

ENDOCRINE  
PATHOLOGY  
OF THE OVARY

MORRIS AND SCULLY

*Endocrine Pathology  
of the Ovary*

Endocrine Pathology  
of the Ovary

# ENDOCRINE PATHOLOGY OF THE OVARY

---

---

**JOHN McLEAN MORRIS, M.D.**

ASSOCIATE PROFESSOR OF GYNECOLOGY, YALE UNIVERSITY  
SCHOOL OF MEDICINE, NEW HAVEN, CONNECTICUT

**ROBERT E. SCULLY, M.D.**

CLINICAL ASSOCIATE IN PATHOLOGY, HARVARD MEDICAL  
SCHOOL; ASSOCIATE PATHOLOGIST, MASSACHUSETTS GEN-  
ERAL HOSPITAL, BOSTON, MASSACHUSETTS

*With 75 illustrations*

---

LONDON

1958

HENRY KIMPTON

Copyright © 1958 by  
THE C. V. MOSBY COMPANY

*(All rights reserved)*

PRINTED IN THE UNITED STATES OF AMERICA

LIBRARY OF CONGRESS CATALOG CARD NUMBER 58-6572



*Dedicated With Admiration and Affection*

*to*

JOE VINCENT MEIGS, M.D.

Dedicated With Reverence and Affection

to

JOE VINCENT MEIGS M.D.

## PREFACE

The purpose of this book is to correlate the pathologic changes occurring in the ovary with the accompanying clinical endocrine findings and to evaluate both in the light of the material available for study. It is our hope that it may prove of value to the gynecologist, pediatrician, or internist, who, confronted by a clinical picture of endocrine disorder, may wish more information as to the possible underlying ovarian abnormalities. In addition, it is intended to assist the pathologist in the identification of such morphologic changes, as well as to acquaint him with their functioning potentialities.

The cases of functioning ovarian tumors and related disorders observed at the Massachusetts General Hospital have been reviewed. Some of the opinions presented are based on studies of the microscopic pathology of cases from the Peter Bent Brigham Hospital, New England Deaconess Hospital, Boston City Hospital, and Yale Medical Center. Dr. Arthur Hertig has been kind enough to permit us to use cases from the Free Hospital for Women, Brookline, and we are grateful for his advice. We should like to express our appreciation to Dr. Lars Santesson for permitting us to use material at the Radiumhemmet, Stockholm, and to the late Dr. Emil Novak for his kindness in allowing us to examine the functioning tumors in the Ovarian Tumor Registry, Baltimore. In addition, we wish to thank Dr. Magnus Haynes, the Chelsea Hospital for Women, London, Dr. Ernst Navratil, Universitäts Frauenklinik, Graz, Austria, Dr. Jacques Varangot, Paris, and Dr. Gunnar Teilum, Copenhagen, for the opportunity of seeing some of their cases.

We are indebted to the late Dr. Tracy Mallory, and Doctors Benjamin Castleman, Somers Sturgis, Janet McArthur, Fuller Albright, and especially Joe V. Meigs and Arthur T. Hertig, for their encouragement and help with this work.

John McLean Morris  
Robert E. Scully



## PREFACE

The purpose of this book is to correlate the pathological changes occurring in the ovary with the accompanying clinical and endocrine findings and to evaluate both in the light of the material available for study. It is our hope that it may prove of value to the gynecologist, pathologist, or internist who confronted by a clinical picture of endocrine disorder, may wish more information as to the possible underlying ovarian abnormalities. In addition it is intended to assist the pathologist in the identification of such morphologic changes, as well as to acquaint him with their functioning potentialities.

The cases of functioning ovarian tumors and related disorders observed at the Massachusetts General Hospital have been reviewed. Some of the opinions presented are based on studies of the microscopic pathology of cases from the Peter Bent Brigham Hospital, New England Deaconess Hospital, Boston City Hospital, and Yale Medical Center. Dr. Arthur Hertig has been kind enough to permit us to use cases from the Face Hospital for Women, Brooklyn, and we are grateful for his advice. We should like to express our appreciation to Dr. Lars Santesson for permitting us to use material at the Radhymnasium, Stockholm, and to the late Dr. Emil Novak for his kindness in allowing us to examine the functioning tumors in the Ovarian Tumor Registry, Baltimore. In addition, we wish to thank Dr. Magnus Harned, the Chelsea Hospital for Women, London; Dr. Ernst Navroth, Universität Frankfurt; Dr. Gustav Voss, Dr. Jacques Vernet, Paris, and Dr. Gunnar Telling, Copenhagen, for the opportunity of seeing some of their cases.

We are indebted to the late Dr. Tracy Mallory and Doctors Hespanha, Castleman, Somers, Sturgis, Janet McArthur, Fuller Albright, and especially to V. Meigs and Arthur T. Hertig for their encouragement and help with this work.

John McLean Morris  
Robert E. Scully

# CONTENTS

<b>I. INTRODUCTION</b> .....	<b>15</b>
THE CELLS OF THE GONADS .....	15
EMBRYOLOGY OF THE GONADS .....	22
SEXUAL DIFFERENTIATION AND SEX HORMONE PRODUCTION .....	23
HERMAPHRODITISM AND PSEUDOHERMAPHRODITISM .....	23
SEX HORMONES AND SEX CHARACTERISTICS .....	24
HORMONE PRODUCTION BY THE TESTIS .....	24
HORMONE PRODUCTION BY THE OVARY .....	25
BISexual EFFECTS OF HORMONES .....	26
HORMONE ASSAYS .....	27
GONADOTROPHINS .....	27
FOLLICLE-STIMULATING HORMONE (FSH) .....	27
CHORIONIC GONADOTROPHIN .....	29
LUTEINIZING HORMONE (LH, ICSH) .....	29
ESTROGENS .....	29
PROGESTERONE .....	31
PREGNANETRIOL .....	32
ANDROGENS .....	32
17-KETOSTEROIDS .....	32
CORTICOIDs .....	33
CLASSIFICATION OF ENDOCRINE EFFECTS .....	33
ESTRINISM .....	33
DEFEMINIZATION .....	35
MASCULINIZATION .....	35
HYPERADRENOCORTICISM .....	36

<b>2. NONNEOPLASTIC ABNORMALITIES OF THE OVARY WITH ENDOCRINE EFFECT</b>	<b>40</b>
SINGLE FOLLICLE CYSTS	40
POLYCYSTIC OVARIES AND HYPERTHECOSIS	42
POLYCYSTIC OVARIES AND ESTRINISM	44
POLYCYSTIC OVARIES AND THE STEIN-LEVENTHAL SYNDROME	44
HYPERTHECOSIS AND VIRILISM	46
ETIOLOGY	48
TREATMENT	50
CORTICAL STROMAL HYPERPLASIA	51
HILAR LEYDIG CELL (HILUS CELL) HYPERPLASIA	54
INTERSEXUAL INDIVIDUALS WITH FEMALE CONFIGURATION: TESTICULAR FEMINIZATION AND GONADAL DYSGENESIS	58
<b>3. CLASSIFICATION OF FUNCTIONING OVARIAN TUMORS</b>	<b>62</b>
<b>4. GRANULOSA-THECA CELL TUMORS</b>	<b>65</b>
HISTORY	65
INCIDENCE	65
PATHOLOGY OF GRANULOSA CELL TUMORS	65
PATHOLOGY OF THECOMAS	73
HISTOGENESIS AND ETIOLOGY	75
ENDOCRINE EFFECTS	76
PROGNOSIS AND TREATMENT	78
CASE REPORTS	79
<b>5. SERTOLI-LEYDIG CELL TUMORS</b>	<b>82</b>
HISTORY	82
INCIDENCE	83
PATHOLOGY	83
HISTOGENESIS	91
ENDOCRINE EFFECTS	91
PROGNOSIS AND TREATMENT	92
CASE REPORTS	93

6. SEX CORD-MESENCHYME TUMORS OF INDETERMINATE OR MIXED CELL TYPES .....	97
INDETERMINATE TUMORS .....	97
MIXED TUMORS .....	97
7. LIPOID CELL TUMORS .....	103
INCIDENCE .....	103
PATHOLOGY .....	104
ADRENAL-LIKE TUMORS .....	104
LEYDIG (HILUS) CELL TUMORS .....	104
HYPERNEPHROMAS .....	106
LUTEOMAS .....	107
HISTOGENESIS .....	108
ENDOCRINE EFFECTS .....	109
PROGNOSIS AND TREATMENT .....	114
8. GERMINOMAS, TERATOMAS, AND RELATED TUMORS .....	117
GERMINOMAS .....	117
GONADOBLASTOMAS .....	120
CHORIOCARCINOMAS .....	127
TERATOMAS .....	128
STRUMA OVARIUM .....	129
9. TUMORS WITH "FUNCTIONING STROMA" .....	131
CASE REPORTS .....	133

97	SEX CORRESPONDENCE TUMORS OF INDETERMINATE OR MIXED CELL TYPES
97	Indeterminate Tumors
97	Mixed Tumors
103	LIPID CELL TUMORS
103	Incidence
104	Pathology
104	Adrenal-Like Tumors
104	Lipoma (Lipus) Cell Tumors
106	Hibernomas
107	Liposarcomas
108	Histiocytomas
109	Endocrine Effects
114	Endocrine and Treatment
117	GERMINOMAS, TERATOMAS, AND RELATED TUMORS
117	Germinalomas
120	Gonadoblastomas
127	Choriocarcinomas
128	Teratomas
129	Stromal Ovarian
131	TUMORS WITH FUNCTIONING STROMA
133	Case Reports

*Endocrine Pathology  
of the Ovary*





## Chapter 1

# INTRODUCTION

## THE CELLS OF THE GONADS

The gonadal cells that may be involved in endocrine disturbances undergo striking changes in appearance during their natural life spans.<sup>8-10</sup> An appreciation of the range of structure exhibited by these cells and of any specific morphologic features they may possess is essential to interpretation of ovarian endocrine pathology. The ovarian cells that may have endocrine significance include the granulosa and theca cells of the follicle and of the corpus luteum, the ovarian stromal cells and their luteinized derivatives, and the hilar Leydig cells. In ovarian tumors, counterparts of the Sertoli and Leydig cells of the testis also are encountered. Since rests of adrenal cortex cells are not uncommon in the vicinity of the gonads, these also merit attention.

In the undeveloped or primordial follicle, the granulosa cells envelop the ovum as a single layer of flat, cuboidal, or columnar epithelial cells, constituting the so-called follicular epithelium (Figs. 1 and 2). As the follicle begins to grow and cavitate, the granulosa cells proliferate, become rounder, and are characterized by uniform spherical nuclei, frothy cytoplasm that stains weakly, and indistinct cell borders (Fig. 3). At this stage characteristic small round cavities (Call-Exner bodies) may appear among the cells. These often contain a few shrunken nuclei and homogeneous eosinophilic colloid, which may be scalloped along its circumference. The Call-Exner body has a distinctive appearance and is one of the most specific morphologic features of granulosa cells, especially in neoplastic growth (Fig. 30). After ovulation, the granulosa cells develop into the large polyhedral granulosa-lutein cells characterized by abundant deeply staining cytoplasm that contains fine fat vacuoles in its peripheral zone (Fig. 4). As the corpus luteum involutes, the granulosa-lutein cells gradually decrease in

size, their cytoplasm becomes spongy and laden with coarse fat droplets, their nuclei shrink (Fig. 5), and eventually they disappear.

The theca cells undergo less spectacular developmental changes than the granulosa cells. Unrecognizable in the primordial follicle, they make their appearance in the developing follicle at the junction of the granulosa cell layer and the ovarian stroma. Two layers of theca cells, often poorly demarcated from one another, may be recognized. The theca interna cells are rounded, contain variable amounts of fat in their cytoplasm, and resemble epithelial cells (Fig. 3). The theca externa cells are plump and spindle-shaped, resembling fibroblasts. In many follicles including cystic and atretic forms, only the theca interna component is seen clearly (Figs. 12 and 13). In the corpus luteum, the theca interna cells are rounded and laden with fat (Fig. 4). In all but the earliest stages, they are considerably smaller than the granulosa-lutein cells.

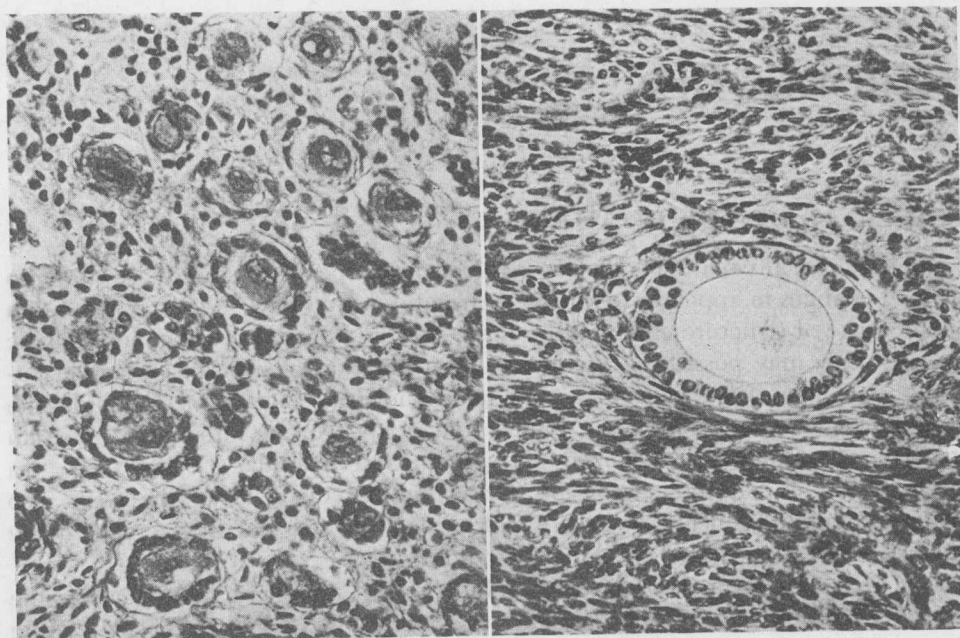


Fig. 1.

Fig. 2.

Fig. 1.—Ovary of newborn premature infant (31 weeks).  $\times 300$ . Note primordial follicles composed of ova surrounded by follicular epithelium. Between the follicles is cellular ovarian stroma.

Fig. 2.—Primordial follicle showing sharply demarcated cuboidal epithelium surrounding pale ovum.  $\times 300$ .

The theca interna cells of the corpus luteum are called theca-lutein or paralutein cells. These terms also have been applied to theca interna cells unassociated with corpora lutea, whenever such cells acquire abundant foamy or granular cytoplasm and resemble true theca-lutein cells. Thus, the term "luteinization of the theca interna" may refer to changes taking place in follicles prior to puberty or in cystic and atretic follicles of mature women, as well as to the characteristic