

VULVA VAGINA UTERUS  
TUMORS OF FEMALE  
SEX ORGANS

part 2 + part 2 supplement

HERTIG + GORE

# TUMORS OF THE FEMALE SEX ORGANS

Part 2

## TUMORS OF THE VULVA, VAGINA AND UTERUS

Arthur T. Hertig, M.D.

and

Hazel Gore, M.B., B.S.

ARMED FORCES INSTITUTE OF PATHOLOGY

# ATLAS OF TUMOR PATHOLOGY

Section IX—Fascicle 33

## TUMORS OF THE FEMALE SEX ORGANS

Part 2

### TUMORS OF THE VULVA, VAGINA AND UTERUS

by

Arthur T. Hertig, M.D.

Shattuck Professor of Pathological Anatomy  
Harvard Medical School, Boston, Massachusetts  
Consultant in Pathology

Boston Lying-in Hospital, Boston, Massachusetts  
Free Hospital for Women, Brookline, Massachusetts  
and

Hazel Gore, M.B., B.S.

Associate in Pathology, Harvard Medical School, Boston, Massachusetts  
Formerly  
Associate Pathologist, Free Hospital for Women, Brookline, Massachusetts

Published by the

ARMED FORCES INSTITUTE OF PATHOLOGY

Under the Auspices of the

SUBCOMMITTEE ON ONCOLOGY

of the

COMMITTEE ON PATHOLOGY

of the

DIVISION OF MEDICAL SCIENCES

of the

NATIONAL ACADEMY OF SCIENCES—NATIONAL  
RESEARCH COUNCIL

Washington, D. C.

1960

Originally submitted for publication March 1955  
Accepted for publication 1959

---

For sale by the American Registry of Pathology  
Armed Forces Institute of Pathology  
Washington 25, D. C. - Price — \$2.50

# ATLAS OF TUMOR PATHOLOGY

Sponsored and Supported

by

AMERICAN CANCER SOCIETY

ANNA FULLER FUND

ARMED FORCES INSTITUTE OF PATHOLOGY

JANE COFFIN CHILDS MEMORIAL FUND FOR MEDICAL RESEARCH

NATIONAL CANCER INSTITUTE, U.S. PUBLIC HEALTH SERVICE

UNITED STATES VETERANS ADMINISTRATION

## ACKNOWLEDGMENTS

The publication of this fascicle has been possible only with the assistance of many people. To them the authors would like to express their sincere thanks. They are grateful to Dr. Hugh Grady for acting as special critic. Dr. Mary Ruth Oldt was very encouraging, patient, and helpful in the preparation of the first draft. Dr. Helen M. Scoville has helped through numerous revisions, and Dr. Catherine W. Blumberg has cooperated in the final revision. They would like to thank the members of the Subcommittee on Oncology of the National Research Council for their careful reading of the manuscript and their constructive criticisms. The authors appreciate Dr. William B. Ober's supervision of some of the photography done at the Armed Forces Institute of Pathology. They also would like to express their thanks to the many Residents and Fellows in Pathology at the Free Hospital for Women and the Boston Lying-in Hospital who have assisted in reviewing the literature and clinical and pathologic material. Mrs. Margaret Hammond and Mrs. Annemarie Hampe have typed the manuscript and to both of them we are most grateful.

Materials and photographs have been contributed by:

Dr. A. F. Anderson, Edinburgh, Scotland; Lt. Col. H. C. Boyd and Maj. W. P. Lochte, Waltham, Mass.; Dr. C. E. Brown, Philadelphia, Pa.; Dr. John Butts, Worcester, Mass.; Dr. Sidney Farber, Boston, Mass.; Dr. Gilbert Friedell, Boston, Mass.; Dr. Sylvia Graham, Boston, Mass.; Dr. R. R. Greene, Chicago, Ill.; Dr. Erle Henriksen, Los Angeles, Calif.; Dr. R. A. Kimbrough, Jr., Philadelphia, Pa.; Dr. J. F. Kuzma, Milwaukee, Wis.; Dr. Olga Leary, Jr., Boston, Mass.; Dr. John McKelvey, Minneapolis, Minn.; Dr. Memoir Marsh, Brooklyn, N.Y.; Dr. Emil Novak, Baltimore, Md.; Dr. Rudolf Osgood, Attleboro, Mass.; Dr. Joseph Porter, Portland, Maine; Dr. S. M. Rabson, Fort Wayne, Ind.; Dr. S. C. Sommers, Boston, Mass.; Dr. F. W. Stewart, New York, N.Y.

Permission to use copyrighted illustrations and other material has been granted by:

C. V. Mosby Co.:

Am. J. Obst. & Gynec.:

55: 917-939, 1948. For fascicle figures 263, 268

56: 23-40, 1948. For fascicle figures 135, 257, 273

58: 867-895, 1949. For fascicle figures 84, 86

58: 924-942, 1949. For fascicle plate VI, and figures 104, 105, 107, 108, 203, 204

64: 807-815, 1952. For fascicle figure 82

68: 1222-1242, 1954. For fascicle figures 130-132, 264, 265, 274-279

Pathology, 1957. For fascicle plates I-D, VII-A, and figures 4, 28, 30, 59, 90, 97, 125, 157, 163, 195, 217, 225, 230, 249

Paul B. Hoeber, Inc.:

Obst. & Gynec.:

3: 150-159, 1954. For fascicle figures 243, 244

6: 1-11, 1955. For fascicle figure 36

6: 147-161, 1955. For fascicle figures 63-65

8: 22-39, 1956. For fascicle figure 185

8: 140-156, 1956. For fascicle figures 179, 182, 186, 189, 190

Grune & Stratton, Inc.:

Progress in Gynecology, 1957. For fascicle figures 67B, 69, 70, 79, 83

American Cancer Society, Inc.:

Cancer:

2: 144-152, 1949. For fascicle figures 20-23

2: 957-963, 1949. For fascicle figures 161, 162, 164

2: 964-971, 1949. For fascicle plate VII-B, and figures 167, 168

7: 75-91, 1954. For fascicle figures 137-140

CA: Bulletin of Cancer Progress, 6: 196-202, 1956. For fascicle figure 76

Blakiston Div., McGraw-Hill Book Co., Inc.:

Human Embryology, 1953. For fascicle figures 258-261

Franklin H. Martin Memorial Foundation:

Surg., Gynec. & Obst., 75: 239-244, 1942. For fascicle figure 67A

Royal College of Surgeons of England:

Ann. R. Coll. Surgeons England, 3: 189-209, 1948. For fascicle figures 17-19

Sherratt & Son:

J. Obst. & Gynaec. Brit. Emp.:

51: 377-385, 1944. For fascicle plate I-A

60: 483-491, 1953. For fascicle figures 109-114

H. K. Lewis & Co., Ltd.:

Brit. J. Dermat., 41: 177-187, 1929. For fascicle plate I-B

American Medical Association:

Arch. Path., 66: 494-503, 1958. For fascicle figure 92

All illustrations are the authors unless otherwise acknowledged. The A.F.I.P. accession numbers are for the identification of negatives at the Armed Forces Institute of Pathology.

Arthur T. Hertig  
Hazel Gore

# TUMORS OF THE VULVA, VAGINA, AND UTERUS

## TABLE OF CONTENTS

	Page No.
VULVA.....	11
Introduction.....	11
Benign Tumors of Epithelial Origin.....	11
Figs. 1, 2	
Papilloma.....	11
Condyloma Acuminatum.....	11
Pigmented Papilloma.....	11
Malignant Tumors of Epithelial Origin.....	14
Figs. 3-23; Plate I	
Carcinoma in Situ.....	14
Bowen's Disease.....	14
Extramammary Paget's Disease.....	15
Melanoma.....	27
Relationship of Leukoplakic Vulvitis to Carcinoma.....	28
Carcinoma.....	29
Basal Cell Carcinoma.....	33
Tumors of Sweat Gland Origin.....	34
Figs. 24-30	
Hidradenoma.....	34
Tumors of Bartholin's Gland.....	40
Figs. 31-34	
Carcinoma.....	40
Sarcoma.....	41
Benign Tumors of Connective Tissue Origin.....	44
Fibroma.....	44
Lipoma.....	44
Hemangioma.....	44
Neurofibroma.....	44
Leiomyoma.....	44
Ganglioneuroma.....	45
Lymphangioma.....	45
Granular Cell Myoblastoma.....	45
Malignant Tumors of Connective Tissue Origin.....	45
Sarcoma.....	45
Endometriosis.....	47
Metastatic Tumors.....	47

	Page No.
URETHRA.....	49
Benign Tumors.....	49
Figs. 35, 36	
Caruncle.....	49
Malignant Tumors.....	50
Fig. 37	
Carcinoma.....	50
Table I.....	51
Melanoma.....	54
Sarcoma.....	54
VAGINA.....	56
Benign Tumors of Epithelial Origin.....	56
Fig. 38	
Papilloma.....	56
Polyp.....	56
Cyst.....	56
Adenosis.....	56
Malignant Tumors of Epithelial Origin.....	57
Figs. 39-46	
Carcinoma.....	57
Endometriosis.....	64
Benign Tumors of Connective Tissue Origin.....	64
Figs. 47-53	
Leiomyoma.....	64
Other Benign Solid Tumors.....	64
Fibroma.....	64
Fibroleiomyoma.....	64
Granular Cell Myoblastoma (Myoblastic Myoma)...	65
Miscellaneous Benign Tumors.....	65
Neurofibroma.....	65
Neuroepithelioma.....	65
Benign Cystic Teratoma (Dermoid Cyst).....	65
Malignant Tumors of Connective Tissue Origin.....	70
Fig. 54	
Sarcoma.....	70
Melanoma.....	70
Secondary Tumors.....	71
Figs. 55-57	
References.....	74
Malignant Mixed Müllerian Tumors.....	78
Figs. 58-61	
References.....	84



	Page No.
CERVIX.....	86
Introduction.....	86
Conditions of Questionable Neoplastic Nature.....	86
Figs. 62-75	
Polyp.....	86
Papilloma.....	90
Squamous Cell Metaplasia.....	91
Leukoplakia of the Cervix.....	98
Carcinoma of Cervix.....	99
Figs. 76-148; Plates II-VI	
Squamous Cell Carcinoma in Situ.....	99
Relationship of Carcinoma in Situ to Carcinoma of the Cervix.....	100
Carcinoma in Situ during Pregnancy and the Puerperium.....	119
Squamous Cell Carcinoma.....	122
Carcinoma in the Cervical Stump.....	132
Biology of Cervical Carcinoma.....	132
Classification of Clinical Stages.....	132
Primary Tumor Radiosensitivity.....	135
Metastases to Lymph Nodes (Radiosensitivity).....	142
Adenocarcinoma.....	143
Cervical Adenocarcinoma of Mesonephric (Wolffian) Origin.....	160
Carcinoma of the Cervix in Pregnancy.....	161
Tumors of Connective Tissue Origin.....	161
Leiomyoma.....	161
Leiomyosarcoma.....	161
Malignant Mixed Müllerian Tumors.....	161
Carcinosarcoma.....	161
Sarcoma Botryoides.....	171
Rare Tumors.....	171
Lymphoma.....	171
Hemangioma.....	171
Hemangioendothelioma.....	171
Ganglioneuroma.....	172
Malignant Melanoma.....	172
Metastatic Tumors.....	172
References.....	172

	Page No.
ENDOMYOMETRIUM.....	177
Benign Tumors of Endometrium.....	177
Figs. 149-156	
Endometrial Polyp.....	177
Placental Polyp.....	182
Malignant Tumors of Endometrium.....	183
Figs. 157-216	
Carcinoma.....	183
Relationship of Endometrial Hyperplasia to Carcinoma.....	185
Relationship of Carcinoma in Situ to Endometrial Carcinoma.....	201
Relationship of Abnormal Bleeding to Carcinoma of the Endometrium.....	202
Histochemistry of Normal, Potentially Malignant, and Malignant Endometrium.....	202
Clinical Staging of Endometrial Carcinoma.....	203
Relationship of Pyometra to Carcinoma of the Endometrium.....	222
Carcinosarcoma.....	223
Adenomyosis Uteri.....	224
Figs. 217-223	
Endolymphatic Stromal Myosis.....	230
Figs. 224-225	
Benign Tumors of Connective Tissue Origin.....	234
Figs. 226-244	
Leiomyoma.....	234
Hemangiopericytoma.....	235
Lipoma.....	235
"Benign Metastasizing Leiomyoma".....	246
Malignant Tumors of Connective Tissue Origin.....	246
Figs. 245-252; Plate VII	
Sarcoma.....	246
Table II.....	247
Leiomyosarcoma.....	247
Endometrial Stromal Sarcoma.....	252
Metastatic Tumors.....	257
Figs. 253-256	
References.....	258

	Page No.
<b>PELVIC SUPPORTING TISSUES</b> .....	262
Introduction.....	262
Figs. 257-261	
Rests, Cysts, and Tumors of Mesonephric (Wolffian) and Para-	
mesonephric (Müllerian) Origin.....	262
Figs. 262-279	
Mesonephric (Wolffian) Rests.....	262
Paramesonephric (Müllerian) Rests.....	262
Cystic Derivatives of Mesonephric and Parameso-	
nephric Structures in the Broad Ligament.....	263
Neoplasms of Mesonephric (Wolffian) Origin in the	
Broad Ligament.....	274
Neoplasms of Paramesonephric (Müllerian) Origin	
in the Broad Ligament.....	274
Mesonephric Rests in the Cervix.....	274
Mesonephric (Gartner's) Duct Rests of the Vagina...	275
References.....	275



# TUMORS OF THE VULVA, VAGINA, AND UTERUS

## VULVA

### INTRODUCTION

The vulva is formed by the labia majora, labia minora, clitoris, mons pubis, and the associated structures of the vestibule including the urethral meatus. Although its component parts are mainly skin and subcutaneous fat with their usual appendages, the vulvar tissue contains mucus secreting and apocrine sweat glands, erectile tissue, wolffian duct remnants, and the insertion of the round ligament with its accompanying pelvic peritoneum. The vulvar tissue is comparable to the sex skin of the higher primates and is similarly subject to influence by the steroid hormones. It may, on occasion, contain accessory breast tissue. Because of this complicated morphologic and functional anatomy, the tumors of the vulva are of diverse origin and of varying degrees of malignancy.

### BENIGN TUMORS OF EPITHELIAL ORIGIN

#### Papilloma

The papilloma is the only widely accepted benign neoplasm of epithelial origin. It is uncommon, usually single but may be multiple, and occurs anywhere on the vulva (fig. 2). Papillomas are usually small but may reach 4 to 5 cm. in diameter. They may occur at any age during adult life.

Papillomas are potentially malignant (3.2 percent for true papillomas, Novak) in contrast to the essential lack of malignant potential in *condyloma acuminatum* (fig. 1). The latter is not a true neoplasm but a hyperplasia. It is probably of viral origin and may arise or grow larger during pregnancy. Most authors (Taussig, 1940; Way, 1951) do not consider *condyloma acuminatum* a predisposing cause of vulvar carcinoma, whereas others (Charlewood and Shippel) have found cases where the cancer appears to have arisen from this papillary tumor-like lesion.

Simple but wide excision of a papilloma, provided careful examination of the adjacent skin shows no evidence of malignant change, is considered adequate therapy.

**Pigmented papilloma** may also occur on the vulva and is similar to such lesions elsewhere on the skin. Other terms for this lesion are acanthotic nevus, seborrheic keratosis, and senile wart.

## PAPILLARY LESIONS ARISING FROM THE SQUAMOUS EPITHELIUM OF THE VULVA

Figure 1. Condyloma acuminatum of vulva. Note pointed or acuminate masses of keratinized epithelium covering a thick arborescent epidermis of papillary pattern. Although this lesion is not a true neoplasm, its pattern and frequently active growth simulate neoplasia. Such a lesion rarely becomes malignant.  $\times 58$ . F.H.W.\* S-50-3800; A.F.I.P. Acc. No. 218754-307.

Figure 2. A true papilloma of the vulva. Note thickened arborescent squamous epithelium with relative lack of keratinization.  $\times 13$ . F.H.W. S-51-511; A.F.I.P. Acc. No. 218754-184.

Figure 3. Photomicrograph showing a squamous cell carcinoma of the vulva which may have arisen on the basis of a papilloma such as seen in figure 2. This also shows an arborescent papillary pattern without keratinization.  $\times 125$ . F.H.W. S-49-4854; A.F.I.P. Acc. No. 298591-3.

---

\*In this and following legends, F.H.W. stands for Free Hospital for Women, Brookline, Mass.



Fig. 1

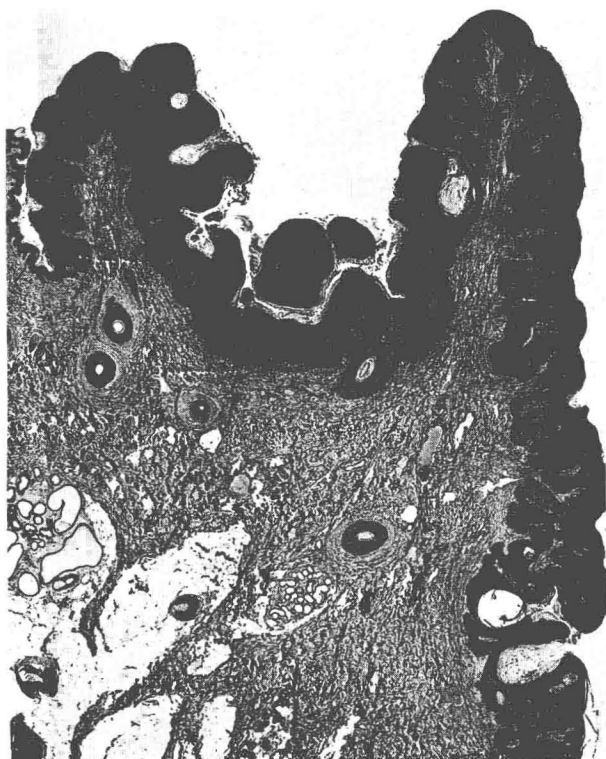


Fig. 2



Fig. 3

## MALIGNANT TUMORS OF EPITHELIAL ORIGIN

### **Carcinoma in Situ**

SYNONYMS AND RELATED TERMS: Bowen's disease; erythroplasia (erythroplakia) of Queyrat; extramammary Paget's disease; intraepidermal carcinoma.

All of these lesions occur on the vulva as well as elsewhere in the body. Willis believes that they are all variants of a single condition and states (p. 290): "For the pathologist there is only one entity, intra-epidermal carcinoma, which, like intra-duct carcinoma of the breast, may long remain confined within epithelial boundaries. Also like intra-duct carcinoma, intra-epidermal carcinoma shows many structural variations, but these do not denote distinct forms of tumour nor call for distinctive names."

Despite this point of view, it is well to describe Bowen's disease and extramammary Paget's disease separately. Bowen's disease appears to be a lesion purely of squamous epithelial origin, whereas extramammary Paget's disease appears to involve both squamous epithelium and apocrine sweat glands, sometimes resulting in a sweat gland carcinoma. The rare erythroplasia of Queyrat may well be a focal variant of Bowen's disease. It occurs on the glans and prepuce of the penis, on the vulva, or in the mouth.

### **Bowen's Disease**

Bowen's disease, an epithelial lesion (pl. I-A; figs. 11, 12) described by Bowen in 1912, may appear anywhere on the skin of middle-aged or elderly patients of either sex "... as slightly raised reddish-brown papular or plaque-like lesions, with crusted or eroded surfaces. The patches are often multiple in the affected region; they slowly enlarge, and may coalesce to form extensive irregular areas. After a long period, usually many years, invasive squamous-cell carcinoma develops . . ." (Willis, p. 287).

It may be added, however, that removal of the crusts leaves a dull red, smooth, moist surface with focal pearly elevations (Knight). The gross description and the account of the clinical course are applicable to the rare case occurring on the vulva. It appears, however, that invasive carcinoma does not inevitably follow Bowen's disease, since only 2 of 100 cases of this disease on file at the Armed Forces Institute of Pathology developed invasive carcinoma, although some patients were followed for 15 years (Grady). According to Jeffcoate and associates, Bowen's disease of the vulva is apt to become an invasive carcinoma when it spreads to mucosal surfaces such as the vagina.

Knight found that Bowen's disease of the vulva occurs between the ages of 25 and 73 years with symptoms, usually pruritis, of three months' to 11 years' duration (average 4.6 years). He considered that Bowen's disease of the vulva is not as rare as has been thought. He found six cases in the files at the Sloane Hospital, and during this same period there were 12 cases of invasive vulvar carcinoma.



Willis described the microscopic structure (p. 288): "The epidermis is thickened and the interpapillary processes broad and blunt. The cells, especially of the spinous layer, show great irregularity of size and shape, including giant or multinucleated forms. Mitotic figures are plentiful, and many of the nuclei are hyperchromatic or distorted. Large rounded pale or vacuolated cells, resembling those of Paget's disease, are often present. The surface may or may not show excessive keratosis. The dermis shows chronic inflammatory changes and abundant lymphoid and plasma cells."

The treatment is by local vulvectomy, since radiation is ineffective (Jeffcoate et al.). The prognosis in patients treated surgically is potentially good, unless the process has become a truly invasive carcinoma or the lesion is too extensive to be removed completely.

### **Extramammary Paget's Disease**

**DEFINITION.** A rare dermatosis limited to the skin of the axilla and anogenital regions of either sex, clinically and pathologically resembling Paget's disease of the breast, and characterized microscopically by the presence of large clear "Paget's cells." These cells are probably metastatic from an underlying carcinoma of apocrine sweat gland origin.

If this is a valid definition (Weiner; Stout; Parsons and Lohlein), it becomes obvious that many cases of so-called extramammary Paget's disease of the vulva only simulate this lesion. In reviews of the literature, many cases have been discarded (Weiner; Pinkus and Gould; Woodruff). Weiner accepted only 8 cases of which 4 had proven carcinoma, 1 an early carcinoma, and 3 apparently had no carcinoma. Woodruff found 21 cases in the literature and added 2 of his own but stated only 3 had underlying invasive carcinoma. Two fatal cases have been reported. In Weiner's case there was a typical clinico-pathologic syndrome of Paget's disease of the vulva with an underlying apocrine sweat gland carcinoma from which the patient died. At autopsy, metastases were found in the regional, inguinal, pelvic, and periaortic nodes, and in the uterus, right tube and ovary, adrenal, liver, and two ribs near the vertebral column. The fatal case reported by Woodruff and Richardson was found at autopsy to have extended to uterus and tubes and to have metastasized to inguinal and retroperitoneal lymph nodes and to skin and peripancreatic tissue.

**AGE INCIDENCE.** Woodruff considers that this lesion occurs at a younger age than does vulvar carcinoma, whereas Weiner found an age range of 35 to 84 years with an average of 62.6 years. Symptoms had been present for periods ranging from several months to eight years.

**GROSS.** The lesion is more commonly found on the labia majora than on the labia minora (Woodruff). It is red, moist, and sharply demarcated with