 and 84 are reproduced by permission of the Editors of the *Journal of Pathology and Bacteriology*, Figures 26 and 76 from the *Journal of Obstetrics and Gynaecology of the British Empire* and Figure 82 from *Guy's Hospital Reports* also by permission. Figure 121 is by Dr Vishnu Sharma. Figures 85, 87 and 93 are by Shri R. Kumaradevan, D.F.A., our photo-artist in Madras, and Figure 149 c was enlarged by Mr F. Jones, F.I.M.L.T. The remainder were photographed and processed by me.

My clinical colleagues have consented to my using their cases. I must thank them for this, as well as for their continued co-operation

and courtesy at all times. Their names in order of seniority are :
(a) in Liverpool, Sir Arthur Gemmell, P. Malpas, M. M. Datnow, T. N. A. Jeffcoate, the late C. MacIntosh Marshall, C. J. K. Hamilton, S. B. Herd, Miss M. H. Mayeur, C. H. de Boer, H. H. Francis ;
(b) in Madras, R. K. K. Thampan, P. Madhavan, M. K. Krishna Menon, Mrs S. Abrahams, Mrs E. V. Kalyani and Madhaviamma (*anglice* Mrs Krishna Menon).

Chapters XV and XVI have been read by Dr J. S. Elwood and Chapters I and XII by Dr J. A. Loraine. They have made many valuable suggestions but naturally cannot be held responsible for what is stated in these chapters. Finally, the whole typescript has been read by Sir Arthur Gemmell, despite illness and other preoccupations. He has made many valuable suggestions and criticisms and in particular has prevented many blunders over clinical matters.

R. E. REWELL.

LIVERPOOL, 1960.

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CHAPTER I

THE MENSTRUAL CYCLE

THE best and most detailed description of the histological changes in tube and endometrium probably remains that of Schroeder (1930), whose figures have often been reprinted in standard textbooks, sometimes without acknowledgment. The study of the endocrinology of reproduction dates from the work of Marshall and Jolly in 1906, who investigated lactation and oestrus in ewes and discovered that removal of the ovary brought the cycles to an end and that the corpus luteum controlled implantation of the ovum. They postulated that the ovary produced, *i.e.*, one that stimulated the uterus to undergo the changes of oestrus. Other important dates are 1927, when Allen showed that oestrogens administered to ovariectomised Rhesus monkeys produced uterine bleeding, and the demonstration round about 1930 that ovarian hormonal activity was controlled by the pituitary, *e.g.*, Evans, Meyer and Simpson (1932). The whole subject is thus little more than fifty years old, while knowledge of the hormones involved is only about thirty years old. In this time the subject has grown to the present vast proportions.

Moreover, similar observations have been extended to many species, and it can be assumed safely that all mammalian females show a regular reproductive cycle, comparable in its essentials to that of the human. There is no necessity to go into details here, and the variations indeed are great. Most mammals are characterised by a much slower cycle than the Primates, the uterus remaining quiescent between periods of oestrus and then cramming the changes into a brief time round about ovulation. External factors, such as changes in length of daylight, may initiate the process, acting through the hypothalamus (Marshall, 1942) which in turn affects the pituitary, and this the ovaries, until the chain of cause and effect ends at the uterus. Preparation may be made for an ovulation which never occurs, *e.g.*, in the rabbit where follicles ripen but are not discharged unless the animal is 'ridden' by a male. Mechanical stimulation to the neck of the female is enough and there is no need for the vagina to be penetrated (Marshall, 1942). Only in the Primates does the cycle appear to be as regular and rapid as in the

human, but the basic changes of pituitary stimulation, ovulation and two phases in the endometrium (those before and after ovulation) appear to be essentially the same in all species, however much they may vary in details of timing. This fundamental arrangement of hypothalamus, pituitary, ovary and uterus occurs apparently in all placental animals, even when the placenta is strictly not comparable to that of mammals, *e.g.*, in certain species of viviparous snakes (Asdell, 1928; Clausen, 1940) and the placental dogfish, *Mustelus canis* (Hisaw and Abramowitz, 1937, although this report was only a preliminary one and the work was apparently interrupted by the war of 1939-45). Anyone wishing to follow the comparative aspect further can do no better than start with the three volumes of *Marshall's Physiology of Reproduction*, the second edition of which (edited by Dr A. S. Parkes) was published in 1950, only a few days after the death of Dr F. H. A. Marshall. The various hormones involved are all closely related chemically in the different species and are obviously of very ancient origin in phylogeny. This makes work with animals of one species using the hormones of another, a relatively easy matter, but naturally there are small differences in the response of different species to an endocrine extract from one of them, while the same species may respond in slightly different ways to extracts from homologous glands from different animals. This may appear obvious, but many mistakes have arisen over the point, and papers have even been published in which the species used, either as the source of an extract or to study its effects, have not been stated clearly. An excellent example of confusion is between the gonadotrophin of the serum of the pregnant mare and that obtained from the human placenta. Much work with the former substance is now seen to have little relation to what would happen were the gonadotrophin of other placentas or pituitaries to be used, as the mare has a unique placental structure which produces a hormone which is peculiar to it.

HISTOLOGY OF THE ENDOMETRIAL CYCLE

Since so many excellent accounts are available in elementary textbooks of anatomy, histology and physiology, it seems unnecessary to describe the changes in detail yet once more. A brief account will be given, therefore, with concentration on points that are often omitted in simple accounts or over which the author has found students to experience difficulty.

Early Oestrogenic Phase.—This starts after the end of menstruation, *i.e.*, is best considered as beginning on the third or fourth day of the normal cycle as calculated in clinical practice, where the first day of the menstrual flow is taken as the start. When the endometrium is shed in menstruation, a thin layer is left consisting of stroma with simple glands torn across at their free ends. The surface epithelium, however, is rapidly re-formed between these ends. Curettings taken near the end of menstruation will contain some tissue still breaking away, some that has done so and some showing early proliferative appearances already.

Once menstruation is over, however, the appearances in curettings will be almost the same for the next few days, until about the eighth or tenth day of the cycle, although in blocks from hysterectomy specimens the endometrium will be seen to increase steadily in thickness. The glands are simple and almost straight in outline when cut longitudinally, although they may branch in the part somewhat more superficial than the basal layers (Fig. 1). The epithelial cells are columnar and evenly arranged. The cells of the stroma are closely packed and plump, although they may appear somewhat shrunken in material that has not been fixed rapidly enough. Both stromal and epithelial cells show mitoses (Fig. 2 A), and these are far more numerous in the glands than in the stromal cells. The glands do not increase obviously in diameter, *i.e.*, grow only in one dimension as a result of these cell divisions, but the stroma is growing in three dimensions and by fewer divisions, with the result that the glands become markedly coiled as the phase proceeds, especially in their basal parts. Nearer

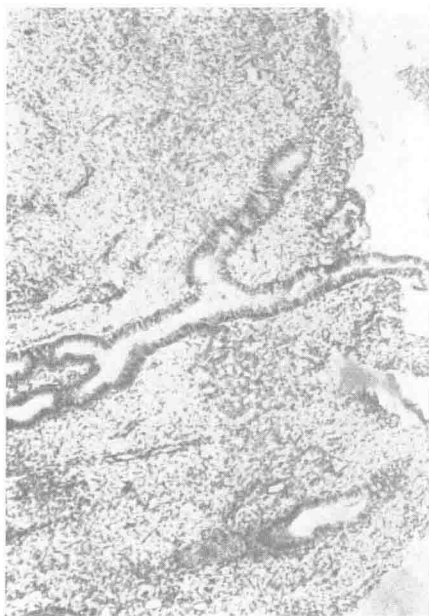


FIG. 1
Branching gland of endometrium.
Proliferative phase. $\times 40$.

the uterine cavity they tend to run straight towards the surface, so that their whole shape may be compared with a snake rising to strike. The stroma does increase in volume, more than the cell divisions within it allow, by the accumulation of oedema fluid between the cells, especially between the straight-running glands

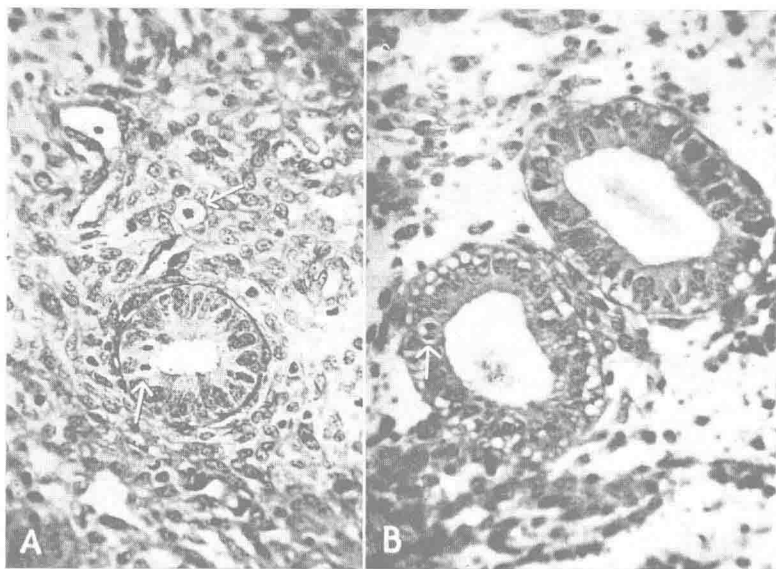


FIG. 2

A, Proliferative endometrium. Mitoses in gland and stroma. $\times 240$. B, Early progesterational endometrium. Glands show clear subnuclear vacuoles, but mitoses in addition. Stroma shows 'oedema.' $\times 240$.

near the surface, but as the phase proceeds the oedema becomes obvious at all levels, the cells of the stroma becoming concentrated round the coiled glands and the oedema being farther from the glands (Fig. 3). The intercellular fluid at this stage does contain water and is presumably true oedema (McLennan and Koets, 1953).

Later Oestrogenic Phase.—From about the eighth or tenth day of the cycle until the time of ovulation the appearances are somewhat different, and are conveniently considered as forming a distinct pattern of their own. The glands remain simple in outline, but coiling has become more marked, while mitoses become fewer and usually cease to occur. Sometimes, however, quite numerous mitoses are found persisting in both glands and stroma well into the progesterational phase, in an endometrium which there is no

reason to consider abnormal (Fig. 2 B). The oedema of the stroma becomes more marked and 'round cells' begin to infiltrate it in increasing numbers. Secretion of mucus by the glands is usually obvious.

At this time a certain amount of 'telescoping' is usual. In

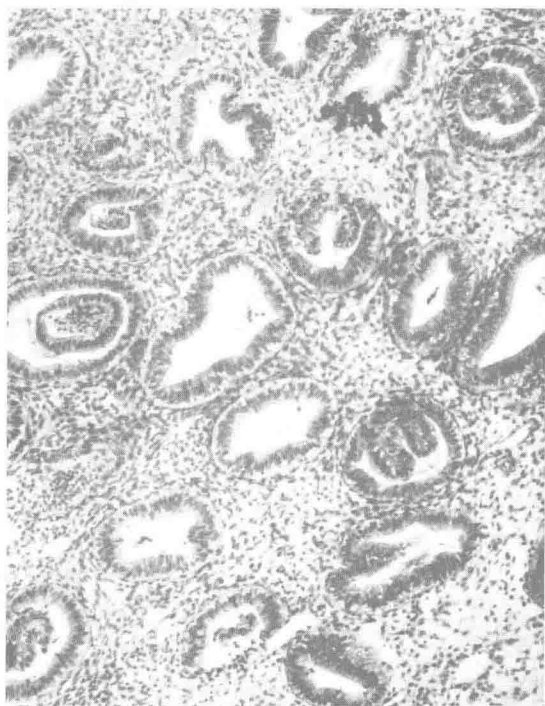


FIG. 3

Early progestational endometrium. Glands show subnuclear vacuolation, but also 'telescoping.' In some this appears as an intussusception, but in others the sprout can be seen to come from the side wall. $\times 104$.

transverse sections of such a gland the appearance is that of an intussusception, but serial sections show that these are sprouts from the side of the lumen (Fig. 3). Hampson and Gerlis (1954) point out that, when progestational change commences, the inner layer of a telescoped gland may not show the change although the outer layer does so. They point out also that telescoping is usually in the deeper parts of the glands and postulate an imbalance in the blood supply of the deeper and more superficial parts, whatever