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**SPECIAL ARTICLES**

**ANENCEPHALY**

**HYDROCEPHALY**

**HYPNOSIS**



**HOEBER MEDICAL DIVISION**

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# CLINICAL OBSTETRICS AND GYNECOLOGY

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## CONTRIBUTORS

- JACK DAVIES, M.D. Professor of Anatomy, Washington University Medical School, St. Louis, Missouri
- C. FREDERIC FLUHMAN, M.D. Clinical Professor, Department of Obstetrics and Gynecology, Stanford University School of Medicine, Palo Alto; Chief, Obstetrics and Gynecology, Presbyterian Medical Center, San Francisco, California
- ALBERT Y. KEYORKIAN, M.D. Assistant in Gynecology, Harvard Medical School, Boston; Associate Surgeon, Free Hospital for Women, Brookline, Massachusetts
- EMIL KOTCHER, Sc.D. Associate Professor of Microbiology, The University of Louisville School of Medicine, Louisville, Kentucky
- WARREN R. LANG, M.D. Associate Professor of Obstetrics and Gynecology, The Jefferson Medical College of Philadelphia; Attending Gynecologist, Veterans Administration Hospital of Philadelphia, Philadelphia, Pennsylvania
- BRIAN LITTLE, M.D. Associate in Obstetrics and Gynecology, Harvard Medical School; Associate Director, Department of Obstetrics and Gynecology, Boston City Hospital, Boston, Massachusetts
- JOSEPH P. LONG, M.D. Assistant Professor of Obstetrics and Gynecology, The Jefferson Medical College of Philadelphia, Philadelphia, Pennsylvania
- JOHN B. MONTGOMERY, M.D. Professor and Chairman of the Department of Obstetrics and Gynecology, The Jefferson Medical College of Philadelphia, Philadelphia, Pennsylvania
- ROBERT E. L. NESBITT, JR., M.D. Professor and Chairman of the Department of Obstetrics and Gynecology, State University of New York Upstate Medical Center College of Medicine, Syracuse, New York

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## CONTRIBUTORS (continued)

- J. H. M. PINKERTON, M.D. Professor of Obstetrics and Gynaecology, University of London; Staff, Institute of Obstetrics and Gynaecology, Queen Charlotte's Maternity Hospital, London, England
- LEON N. PRINCE, M.D. Assistant Professor of Clinical Obstetrics and Gynecology, The Jefferson Medical College of Philadelphia, Philadelphia, Pennsylvania
- ABRAHAM E. RAKOFF, M.D. Professor of Obstetrics and Gynecologic Endocrinology, The Jefferson Medical College of Philadelphia; Lecturer in Gynecic Endocrinology, Graduate School of Medicine, University of Pennsylvania; Endocrinologist, Jefferson Hospital, Philadelphia, Pennsylvania
- VISHNU SARMA, M.D. Assistant Professor of Obstetrics and Gynaecology, Stanley Medical College; Staff, The Government Women and Children's Hospital, Madras, India
- BENJAMIN TENNEY, JR., M.D. Clinical Professor, Obstetrics and Gynecology, Harvard Medical School; Director, Department of Obstetrics and Gynecology, Boston City Hospital, Boston, Massachusetts
- ABRAHAM WEINBERG, M.D. Formerly Instructor in Medical Hypnosis and Guest Lecturer, Institute for Research in Hypnosis, Postgraduate Division, Seton Hall College of Medicine and Dentistry, Jersey City, New Jersey; Consultant on Nutrition, Division of Psychiatry, City Hospital, Elmhurst, New York
- RALPH B. WOOLF, M.D. Associate Professor in Obstetrics and Gynecology, Washington University School of Medicine, St. Louis, Missouri
- PAUL B. YOUNGE, M.D. Assistant Clinical Professor of Gynecology, Harvard Medical School, Boston; Associate Chief Surgeon, Free Hospital for Women, Brookline, Massachusetts

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**BENIGN LESIONS  
OF THE CERVIX**



## FOREWORD

TO THE PRACTITIONER of obstetrics and gynecology, the cervix is probably the most important structure in the female. Abnormalities of the cervix constitute a large proportion of the problems with which he copes. Cervical malignancy comprises approximately 10 per cent of all malignancies in the female, second only in incidence to carcinoma of the breast; it accounts for more than half of the cancers of the female genital tract.

In spite of these figures, however, most cervixes which the obstetrician-gynecologist encounters are normal or have benign lesions. Understandably, such lesions receive scant attention in the literature. On the other hand, with the present emphasis in medicine on the detection and prevention of cancer, a symposium of benign cervical changes, some of which must serve as a matrix for subsequent malignancy, is not without pertinence at this time.

We have attempted to highlight the benign cervix in its various phases—anatomy and histology, physiology, microbiology, means of evaluation, erosion, atypia, benign neoplastic lesions, the cervix of pregnancy, the incompetent cervical os, and surgery of the benign cervix. We have given the authors a wide latitude in the interpretation of the subjects assigned. It is thus hoped that important aspects of the nonmalignant cervix are included, not only as they relate to subsequent malignant change, but also with reference to significant data of the benign diseases of this tiny but significant organ.

WARREN R. LANG, M.D.



# HISTOLOGY AND FINE STRUCTURE OF THE ADULT HUMAN CERVIX UTERI

J. DAVIES, M.D., and  
R. B. WOOLF, M.D.

*From the Department of Anatomy, and the Department of  
Obstetrics and Gynecology, Washington University School  
of Medicine, St. Louis, Missouri*

IT IS THE PURPOSE of this paper to review the salient histologic features of the nonmalignant human cervix, illustrating them by observations with the electron microscope. The increased resolving power of this instrument has rendered virtually obsolete many of the less-refined optical methods of visualization used a few years ago in study of the precise form and fine structure of cells and the nature of their relationships with each other and with the vascular and connective tissues. The method has added a new dimension to the study of such structures as the mitochondria, the Golgi apparatus, basement membranes, and inclusion and secretory granules of all types; and it has revealed the nature of structures such as the endoplasmic reticulum, the microsomal particles, and cell membranes which are beyond the limits of resolution of the light microscope. Application of the electron microscope to old basic and applied problems of reproductive biology is in its infancy, and its importance is scarcely realized. It is hoped that the observations in this paper on a very limited group of normal cervixes removed at operation will illustrate some of the possibilities in the use of the electron microscope for the study of old and unsolved problems, of which those of the cervix are but one example.

## MATERIAL AND METHODS

Three specimens of the adult human cervix form the basis of these observations. The specimens with such clinical data as seem pertinent are as follows:

1. N. L. H. (B. H. #362677), age 39, single, Caucasian, gravida 0, normal menstrual history. Cervix grossly normal to inspection. Laparotomy performed

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on eighteenth day of menstrual cycle: bilateral ovarian endometriomas and pelvic endometriosis; the endometrium was premenstrual.

2. A. E. F. (B. H. #169597), age 42, married, Caucasian, gravida 3, para 3, normal menstrual history prior to third pregnancy. Following birth of third child in 1946 patient continued to lactate until present. A laparotomy was performed during 1950, at which time a benign cyst of the right ovary was removed. In conjunction with the persistent lactation the patient had been essentially amenorrheal up to 1 year ago without gross involution of the genital structures. Cyclic sex hormone therapy was used on many occasions and caused episodes of withdrawal uterine bleeding. The patient was thought to possess a form of "hypothalamic" amenorrhea. Spontaneous but irregular menses resumed 9 months prior to laparotomy, which was performed because of a persistent right ovarian mass. The last spontaneous menstrual period occurred 4 months earlier. The cervix was grossly normal to inspection. Histologically the endometrium was proliferative and an ovarian corpus-luteum cyst and luteinized follicle cyst were present.

3. N. A. A. (B. H. #362932), age 27, married, Caucasian, gravida 1, para 0. The patient was pregnant approximately 27 weeks. A living infant weighing approximately 1200 gm. was delivered by cesarean section, following which hysterectomy was performed in conjunction with surgery for adenocarcinoma of the rectosigmoid colon.

The cervixes were opened along their length, usually not later than 30 to 60 minutes after removal. Full-thickness sections from the wall of the cervix along the axis of the cervical canal were made and fixed in Bouin's solution for ordinary histologic study. For electron microscopy small pieces of the mucosa of the portio externa and endocervical region (about 2 mm. square) were fixed for 1 hour in 1 per cent osmic acid buffered with White's saline solution.<sup>31</sup> The pieces were then dehydrated through graded concentrations of ethyl alcohol (10-40 per cent) and then through mixtures of ethyl and butyl alcohol to 100 per cent butyl alcohol, in which they were stored overnight. The next morning they were immersed for 1 hour in propylene glycol and embedded in English Araldite.<sup>31</sup> Thin sections were cut on a Porter-Blum microtome, mounted on copper grids coated with collodion, stained for several hours with a saturated solution of uranyl acetate in water and examined in an RCA electron microscope, model EMU-3C. Orientation of the sections before ultra-thin sectioning was obtained by cutting thick sections at about 1  $\mu$  and examining these in the phase contrast microscope.

Tissues for light microscopy, being of considerable size, were double embedded in paraffin and celloidin and cut at approximately 10  $\mu$  on a sliding microtome. Staining was with Harris' hematoxylin and with

eosin. The periodic acid Schiff (PAS) stain was carried out on the sections before and after incubation with saliva to remove glycogen.

## OBSERVATIONS

### *Light Microscopy: Portio Externa*

The epithelium of the portio externa of the three women observed by light microscopy is illustrated at the same magnification in Fig. 1-4. For convenience of description the stratified squamous epithelium of this area will be arbitrarily divided into four layers, though there is a gradual transition between the layers and not a clear distinction between them. The four layers are: (1) a basal layer, (2) a parabasal layer, (3) an intermediate layer, and (4) a superficial layer. The basal layer, which rests on the cervical stroma, is a single layer of cuboidal or low columnar cells in the nonpregnant women (Fig. 1, 3, 4). These cells have prominent nuclei and a relatively small amount of cytoplasm which is moderately basophilic. The basement membrane between the basal cells and the stroma is straight (Fig. 1) or slightly undulating (Fig. 3, 4). The basement membrane is visible in ordinary hemotoxylin preparations as a thin line but is sharply delineated in preparations stained with the PAS method (Fig. 3, 4). In pregnancy the basal layer consists of several layers of deeply basophilic cells, some of which are in mitosis. The epithelium margin bordering the cervical stroma and the basement membrane is thrown into folds and the stroma extends deeply into the basal layer as "pegs" or papillae (Fig. 2).

The second or parabasal layer consists of several rows of polyhedral cells, three or four rows in thickness in the nonpregnant women (Fig. 1, 3, 4) and about six rows in the pregnant woman (Fig. 2). The cytoplasm of these cells is moderately basophilic, the degree of basophilia decreasing in the direction of the surface of the epithelium. The nuclei are less basophilic and show a more finely divided chromatin than do those of the basal layer. The intercellular areas become more clearly marked in the superficial rows of the second layer and begin to stain delicately with the PAS method (Fig. 4). The nuclei of many cells in Fig. 1 appear distorted by a large paranuclear vacuole which in some cases compresses the nucleus to a thin crescent. Many cells showed this change in the case of A. E. F. (Fig. 1), but only occasional cells in the case of N. L. H. (Fig. 4). This paranuclear vacuole will be referred to again, when the electron microscopic observations are discussed at

