INTERNATIONAL HISTOLOGICAL CLASSIFICATION OF TUMOURS

No. 9

HISTOLOGICAL TYPING
OF OVARIAN TUMOURS

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ALREADY PUBLISHED IN THIS SERIES:

No. 1. Histological typing of lung tumours, by Leiv Kreyberg in collaboration with A. A. Liebow and E. A. Uehlinger (1967)


No. 3. Histological typing of soft tissue tumours, by F. M. Enzinger in collaboration with R. Lattes and H. Torloni (1969)


No. 7. Histological typing of salivary gland tumours, by A. C. Thackray in collaboration with L. H. Sobin (1972)

No. 8. Cytology of the female genital tract, by G. Riotton and W. M. Christopherson in collaboration with R. Lunt (1973)

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GENERAL PREFACE TO THE SERIES

Among the prerequisites for comparative studies of cancer are international agreement on histological criteria for the classification of cancer types and a standardized nomenclature. At present, pathologists use different terms for the same pathological entity, and furthermore the same term is sometimes applied to lesions of different types. An internationally agreed classification of tumours, acceptable alike to physicians, surgeons, radiologists, pathologists and statisticians, would enable cancer workers in all parts of the world to compare their findings and would facilitate collaboration among them.

In a report published in 1952,1 a subcommittee of the WHO Expert Committee on Health Statistics discussed the general principles that should govern the statistical classification of tumours and agreed that, to ensure the necessary flexibility and ease in coding, three separate classifications were needed according to (1) anatomical site, (2) histological type, and (3) degree of malignancy. A classification according to anatomical site is available in the International Classification of Diseases.2

The question of establishing a universally accepted classification by histological type has received much attention during the last 20 years and a particularly valuable Atlas of Tumor Pathology—already numbering more than 40 volumes—is being published in the USA by the Armed Forces Institute of Pathology under the auspices of the National Research Council. An Illustrated Tumour Nomenclature in English, French, German, Latin, Russian, and Spanish has also been published by the International Union Against Cancer (UICC).

In 1956 the WHO Executive Board passed a resolution3 requesting the Director-General to explore the possibility that WHO might organize centres in various parts of the world and arrange for the collection of human tissues and their histological classification. The main purpose of such centres would be to develop histological definitions of cancer types and to facilitate the wide adoption of a uniform nomenclature. This resolution was endorsed by the Tenth World Health Assembly in May 19574 and the following month a Study Group on Histological Classification of Cancer Types met in Oslo to advise

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WHO on its implementation. The Group recommended criteria for selecting tumour sites for study and suggested a procedure for the drafting of histological classifications and testing their validity. Briefly, the procedure is as follows:

1. For each tumour site, a tentative histopathological typing and classification is drawn up by a group of experts, consisting of up to ten pathologists working in the field in question.

2. An international reference centre and a number of collaborating laboratories are then designated by WHO to evaluate the proposed classification. These laboratories exchange histological preparations, accompanied by clinical information. The histological typing is then made in accordance with the proposed classification. Subsequently, one or more technical meetings are called by WHO to facilitate an exchange of opinions. If necessary, the classification is amended to take account of criticisms.

3. The international reference centre then prepares sets of microscope slides covering all the proposed histological types and sends these with the revised classification to other pathologists, usually not more than ten, for their comments and suggestions.

4. When replies have been received from all these reviewers, the classification is again revised in accordance with their comments. The international reference centre then prepares up to 100 sets of microscope slides of the various histological types and also drafts a text explaining the basis of the classification. In addition, photomicrographs are taken of the appropriate fields for the preparation of colour plates and 35-mm transparencies.

Since 1958, WHO has established 23 international reference centres covering tumours of the lung; breast; soft tissues; oropharynx; bone; ovaries; salivary glands; thyroid; skin; male urogenital tract; jaws; uterus; stomach and oesophagus; intestines; central nervous system; liver, biliary tract and pancreas; upper respiratory tract; eye; and endocrine glands; as well as oral precancerous conditions; the leukaemias and lymphomas; comparative onco­logy; and exfoliative cytology. This work has involved more than 200 pathologists from over 50 countries. The international reference centres for tumours of the lung; breast; soft tissues; oropharynx; bone; jaws; salivary glands; skin; and ovaries; and for leukaemias and lymphomas have completed their work, and some of the classifications prepared by these centres have already been published (see page 6).

The World Health Organization is indebted to the many pathologists who have participated and are participating in this large undertaking, especially to the heads of the international reference centres and of the collaborating laboratories. The pioneer work of many other international and national organizations in the field of histological classification of tumours has greatly
facilitated the task undertaken by WHO. Finally, WHO wishes to record its appreciation of the co-operation of the International Council of Societies of Pathology (ICSP) which has undertaken to distribute copies of the classifications, with corresponding sets of microscope slides, to national societies of pathology all over the world.
PREFACE TO
HISTOLOGICAL TYPING OF
OVARIAN TUMOURS

The WHO International Reference Centre for the Histological Classification of Ovarian Tumours was established in 1963 in the Research Institute of Oncology of the Academy of Medical Sciences of the USSR, Leningrad, USSR.

At a meeting held in Geneva in 1963, attended by Dr G. Gricouloff (Paris), Dr H. Hamperl (Bonn), Dr F. A. Langley (Manchester), Dr A. Luisi (São Paulo), Dr R. E. Scully (Boston), Dr G. Teilum (Copenhagen), Dr H. Torloni (WHO), and Dr A. J. Tuyns (WHO), a tentative classification of ovarian tumours was drafted. This was then evaluated by the International Reference Centre and its Collaborating Centres, a list of which will be found on p. 5.

Subsequently, the IRC began to distribute material (clinical information and histological sections) from selected cases of ovarian tumours to the 6 collaborating centres for histological typing according to the tentative classification. In all, 511 cases were thus studied by these centres and were reviewed at meetings in 1967 and 1971, attended by the heads of the centres. The classification and selected cases were reviewed by a second group of pathologists designated by WHO (see p. 5) and the final version was then adopted.

The authors then prepared the accompanying text and colour photomicrographs. The latter are reproduced as colour plates in this book and are also available as a collection of transparencies intended especially for teaching purposes. To help pathologists who might wish to know the corresponding terms in French, Russian, and Spanish, translations of the classification into these languages are also given, immediately following the English version.

It will, of course, be appreciated that the classification reflects the present state of knowledge and modifications are almost certain to be needed as experience accumulates. Furthermore, it necessarily represents a majority view, from which some pathologists may wish to dissent. It is nevertheless hoped that, in the interests of international cooperation, all pathologists will try to use the classification as put forward. Criticisms and suggestions for its improvement will be welcomed.

1 Representative of the International Federation of Gynecology and Obstetrics.
The publications in the series International Histological Classification of Tumours are not intended to serve as textbooks but rather to promote the adoption of a uniform terminology and categorization of tumours that will facilitate and improve communication among cancer workers. For this reason, the literature references have been intentionally kept to a minimum and readers are referred to standard works on the subject for extensive bibliographies.¹

¹ The following are some of the principal works that may be found useful for this purpose:

Tellum, G. (1971) Special tumors of ovary and testis, Philadelphia, Lippincott
INTRODUCTION

This classification is based primarily on the microscopic characteristics of the tumours and thus reflects the nature of morphologically identifiable cell types and patterns. Time-honoured and widely used terms have generally been retained unless they were considered to be seriously misleading. Controversial histogenetic designations have been adopted only when they appear to be the most convenient terms available. An effort has been made to conform to the classification of common epithelial tumours proposed by the International Federation of Gynecology and Obstetrics ¹ and subsequently used in publications from several large centres. It is a matter of controversy whether some of the lesions considered for inclusion in the classification are true neoplasms. With few exceptions we have designated these as tumours because it is difficult to disprove their neoplastic nature, but future experience may alter some of these interpretations. Broad categories of tumours have been divided into numerous subtypes throughout the classification in order to stimulate the investigation of smaller and possibly distinctive groups as well as general classes.

Because ovarian tumours are often composed of combinations of several types that may vary in their biological behaviour, it is important that the diagnostic terms chosen include all the varieties encountered and indicate as accurately as possible the proportion and distribution of each; an accompanying description of the microscopic characteristics may be helpful for this purpose.

Grading of malignant tumours or a modifying phrase indicating the degree of their differentiation has been widely recommended. According to some investigators this approach has proven to be of prognostic significance in evaluating certain types of ovarian tumour, but of doubtful value in others; it deserves continuing investigation in relation to all types, particularly as new methods of therapy evolve.

Because the ovarian stroma is specialized, it may be stimulated by the growth of a variety of tumours, either benign or malignant, primary or metastatic, to assume the morphological appearance of steroid-hormone-secreting tissue and to produce androgens, oestrogens, and rarely progestogens. Therefore, a complete microscopic evaluation of an ovarian tumour requires an appraisal of the appearance of the stroma, both inside the tumour and at its periphery. The occasional tumours in which evidence

exists that the stroma is endocrinologically active have been designated by some authors "tumours with functioning stroma". Although we have not included this term in the classification, it is useful in the investigation of this physiological phenomenon, which appears to occur only in ovarian tumours and not in tumours of other endocrine glands. In terms of function, it must also be emphasized that a variety of paraendocrine effects, such as hypercalcaemia, hypoglycaemia, and Cushing's syndrome, as well as disorders such as haemolytic anemia, may rarely be related to the presence of an ovarian tumour.

Sometimes it is necessary to base the diagnosis of an ovarian tumour on the microscopic examination of a metastatic deposit when this is the only tissue available. For example, the pathologist may receive an omental implant, but no sample of the primary tumour when laparotomy reveals it to be inoperable. It must be realized that although such a specimen is not ideal for diagnostic purposes and may even be misleading in an occasional case, its interpretation is necessary in order to avoid bias in analysing the results of treatment.

Rarely, phenotypic females have gonadal tumours arising in testicular rather than ovarian tissue (e.g., tumours in patients with testicular feminization, or the androgen-insensitivity syndrome). These tumours will be considered in a future publication in this series dealing with testicular tumours.

Finally it must be emphasized that the optimum microscopic evaluation of an ovarian tumour requires prompt fixation of small samples of tissue and that rubbing serosal surfaces and the linings of cysts detaches cells the interpretation of which is essential to a diagnosis.

Eponyms and synonyms are used only if they have been widely used in the literature or if their use is considered to be important for an understanding of the tumours. In such cases the preferred term is given first, followed by the synonym in square brackets.

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HISTOLOGICAL CLASSIFICATION
OF OVARIAN TUMOURS

I. COMMON “EPITHELIAL” TUMOURS

A. SEROUS TUMOURS

1. Benign
   (a) cystadenoma and papillary cystadenoma
   (b) surface papilloma
   (c) adenofibroma and cystadenofibroma

2. Of borderline malignancy [carcinomas of low malignant potential]
   (a) cystadenoma and papillary cystadenoma
   (b) surface papilloma
   (c) adenofibroma and cystadenofibroma

3. Malignant
   (a) adenocarcinoma, papillary adenocarcinoma, and papillary
cystadenocarcinoma
   (b) surface papillary carcinoma
   (c) malignant adenofibroma and cystadenofibroma

B. MUCINOUS TUMOURS

1. Benign
   (a) cystadenoma
   (b) adenofibroma and cystadenofibroma

2. Of borderline malignancy [carcinomas of low malignant potential]
   (a) cystadenoma
   (b) adenofibroma and cystadenofibroma

3. Malignant
   (a) adenocarcinoma and cystadenocarcinoma
   (b) malignant adenofibroma and cystadenofibroma
C. ENDOMETRIOID TUMOURS

1. Benign
   (a) adenoma and cystadenoma
   (b) adenofibroma and cystadenofibroma

2. Of borderline malignancy [carcinomas of low malignant potential]
   (a) adenoma and cystadenoma
   (b) adenofibroma and cystadenofibroma

3. Malignant
   (a) carcinoma
      (i) adenocarcinoma
      (ii) adenoacanthoma
      (iii) malignant adenofibroma and cystadenofibroma
   (b) endometrioid stromal sarcomas
   (c) mesodermal [müllerian] mixed tumours, homologous and heterologous

D. CLEAR CELL [MESONEPHROID] TUMOURS

1. Benign: adenofibroma

2. Of borderline malignancy [carcinomas of low malignant potential]

3. Malignant: carcinoma and adenocarcinoma

E. BRENNER TUMOURS

1. Benign

2. Of borderline malignancy [proliferating]

3. Malignant

F. MIXED EPITHELIAL TUMOURS

1. Benign

2. Of borderline malignancy

3. Malignant

G. UNDIFFERENTIATED CARCINOMA

H. UNCLASSIFIED EPITHELIAL TUMOURS
II. SEX CORD STROMAL TUMOURS

A. GRANULOSA-STROMAL CELL TUMOURS

1. Granulosa cell tumour
2. Tumours in the thecoma-fibroma group
   (a) thecoma
   (b) fibroma
   (c) unclassified

B. ANDROBLASTOMAS; SERTOLI-LEYDIG CELL TUMOURS

1. Well differentiated
   (a) tubular androblastoma; Sertoli cell tumour [tubular adenoma of Pick]
   (b) tubular androblastoma with lipid storage; Sertoli cell tumour with lipid storage [folliculome lipidique of Lecène]
   (c) Sertoli–Leydig cell tumour [tubular adenoma with Leydig cells]
   (d) Leydig cell tumour; hilus cell tumour
2. Of intermediate differentiation
3. Poorly differentiated [sarcomatoid]
4. With heterologous elements

C. GYNANDROBLASTOMA

D. UNCLASSIFIED

III. LIPID [LIPOID] CELL TUMOURS

IV. GERM CELL TUMOURS

A. DYSGERMINOMA

B. ENDODERMAL SINUS TUMOUR
C. EMBRYONAL CARCINOMA

D. POLYEMBRYOMA

E. CHORIOCARCINOMA

F. TERATOMAS

1. Immature
2. Mature
   (a) solid
   (b) cystic
      (i) dermoid cyst [mature cystic teratoma]
      (ii) dermoid cyst with malignant transformation
3. Monodermal and highly specialized
   (a) struma ovarii
   (b) carcinoid
   (c) struma ovarii and carcinoid
   (d) others

G. MIXED FORMS

V. GONADOBLASTOMA

A. PURE

B. MIXED WITH DYSGERMINOMA OR OTHER FORM OF GERM CELL TUMOUR

VI. SOFT TISSUE TUMOURS NOT SPECIFIC TO OVARY

VII. UNCLASSIFIED TUMOURS

VIII. SECONDARY [METASTATIC] TUMOURS
IX. TUMOUR-LIKE CONDITIONS

A. Pregnancy luteoma

B. Hyperplasia of ovarian stroma and hyperthecosis

C. Massive oedema

D. Solitary follicle cyst and corpus luteum cyst

E. Multiple follicle cysts [polycystic ovaries]

F. Multiple luteinized follicle cysts and/or corpora lutea

G. Endometriosis

H. Surface-epithelial inclusion cysts [germinal inclusion cysts]

I. Simple cysts

J. Inflammatory lesions

K. Parovarian cysts
CLASSIFICATION HISTOLOGIQUE
DES TUMEURS OVARIENNES

I. TUMEURS «ÉPITHELIALES» COMMUNES

A. TUMEURS SÉREUSES

1. Bénignes
   (a) cystadénome et cystadénome papillaire
   (b) papillome de surface
   (c) adénofibrome et cystadénofibrome

2. À la limite de la malignité [carcinomes de faible potentiel de malignité]
   (a) cystadénome et cystadénome papillaire
   (b) papillome de surface
   (c) adénofibrome et cystadénofibrome

3. Malignes *
   (a) adénocarcinome, adénocarcinome papillaire et cystadénocarcinome papillaire
   (b) carcinome papillaire de surface
   (c) adénofibrome et cystadénofibrome malins

B. TUMEURS MUCINEUSES

1. Bénignes
   (a) cystadénome
   (b) adénofibrome et cystadénofibrome

2. À la limite de la malignité [carcinome de faible potentiel de malignité]
   (a) cystadénome
   (b) adénofibrome et cystadénofibrome

3. Malignes
   (a) adénocarcinome et cystadénocarcinome
   (b) adénofibrome et cystadénofibrome malins.

* Carcinome et adénocarcinome sont synonymes d'épithélioma et épithélioma glandulaire.
C. Tumeurs endométrioïdes

1. Bénignes
   (a) adénome et cystadénome
   (b) adénofibrome et cystadénofibrome
2. À la limite de la malignité [carcinome de faible potentiel de malignité]
   (a) adénome et cystadénome
   (b) adénofibrome et cystadénofibrome
3. Malignes
   (a) carcinome
      (i) adénocarcinome
      (ii) adénoacanthome
      (iii) adénofibrome malin et cystadénofibrome malin
   (b) sarcomes endométrioïdes du type stromal
   (c) tumeurs mixtes mésodermiques [mülleriennes] homologues et hétérologues

D. Tumeurs à cellules claires [mésonephroïdes]

1. Bénignes: adénofibrome
2. À la limite de la malignité [carcinome de faible potentiel de malignité]
3. Malignes: carcinome et adénocarcinome

E. Tumeurs de Brenner

1. Bénignes
2. À la limite de la malignité
3. Malignes

F. Tumeurs mixtes épithéliales

1. Bénignes
2. À la limite de la malignité
3. Malignes

G. Carcinomes indifférenciés

H. Tumeurs épithéliales non classées
II. TUMEURS DU MÉSENCHYME DES « CORDONS SEXUELS »

A. TUMEURS À CELLULES DE LA GRANULOSA ET STROMALES

1. Tumeur à cellules de la granulosa
2. Tumeurs du groupe fibro-thécal
   (a) Thécome
   (b) Fibrome
   (c) Non classées

B. ANDROBLASTOME; TUMEURS À CELLULES DE SERTOLI ET LEYDIG

1. Tumeurs bien différenciées
   (a) androblastome tubulaire; tumeur à cellules de Sertoli [adénome tubulé de Pick]
   (b) androblastome tubulaire, à cellules lipidiques; tumeur à cellules de Sertoli lipidiques [folliculome lipidique de Lecène]
   (c) tumeur à cellules de Sertoli et de Leydig
   (d) tumeur à cellules de Leydig; tumeur à cellules du hile

2. A différenciation intermédiaire

3. Peu différenciées [sarcomatoïdes]

4. Avec éléments hétérologues

C. GYNAandroblastome

D. NON CLASSÉES

III. TUMEURS À CELLULES LIPIDIQUES [LIPOIDIIQUES]

IV. TUMEURS DES CELLULES GERMINALES

A. DYSGERMINOME

B. TUMEUR DU SINUS ENDODERMIQUE
C. **Carcinome embryonnaire**

D. **Polyembryome**

E. **Choriocarcinome**

F. ** tératomes**

   1. Immature

   2. Mature
      (a) solide
      (b) kystique
         (i) kyste dermoïde
         (ii) kyste dermoïde avec transformation maligne

   3. Monodermiques et hautement spécialisés
      (a) goître ovarien [struma ovarii]
      (b) carcinoïde
      (c) goître ovarien et carcinoïde
      (d) autres

G. **formes mixtes**

V. **Gonadoblastome**

A. **pur**

B. ** Associé avec un dysgerminome ou d'autres formes de tumeur des cellules germinales**

VI. **Tumeurs des tissus mois non spécifiques**

VII. **Tumeurs non classées**

VIII. **Tumeurs secondaires [méstatatiques]**
IX. LÉSIONS PSEUDO-TUMORALES

A. Lutéome de la grossesse

B. Hyperplasie du stroma ovarien et Hyperthécose

C. Œdème massif

D. Kyste folliculaire solitaire et Kyste du corps jaune

E. Kystes folliculaires multiples [ovaires polykystiques]

F. Follicules kystiques lutiéinisés multiples et/ou Corps jaunes multiples

G. Endométriose

H. Kystes par inclusion de l’ épithélium de surface [kystes germi- natifs par invagination]

I. Kystes simples

J. Lésions inflammatoires

K. Kystes parovariens
ГИСТОЛОГИЧЕСКАЯ КЛАССИФИКАЦИЯ ОПУХОЛЕЙ ЯИЧНИКОВ

I. «ЭПИТЕЛИАЛЬНЫЕ» ОПУХОЛИ

А. Серозные опухоли

1. Доброкачественные:
   a) цистаденома и папиллярная цистаденома
   b) поверхностная папиллома
   в) аденофиброма и цистаденофиброма

2. Пограничные [потенциально низкой степени злокачественности]:
   a) цистаденома и папиллярная цистаденома
   b) поверхностная папиллома
   в) аденофиброма и цистаденофиброма

3. Злокачественные:
   a) аденокарцинома, папиллярная аденокарцинома и папиллярная цистадепокарцинома
   b) поверхностная папиллярная карцинома
   в) злокачественная аденофиброма и цистаденофиброма

Б. Муцинозные опухоли

1. Доброкачественные:
   a) цистаденома
   b) аденофиброма и цистаденофиброма

2. Пограничные [потенциально низкой степени злокачественности]:
   a) цистаденома
   b) аденофиброма и цистаденофиброма

3. Злокачественные:
   a) аденокарцинома и цистадекарцинома
   b) злокачественная аденофиброма и цистаденофиброма

— 27 —
В. Эндометриоидные опухоли

1. Доброкачественные:
   a) аденома и цистаденома
   b) аденофиброма и цистаденофиброма

2. Пограничные [потенциально низкой степени злокачественности]:
   a) аденома и цистаденома
   b) аденофиброма и цистаденофиброма

3. Злокачественные:
   a) карцинома
      i) adenокарцинома
      ii) аденокактома
      iii) злокачественная аденофиброма и цистаденофиброма
   b) эндометриоидная стромальная саркома
   в) мезодermalные [мюллеровы] смешанные опухоли, гомологичные и гетерологичные

Г. Светлоклеточные [мезоцендроидные] опухоли

1. Доброкачественные: аденофиброма

2. Пограничные [потенциально низкой степени злокачественности]

3. Злокачественные: карцинома и аденокарцинома

Д. Опухоли Бреннера

1. Доброкачественные

2. Пограничные [пограничной злокачественности]

3. Злокачественные

Е. Смешанные эпителиальные опухоли

1. Доброкачественные

2. Пограничные [пограничной злокачественности]

3. Злокачественные

Ж. Недифференцированная карцинома

3. Неклассифицируемые эпителиальные опухоли
II. ОПУХОЛИ СТРОМЫ ПОЛОВОГО ТЯЖА

А. Гранулемо–стромальноклеточные опухоли

1. Гранулемоклеточная опухоль
2. Группа теком–фиброн
   а) текома
   б) фиброма
   в) неклассифицируемые

Б. Андробластомы; опухоли из клеток Сертоли и Лейдига

1. Высокодифференцированные
   а) тубулярная андробластома; опухоль из клеток Сертоли
   б) тубулярная андробластома с накоплением липидов; опухоль из клеток Сертоли с накоплением липидов [липидная фолликулома Лесена]
   в) опухоль из клеток Сертоли и Лейдига
   г) опухоль из клеток Лейдига; опухоль из хилосных клеток

2. Промежуточной [переходной] дифференцировки
3. Низкодифференцированные [саркоматоидные]
4. С гетерологическими элементами

В. Гинандробластома

Г. Неклассифицируемые опухоли стромы полового тяжа

III. ЛИПИДНКОЛЕТОЧНЫЕ [ЛИПОИДНКОЛЕТОЧНЫЕ] ОПУХОЛИ

IV. ГЕРМИНОГЕННЫЕ ОПУХОЛИ

А. Дистерминома

Б. Опухоль эндодермального синуса
В. ЭМБРИОНАЛЬНАЯ КАРЦИНОМА

Г. ПОЛИЭМБРИОМА

Д. ХОРИОНЭПITЕЛЮМА

Е. ТЕРАТОМЫ

1. Незрелые
2. Зрелые:
   а) солидные
   б) кистозные:
      i) дермоидная киста
      ii) дермоидная киста с малигнизацией
3. Монодермальные [высоко специализированные]:
   а) струма яичника
   б) карциноид
   в) струма яичника и карциноид
   г) другие

Ж. СМЕШАННЫЕ ГЕРМИНОГЕННЫЕ ОПУХОЛИ

V. ГОНАДОБЛАСТОМА

А. ЧИСТАЯ [Без примеси других форм]

Б. СМЕШАННАЯ С ДИСГЕРМИНОМОЙ И ДРУГИМИ ФОРМАМИ ГЕРМИНОГЕННЫХ ОПУХОЛЕЙ

VI. ОПУХОЛИ МЯГКИХ ТКАНЕЙ НЕСПЕЦИФИЧНЫЕ ДЛЯ ЯИЧНИКОВ

VII. НЕКЛАССИФИЦИРОВАННЫЕ ОПУХОЛИ

VIII. ВТОРИЧНЫЕ [МЕТАСТАТИЧЕСКИЕ] ОПУХОЛИ
IX. ОПУХОЛЕВИДНЫЕ ПРОЦЕССЫ

А. ЛЮТЕОМА БЕРЕМЕННОСТИ

Б. ГИПЕРПЛАЗИЯ СТРОМЫ ЯЧНИКА И ГИПЕРТЕКЗОЗ

В. МАССИВНЫЙ ОТЕК ЯЧНИКА

Г. ЕДИНИЧНАЯ ФОЛЛИКУЛЯРНАЯ КИСТА И КИСТА ЖЕЛТОГО ТЕЛА

Д. МНОЖЕСТВЕННЫЕ ФОЛЛИКУЛЯРНЫЕ КИСТЫ [ПОЛИКИСТОЗНЫЕ ЯЧНИКИ]

Е. МНОЖЕСТВЕННЫЕ ЛЮТЕИНИЗИРОВАННЫЕ ФОЛЛИКУЛЯРНЫЕ КИСТЫ И (ИЛИ) ЖЕЛТЫЕ ТЕЛА

Ж. ЭНДОМЕТРИОЗ

З. ПОВЕРХНОСТНЫЕ ЭПИТЕЛИАЛЬНЫЕ КИСТЫ ВКЛЮЧЕНИЯ [ГЕРМИНАЛЬНЫЕ КИСТЫ ВКЛЮЧЕНИЯ]

И. ПРОСТЫЕ КИСТЫ

К. ВОСПАЛИТЕЛЬНЫЕ ПРОЦЕССЫ

Л. ПАРАОВАРИАЛЬНЫЕ КИСТЫ
CLASIFICACION HISTOLOGICA
DE LOS TUMORES DEL OVARIO

I. TUMORES «EPITELIALES» COMUNES

A. TUMORES SEROSOS

1. Benignos
   a) cistoadenoma y cistoadenoma papilar
   b) papiloma superficial
   c) adenofibroma y cistoadenofibroma

2. En el límite de la malignidad [carcinomas de bajo potencial maligno]
   a) cistoadenoma y cistoadenoma papilar
   b) papiloma superficial
   c) adenofibroma y cistoadenofibroma

3. Malignos
   a) adenocarcinoma, adenocarcinoma papilar y cistoadenocarcinoma papilar
   b) carcinoma papilar superficial
   c) adenofibroma y cistoadenofibroma malignos

B. TUMORES MUCINOSOS

1. Benignos
   a) cistoadenoma
   b) adenofibroma y cistoadenofibroma

2. En el límite de la malignidad [carcinoma de bajo potencial maligno]
   a) cistoadenoma
   b) adenofibroma y cistoadenofibroma

3. Malignos
   a) adenocarcinoma y cistoadenocarcinoma
   b) adenofibroma y cistoadenofibroma malignos
C. TUMORES ENDOMETRIOIDES

1. Benignos
   a) adenoma y cistoadenoma
   b) adenofibroma y cistoadenofibroma

2. En el límite de la malignidad [carcinomas de bajo potencial maligno]
   a) adenoma y cistoadenoma
   b) adenofibroma y cistoadenofibroma

3. Malignos
   a) carcinoma
      i) adenocarcinoma
      ii) adenoacantoma
      iii) adenofibroma maligno y cistoadenofibroma maligno
   b) sarcomas estromáticos endometrioides
   c) tumores mesodérmicos mixtos [mullerianos], homólogos y heterólogos

D. TUMORES DE CÉLULAS CLARAS [MESONEFROIDES]

1. Benignos: adenofibroma

2. En el límite de la malignidad [carcinomas de bajo potencial maligno]

3. Malignos: carcinoma y adenocarcinoma

E. TUMORES DE BRENNER

1. Benignos

2. En el límite de la malignidad

3. Malignos

F. TUMORES EPITELIALES MIXTOS

1. Benignos

2. En el límite de la malignidad

3. Malignos

G. CARCINOMA INDIFERENCIADO

H. TUMORES EPITELIALES NO CLASIFICADOS
II. TUMORES DE LOS CORDONES SEXUALES-ESTROMA

A. TUMORES DE CÉLULAS GRANULOSO-ESTROMÁTICAS

1. Tumor de células de la granulosa
2. Tumores del grupo tecoma-fibroma
   a) tecoma
   b) fibroma
   c) no clasificados

B. ANDROBLASTOMAS; TUMORES DE CÉLULAS DE SERTOLI-LEYDIG

1. Bien diferenciados
   a) androblastoma tubular; tumor de células de Sertoli [adenoma tubular de Pick]
   b) Androblastoma tubular con depósito lipídico; tumor de células de Sertoli con depósito lipídico [folículo lipídico de Lecène]
   c) tumor de células de Sertoli-Leydig
   d) tumor de células de Leydig; tumor de células hiliares
2. Medianamente diferenciados
3. Poco diferenciados [sarcomatoides]
4. Con elementos heterólogos

C. GINANDROBLASTOMA

D. NO CLASIFICADOS

III. TUMORES DE CÉLULAS LIPÓIDEAS

IV. TUMORES DE CÉLULAS GERMINALES

A. DISGERMINOMA

B. TUMOR DE LOS SENOS ENDODÉRMICOS
C. CARCINOMA EMBRIONARIO

D. POLIEMBRIOMA

E. CORIOCARCINOMA

F. TERATOMAS
   1. Inmaduros
   2. Maduros
      a) sólidos
      b) quísticos
         i) quistes dermoides
         ii) quistes dermoides con transformación maligna
   3. Monodérmicos y altamente especializados
      a) estruma ovárico
      b) carcinoide
      c) estruma ovárico y carcinoide
      d) otros

G. FORMAS MIXTAS

V. GONADOBLASTOMA

A. PURO

B. ASOCIADO A UN DISGERMINOMA Y A OTRAS FORMAS DE TUMORES DE CÉLULAS GERMINALES

VI. TUMORES DE TEJIDOS BLANDOS NO ESPECÍFICOS DEL OVARIO

VII. TUMORES NO CLASIFICADOS

VIII. TUMORES SECUNDARIOS [METASTÁTICOS]
IX. LESIONES SEUDOTUMORALES

A. LUTEOMA GRAVIDICO

B. HIPERPLASIA DEL ESTROMA OVÁRICO E HIPERTECOSIS

C. EDEMA MASIVO

D. QUISTE FOLICULAR SOLITARIO Y QUISTE DEL CUERPO LÚTEO

E. QUISTES FOLICULARES MÚLTIPLES [OVARIOS POLIQUISTICOS]

F. QUISTES FOLICULARES LUTEINIZADOS MÚLTIPLES Y/O CUERPOS LÚTEOS

G. ENDOMETRIOSIS

H. QUISTES POR INCLUSIÓN DEL EPITELIO SUPERFICIAL [QUISTES POR INCLUSIÓN GERMINAL]

I. QUISTES SIMPLES

J. LESIONES INFLAMATORIAS

K. QUISTES PARAOVÁRICOS
DEFINITIONS AND EXPLANATORY NOTES

I. COMMON "EPITHELIAL" TUMOURS

Tumours composed of one or more of several types of epithelium and stroma in a variety of combinations and generally considered to be derived from the surface (coelomic) epithelium (mesothelium) covering the ovary and from the underlying ovarian stroma (Fig. 1).

The word "common" has been applied because the majority of ovarian tumours belong in this general category. Origins other than surface epithelium are possible for some of these tumours.

A form of common epithelial tumour intermediate between one that is morphologically clearly benign and one that is obviously malignant has been termed a tumour "of borderline malignancy", or a "carcinoma of low malignant potential". This type of tumour can be defined as one that has some, but not all, of the morphological features of malignancy; those present include in varying combinations: stratification of the epithelial cells, apparent detachment of cellular clusters from their sites of origin, and mitotic activity and nuclear abnormalities intermediate between those of clearly benign and unquestionably malignant tumours of a similar cell type; on the other hand, obvious invasion of the adjacent stroma is lacking. Tumours with epithelial cell proliferation or atypicality of a minor degree should be placed in the benign category.

The assessment of stromal invasion may be difficult or even impossible in certain cases. It can be accomplished most easily in the examination of serous cystic tumours, which are usually composed of large cysts lined by neoplastic epithelial cells. The value of making a distinction between borderline and unquestionably malignant forms has not yet been clearly demonstrated for common epithelial tumours other than those in the serous category, nor is it certain that it is possible to achieve uniformly applicable criteria for making such a distinction. However, an attempt to apply this approach to all common epithelial tumours is recommended for purposes of investigation. Benign, borderline and malignant forms of any of the neoplastic types listed below may coexist in any one tumour.

It must be emphasized that tumours of borderline malignancy occasionally implant on the peritoneum and that such implants may be invasive; rarely, distant metastases occur. However, in order that the diagnosis be
morphologically objective and have prognostic significance it must be based exclusively on an examination of the ovarian tumour without consideration of whether spread beyond the ovary has taken place. The practical validity of this diagnostic approach has been demonstrated by the high survival rate of patients with serous tumours of borderline malignancy, even when these were complicated by peritoneal implants,¹ as well as by the typically indolent course of these tumours when they have spread beyond the ovary and the occasional spontaneous regression of peritoneal implants.²

The descriptive prefixes "adeno-" and "cystadeno-" and the adjective "papillary" should be added to the more specific designation of a tumour whenever appropriate. The suffix "-fibroma" should be used when a tumour, with the exception of the Brenner tumour, is composed predominantly of stroma derived from the ovarian stroma. If the neoplastic epithelium is growing primarily on the peritoneal surface of the ovary, the word "surface" is an appropriate addition to the diagnostic term. The adjective indicating the epithelial cell type should generally be placed first among the descriptive words.

A. SEROUS TUMOURS (Fig. 2–16)

Tumours composed of epithelium resembling that of the fallopian tube or the surface epithelium of the ovary; ciliated cells are found almost always in the benign serous tumours, usually in those of borderline malignancy and rarely in the carcinomatous forms.

Psammoma bodies may be present, at times in great profusion, but do not in themselves indicate malignancy. The tumour cells may produce considerable mucin, which is almost entirely extracellular. The borderline and carcinomatous forms typically have a well developed papillary pattern, but the carcinoma is often predominantly solid in its architecture. The neoplastic epithelium may line cysts, the external surface of the ovary, or both.

B. MUCINOUS TUMOURS (Fig. 17–27)

Tumours, the epithelial element of which includes a prominent component of mucin-filled cells. The epithelium may resemble endocervical or enteric epithelium, occasionally containing argentaffin cells and rarely Paneth cells.

Tumours in the mucinous category may be associated with pseudomyxoma peritonei, but the presence of this complication per se does not

warrant a morphological diagnosis of malignancy of the ovarian tumour. When a mucocelle of the appendix is present in addition to a mucinous ovarian mass, it may be impossible to determine whether the former, the latter, or both are the primary sites of involvement. For practical purposes in such cases, the ovarian mass is regarded as a primary tumour, but the additional presence of the appendiceal lesion must also be recorded.¹

The possibility of metastatic adenocarcinoma, particularly of large-intestinal origin, should always be considered in cases of tumours having the appearance of mucinous adenocarcinoma; in some instances a metastasis cannot be excluded solely on the basis of an examination of the ovarian tumour.

C. ENDOMETRIOID TUMOURS (Fig. 30–39)

Tumours having the microscopic features of one or more of the typical forms of endometrial neoplasia.

Although endometriosis, which is composed of epithelium and stroma of endometrial type (Fig. 28 & 29), may have the gross features of a neoplasm, may form nodules resembling endometrial polyps, and may be present in association with a variety of tumours in the common epithelial category (Fig. 29), this disorder lacks many of the features of neoplasia and has been classified as a tumour-like condition. A small number of endometrioid tumours can be shown to have arisen in endometriosis (Fig. 31), but the demonstration of such an origin is not required for the diagnosis.

The cells of endometrioid tumours may produce mucin, which is predominantly extracellular. Squamous differentiation of the neoplastic cells is common and if present in an endometrioid carcinoma, justifies the diagnosis of adenoacanthoma; the squamous cells of the adenoacanthoma may have a benign or a malignant appearance. The prognostic significance of cytologic malignancy of the squamous cells has not yet been determined. Endometrioid carcinomas may have a markedly papillary pattern, which is unusual in carcinomas of the endometrium.

Often an endometrioid carcinoma of the ovary is associated with a carcinoma of the endometrium that appears similar on microscopic examination. In such cases it may be impossible to determine whether either or both tumours are primary, and the presence and extent of each should be recorded in the diagnosis.

The mesodermal (mullerian) mixed tumours of the ovary are similar to those encountered more commonly in the body of the uterus, containing elements derived exclusively from mesoderm. These tumours may be homologous (carcinosarcomas) or contain heterologous elements such as skeletal

muscle, cartilage, osteoid and bone. Unlike the immature teratoma, which occurs almost always in children or young women, the mesodermal mixed tumour is encountered almost exclusively in menopausal or postmenopausal women. The cartilage that is found in heterologous mesodermal mixed tumours typically has bizarre nuclei similar to those that may be seen in chondrosarcomas (Fig. 39), whereas the cartilage in immature teratomas characteristically has an embryonal appearance (Fig. 99). The carcinomatous element of the mesodermal mixed tumour resembles various types within the common “epithelial” category (Fig. 38); in contrast the malignant epithelium of the immature teratoma is typically of an embryonal type. Finally, the immature teratoma also contains structures of ectodermal (commonly neuroectodermal) and/or endodermal derivation.

D. CLEAR CELL [MESONEPHROID] TUMOURS (Fig. 40–45)

Tumours composed of (a) clear cells containing glycogen and resembling those of the renal cell carcinoma and/or (b) “hobnail”, or peg-shaped, cells lining small cysts and tubules; “hobnail” cells are characterized by scant cytoplasm and large nuclei that project into the lumen.

Cells with abundant eosinophilic cytoplasm may also be seen. Mucin secretion is often present within the cysts and tubules, but is absent intracellularly. The patterns encountered include solid, glandular, tubular, papillary, and microcystic, or combinations thereof.

The terms “mesonephroma”, “mesonephric carcinoma” and “mesometanephric carcinoma” have been avoided because of the questionable relation of these tumours to the mesonephros or metanephros.

On very rare occasions, a renal cell carcinoma metastasizes to the ovary and may be confused with a primary clear cell carcinoma. This tumour must also be distinguished from the endodermal sinus tumour, the dysgerminoma and the lipid cell tumour.

E. BRENNER TUMOURS (Fig. 46–52)

Fibroepithelial tumours composed of stroma derived from the ovarian stroma and nests of polyhedral or rounded epithelial cells of transitional, or urothelial, type; these cells often contain grooved, “coffee-bean” nuclei.

The nests may form glands or cysts lined by flat, cuboidal or columnar cells; these cells often contain mucin and are occasionally ciliated. Cells of transitional cell type predominate; squamous cells may also be present.
Most Brenner tumours are benign. Because the small number of borderline forms reported in the literature have not been proven to be malignant clinically, certain authors prefer the term "proliferating Brenner tumour" to "borderline malignancy". The designation "malignant Brenner tumour" is used when carcinomatous change has taken place in the predominant cell type with the development of either a transitional cell or squamous cell carcinoma. A predominantly mucinous carcinoma in which Brenner elements are also present should be classified as either a mucinous carcinoma or a mixed epithelial tumour, depending on the quantity of the Brenner element present (see below).

F. MIXED EPITHELIAL TUMOURS (Fig. 53)

Tumours composed of a mixture of two or more of the five types described above.

When only a small quantity of a second or third type of epithelium is present, the tumour should be classified according to the predominant element. For example, endometrioid carcinomas, like carcinomas of the uterine body, occasionally contain foci of glands lined by mucin-filled epithelial cells, but their quantity is usually insufficient to warrant a diagnosis of a mixed epithelial tumour.

G. UNDIFFERENTIATED CARCINOMA (Fig. 54)

A malignant tumour of epithelial structure that is too poorly differentiated to be placed in any of the other groups.

Although it may not be possible to establish the origin of many of these tumours, they have been included in the common epithelial category in view of the frequently observed transitions between them and clearly recognizable forms of common epithelial carcinoma. Rare foci of differentiation, such as gland formation, psammoma body formation, or mucin production, do not exclude the diagnosis of undifferentiated carcinoma.

H. UNCLASSIFIED EPITHELIAL TUMOURS

Tumours of common epithelial type with features intermediate between two or more of the specific categories.

For example, it may be difficult, or even impossible, to differentiate a serous adenofibroma from an endometrioid adenofibroma in certain cases.

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The problem of making a specific diagnosis is encountered particularly often in cases of poorly differentiated adenocarcinomas or papillary adenocarcinomas. Careful study and extensive sampling is desirable in order to make specific diagnoses in such instances.

II. SEX CORD STROMAL TUMOURS

Tumours containing granulosa cells, theca cells, collagen-producing stromal cells, Sertoli cells, Leydig cells, and cells resembling their embryonic precursors, singly or in various combinations.

These tumours have also been designated gonadal stromal tumours; sex cord-mesenchyme tumours; and mesenchymomas. The generic term chosen is not intended to reflect a commitment to any one theory of gonadogenesis, but only acknowledges the presence in these tumours of two distinct categories of ovarian and testicular homologous cell types: granulosa and Sertoli cells (sex cord elements) and theca and Leydig cells (stromal elements).

A. GRANULOSA-STROMAL CELL TUMOURS

Tumours containing granulosa cells, theca cells, and stromal cells resembling fibroblasts singly or in various combinations.

1. Granulosa cell tumour (Fig. 55-62)

A tumour of female cell types containing more than a small component of granulosa cells.

The cells may be arranged in a variety of patterns, including follicular (microfollicular and macrofollicular), trabecular, insular, and diffuse (sarcomatoid). Usually a combination of patterns exists in any one tumour, and theca cells are present in addition to granulosa cells; either cell type may be luteinized (i.e., contain abundant cytoplasm and have a morphological appearance similar to that of cells of the corpus luteum). The microfollicular pattern is characterized by the presence of the distinctive Call-Exner bodies (Fig. 55 & 56).

Adenocarcinomas with small, uniform glands may resemble superficially microfollicular granulosa cell tumours and are often misdiagnosed as such; a similar problem in differential diagnosis exists for undifferentiated carcinomas and diffuse granulosa cell tumours. The most specific diagnostic feature of the granulosa cell tumour, in addition to its characteristic patterns, is the appearance of its nuclei, which may be either irregular in shape, with their long axes directed haphazardly, or round and uniform; although mitoses may be numerous, the nuclei typically lack the pleomorphism and
hyperchromatism of the nuclei of adenocarcinomas and undifferentiated carcinomas; the presence of nuclear grooving in granulosa cells is often helpful in the differential diagnosis (Fig. 59).

The distinction of the microfollicular granulosa cell tumour from primary and metastatic carcinoid tumours is discussed below.

Granulosa cell tumours are usually oestrogenic, but may be inactive or rarely androgenic. They are clinically malignant in a minority of cases; the course of malignancy is usually low-grade, being characterized by a slow evolution or a late recurrence.

2. Thecoma-fibroma group

Tumours forming a continuous spectrum from those composed entirely of cells resembling fibroblasts and producing collagen to those containing a predominance of cells resembling lipid-rich theca cells.

(a) Thecoma [theca cell tumour] (Fig. 63–66)

A stromal tumour, many cells of which contain abundant lipid-rich cytoplasm and resemble theca cells.

The fibrous component varies in quantity. Thecomas should be differentiated from diffuse granulosa cell tumours; reticulin staining, which reveals an abundance of fibrils investing individual theca cells and relatively little within aggregates of granulosa cells, is often helpful in the differential diagnosis (Fig. 62 & 65). The thecoma is typically oestrogenic and almost invariably benign.

(b) Fibroma (Fig. 67 & 68)

A stromal tumour composed of spindle cells producing abundant collagen.

Some tumours are markedly oedematous (Fig. 68); these are more apt to be associated with ascites and hydrothorax (Demons-Meigs syndrome) than those containing little intercellular fluid. It is possible that an occasional fibroma is derived from nonspecific fibrous tissue within the ovary rather than from the ovarian stroma. The fibroma is non-functioning.

(c) Unclassified

Stromal tumours intermediate between the thecoma and fibroma in morphological appearance.

B. ANDROBLASTOMAS; SERTOLI-LEYDIG CELL TUMOURS

Tumours containing Sertoli and Leydig cells of varying degrees of maturity; indifferent gonadal cells of embryonal appearance are present in certain cases.
The term "arrhenoblastoma", although widely used, is not considered appropriate because it carries the connotation of masculinization. Although most of these tumours are virilizing, some are endocrinologically inactive and others are oestrogenic, in keeping with the oestrogenic potential of the normal testis. The designation "androblastoma" is preferred by some investigators because it reflects the wide range of differentiation of these tumours, which recapitulate, in an imperfect manner, stages of testicular development. The term "Sertoli-Leydig cell tumours" is the choice of others because it indicates the nature of the cell types that are present in these tumours in either mature or immature form. Both designations enjoy wide acceptance and are listed as alternatives in the classification.

The well differentiated forms of these tumours are almost always benign, while those less mature are more apt to be malignant.

The various cellular components combine in diverse and often distinctive patterns to produce identifiable subgroups.

1. Well differentiated

(a) Tubular androblastoma; Sertoli cell tumour [tubular adenoma of Pick] (Fig. 69–71)

A tumour composed entirely or almost entirely of Sertoli cells forming well defined tubules.

The tubules may have lumens or be solid like those of the prepubertal testis. The Sertoli cells may contain lipid in minor quantities. Leydig cells may be present in small numbers.

(b) Tubular androblastoma with lipid storage; Sertoli cell tumour with lipid storage [folliculome lipidique of Lecène] (Fig. 72–74)

A tumour composed of Sertoli cells distended with lipid and arranged in a tubular pattern.

Like its counterpart in the testis, this tumour may be associated with oestrogenic manifestations. It should be distinguished on microscopical examination from non-tubular lipid cell tumours, which are usually masculinizing.

(c) Sertoli-Leydig cell tumour [tubular adenoma with Leydig cells] (Fig. 75)

A tumour containing more than a small component of Leydig cells as well as Sertoli cells arranged in a tubular pattern.

It may be androgenic or oestrogenic.

(d) Leydig cell tumour; Hilus cell tumour (Fig. 76)

A tumour composed entirely of Leydig cells.

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1 Teilmann, G. (1958) Cancer (Philad.), 11, 769.
This tumour may represent a unilateral development of an androblastoma, or Sertoli-Leydig cell tumour, or arise directly from the Leydig cells that are normally present in the ovarian hilus (hilus cells). It cannot be differentiated with certainty from the lipid cell tumour unless crystalloids of Reinke can be identified in the cytoplasm of its cells (Fig. 76). The typical endocrine effect is virilization.

2. Of intermediate differentiation (Fig. 77–78)

Tumours in which immature Sertoli cells are typically arranged diffusely, in islands, or in cords resembling testicular embryonic sex cords; well-defined tubules may be present and mature Leydig cells are usually also identifiable.

3. Poorly differentiated [sarcomatoid] (Fig. 79)

Tumours largely composed of tissue resembling that of the indifferent gonad; these tumours may resemble sarcomas.

4. With heterologous elements (Fig. 80)

Tumours of intermediate or poor differentiation that contain, in addition to the components described under (2) or (3), cell types foreign to the developing gonad; these include tubules and cysts lined by mucus-filled epithelial cells and argentaffin cells, cartilage, and skeletal muscle.

These tumours have not been classified as teratomas because they have not been reported to contain the wide variety of tissues encountered in typical teratomas; moreover, tissue of gonadal type has rarely, if ever, been identified as part of a teratoma.

C. GYNANDROBLASTOMA

A very rare tumour in which collections of granulosa cells with typical Call-Exner bodies coexist with hollow tubules lined by Sertoli cells.

The term is only morphological and does not imply a specific type of hormone production. This tumour is also known as sex cord stromal tumour of mixed cell types.

D. UNCLASSIFIED (Fig. 81)

Tumours in which sex cord and/or stromal elements are present although they cannot be specifically identified as either ovarian or testicular in type.
This category includes the rare "sex cord tumour with annular tubules",¹ which is commonly multifocal and of microscopic size. It is seen disproportionately often in patients with the Peutz-Jeghers syndrome, and is characterized by simple and complex ring-shaped solid tubules containing cells of Sertoli or granulosa type, by the presence of hyaline bodies, and by a tendency to calcify in a manner similar to that of the gonadoblastoma (Fig. 81).

III. LIPID [LIPOID] CELL TUMOURS (Fig. 82–85)

Tumours composed of cells that resemble Leydig, lutein, and adrenal cortical cells, but cannot be identified specifically as any one of the three types.

These tumours are also known as adrenal-like tumours. The cells contain varying amounts of intracellular lipid, and although usually virilizing may be non-functioning. A few have been associated with some of the manifestations of Cushing's syndrome, but none with the complete syndrome or with evidence of cortisol secretion. These tumours are generally thought to be of lutein cell or Leydig cell origin; a derivation from adrenal cortical rests has not been proven in any case. Therefore, although lipid cell tumours are generally considered as a separate group, they may belong more properly within Category II (sex cord stromal tumours). A minority of these neoplasms are malignant.²

IV. GERM CELL TUMOURS

A broad category of tumours including undifferentiated forms; in some tumours extra-embryonic structures predominate; in others immature and/or mature structures that may be derived from any or all of the three embryonic layers (ectoderm, mesoderm, and endoderm) are present.

A. DYSGERMINOMA (Fig. 86–88)

A tumour of uniform appearance composed of large, rounded, clear cells that resemble primordial germ cells both morphologically and histochmically.

The cells may be arranged diffusely or in islands or strands separated by varying amounts of fibrous tissue infiltrated by lymphocytes; granulomas, which may contain Langhans' giant cells, are often present. The cytoplasm of the tumour cells contains glycogen, the presence of which may be of diagnostic aid.

B. ENDODermal SINUS TUMOUR (Fig. 89–93)

A tumour characterized by the presence of a loose vacuolated network of embryonal cells, distinctive perivascular structures resembling the endodermal sinuses of the rat placenta, and both intracellular and extracellular hyaline globules giving a positive periodic acid Schiff reaction.1, 2

This tumour has also been called yolk sac tumour and may contain cysts resembling yolk sac vesicles (polyvesicular vitelline pattern) (Fig. 91 & 92). It is important to distinguish the endodermal sinus tumour from the clear cell [mesonephroid] carcinoma, which has different patterns, lacks endodermal sinuses and hyaline bodies, typically occurs in older women, and has a much better prognosis.

C. EMBRYONAL CARCINOMA

A tumour composed of anaplastic embryonal cells of epithelial appearance growing in a variety of patterns—acinar, tubular, papillary and solid.

This tumour, which is commonly encountered in the testis, is very rare in the ovary, where the endodermal sinus tumour accounts for almost all the highly malignant embryonal epithelial tumours.

D. POLYEMBRYOMA (Fig. 94) 3

A very rare tumour composed predominantly of embryonic bodies.

It is also known as polyembryonic embryoma.

E. CHORIOCARCINOMA (Fig. 95–96)

A rare tumour composed of both cytotrophoblast and syncytiotrophoblast.

2 Tellum, G. (1959) Cancer (Philad.), 12, 1092.
Typically these elements are present only as a part of a more complex germ cell tumour. Besides being of germ cell origin, an ovarian choriocarcinoma may possibly arise in an ovarian pregnancy or may spread to the ovary from another site in the genital tract.

F. TERATOMAS

Tumours that are generally composed of several types of tissue representing two or three embryonic layers.

The structures present may be immature, mature, or both. In occasional cases differentiation is only monodermal or may be evidenced by the exclusive or predominant formation of a single highly specialized type of tissue.

1. *Immature teratoma* [embryonal teratoma] (Fig. 97–99)

A teratoma that contains immature (embryonal) structures.

Mature tissue may be present as well. Although most immature teratomas are predominantly solid, an occasional one is predominantly cystic.

2. *Mature teratoma* [adult teratoma]

A teratoma composed exclusively of mature (adult) structures.

(a) *Solid* (Fig. 100-103)

It is important to differentiate immature and mature solid teratomas because of a striking difference in prognosis; while the former are often clinically malignant, the latter are almost invariably benign.¹ The presence of implants of mature glia as well as mature structures of other types on the peritoneum (Fig. 102–103) has not been associated with a malignant clinical course in the reported cases and *per se* does not warrant a diagnosis of malignancy.²

(b) *Cystic*

(i) *Dermoid cyst* [mature cystic teratoma] (Fig. 104–106): A teratoma characterized by a predominance of one or a few cysts lined by epidermis, accompanied by its appendages.

The tumour often contains other ectodermal, especially neuroectodermal derivatives; elements of endodermal and mesodermal origin are also found with great frequency. Occasionally respiratory epithelium or glia forms a portion of the cyst lining.

(ii) Dermoid cyst with malignant transformation (Fig. 107)

Squamous cell carcinoma is the usual form of malignant change; adeno-carcinoma and sarcoma are much less common, and melanoma is very rare.

3. Monodermal and highly specialized teratomas

(a) Struma ovarii (Fig. 108–110)

A teratoma in which thyroid tissue is exclusively present or constitutes a grossly recognizable component of a more complex teratoma.

The tumour often has the appearance of a follicular adenoma rather than normal thyroid parenchyma. A small number of strumas are malignant on microscopical examination, but only a minority of these have been shown to be clinically malignant. Among the tumours that have been reported as "malignant" struma are those combined with carcinoid (see (c) below).

(b) Carcinoid (Fig. 111 & 112)

A tumour of argentaffin cells.

Besides being associated with a struma, a primary carcinoid may be pure, or relatively pure, or may be part of a complex teratoma. Primary carcinoid tumours must be distinguished from metastases of intestinal origin, which are bilateral in a high proportion of cases, and from granulosa cell tumours. See category VIII below.

(c) Struma ovarii and carcinoid (Fig. 113 & 114)

Tumours composed of thyroid tissue intimately associated with ribbons and islands of carcinoid.

In some cases the carcinoid cells have been shown to contain argentaffin granules. These tumours, which have been called "strumal carcinoids" have not been proved to be clinically malignant.

(d) Others

This category includes the epidermoid cyst, which is lined by epidermis without appendages, the sebaceous gland tumour and a rare tumour resembling the retinal anlage tumour. It is possible also that some mucinous tumours, particularly those containing intestinal-type epithelium, belong in

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this category; for convenience, however, all the mucinous tumours are included under heading I.

G. MIXED FORMS

Tumours consisting of a mixture of one or more of the above types (A-F).

Each component should be identified in the diagnostic term chosen and quantified as far as possible.

V. GONADOBLASTOMA (Fig. 115-117)\(^1\)

A tumour composed of two principal cell types: large germ cells similar to those of the dysgerminoma and seminoma, and small cells resembling immature granulosa and Sertoli cells; in addition, the stroma may contain cells resembling lutein and Leydig cells.

Hyaline bodies that simulate Call-Exner bodies are typically present, and foci of calcification are common. In some tumours the nests composed of the two major cell types are circumscribed, but in others the germ cells transgress the margins of the nests and grow as a dysgerminoma or seminoma. Certain tumours appear in the form of a dysgerminoma or a more highly malignant type of germ cell tumour with only small foci of gonadoblastoma within them or at their margins.

Gonadoblastomas arise almost exclusively in patients with dysgenetic ovaries or testes, most of whom are phenotypic females and almost all of whom are chromatin-negative and have a Y-chromosome.

These tumours have also been called dysgenetic gonadomas and gonocytomas II and III. A gonadoblastoma composed entirely of germ cells and sex cord elements corresponds to the gonocytoma II; if the tumour contains additional cells resembling lutein and Leydig cells, it corresponds to the gonocytoma III.\(^2,3\)

VI. SOFT TISSUE TUMOURS NOT SPECIFIC TO THE OVARY

These should be classified according to Histological Typing of Soft Tissue Tumours (see page 6).

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\(^3\) Teter, J. (1960) Gynaecologia (Basel), 150, 84.
VII. UNCLASSIFIED TUMOURS

Primary ovarian tumours that cannot be placed in any of the categories described above.

VIII. SECONDARY [METASTATIC] TUMOURS (Fig. 118-124)

Metastatic deposits may arise from a wide variety of sources. Carcinomas of the breast, genital tract and gastrointestinal tract and tumours of the haematopoietic system are most commonly encountered.

The Krukenberg tumour (Fig. 118 & 119) is a metastasis of distinctive appearance characterized by the presence of mucus-filled signet-ring cells accompanied by a "sarcoma-like" proliferation of the ovarian stroma. This tumour is usually secondary to a gastric carcinoma, but may originate in any organ in which mucinous carcinomas arise, including the breast and intestine. On rare occasions a tumour with the pattern of a Krukenberg tumour appears to be primary in the ovary.

Metastatic carcinoid tumours are important because the primary tumour may be clinically inapparent and the ovarian metastases may be confused with primary ovarian tumours of several types. The more cellular carcinoid tumours must be distinguished from granulosa cell tumours, whilst those that have elicited an exuberant stromal proliferation should be differentiated from Brenner tumours and adenofibromas (Fig. 123). Gland formation, round nuclei with a coarse chromatin pattern and luminal calcific deposits are of diagnostic aid, but the most specific finding, which is not present in every carcinoid tumour, is a cytoplasmic content of argentaffin granules.

Lymphoma and leukaemia may involve the ovary and grow diffusely or in the form of well-defined nests and cords of cells, simulating the pattern of a carcinoma (Fig. 124). Burkitt’s lymphoma is a type that commonly involves the ovaries.¹

IX. TUMOUR-LIKE CONDITIONS

A. PREGNANCY LUTEOMA [NODULAR THECA-LUTEIN HYPERPLASIA] (Fig. 125-128).²

Single or multiple nodules of lutein cells typically developing during an otherwise normal pregnancy.

These nodules are usually discovered incidentally in the last trimester when a caesarean section is being performed, and they may attain a diameter of 15 cm or more. Mitoses may be frequent. Pregnancy luteomas are probably not autonomous tumours, but are dependent on chorionic gonadotrophin stimulation. Occasionally they are virilizing. In a few cases microscopic examination has disclosed degeneration postpartum (Fig. 128).

The pregnancy luteoma should be distinguished from the corpus luteum of pregnancy, the Leydig cell tumour and the lipid cell tumour. The corpus luteum of pregnancy has a festooned margin and contains both granulosa and theca lutein cells; colloid droplets and small foci of calcification are typically present. An association with pregnancy, multiplicity, and mitotic activity are helpful clues in differentiating the pregnancy luteoma from the Leydig cell tumour and the lipid cell tumour, but such a distinction may be difficult in some cases.

B. HYPERPLASIA OF OVARIAN STROMA AND HYPERTHECOSIS (Fig. 129–132)

Bilateral tumour-like enlargements composed of proliferating ovarian stroma; the presence of scattered clusters of lutein cells in the hyperplastic stroma warrants the diagnosis of hypertecosis (luteinization of ovarian stroma).

The exclusive or predominant cell type is a spindle cell that is smaller than that of the fibroma and produces less collagen. These lesions are almost always bilateral, whereas the thecoma is almost always unilateral. Hypertecosis may be associated with endocrine manifestations, which are usually androgenic, but occasionally oestrogenic.

C. MASSIVE OEDEMA OF THE OVARY (Fig. 133)

Marked enlargement of one or both ovaries by an accumulation of oedema fluid in the stroma, separating normal follicular structures.

In some cases the stroma contains lutein cells and the patient is virilized.

D. SOLITARY FOLLICLE CYST AND CORPUS LUTEUM CYST


E. Multiple follicle cysts [polycystic ovaries, Stein-Leventhal ovaries]

F. Multiple luteinized follicle cysts and/or corpora lutea [hyperreactio luteinalis] 1

These may be associated with hydatidiform mole or choriocarcinoma of the uterus, erythroblastosis fetalis, normal twin or singleton pregnancy, and the administration of ovulation-inducing drugs.

The involved ovaries may be of enormous size and undergo torsion, haemorrhage, infarction, or rupture. The disorder may also be complicated by ascites, hydrothorax, and shock. These ovarian enlargements are important to recognize because they simulate neoplasms, but surgical removal is not always necessary.

G. Endometriosis (Fig. 28 & 29)

The relation of endometriosis to ovarian tumours is discussed on page 39.

H. Surface-epithelial inclusion cysts [germinatal inclusion cysts] (Fig. 134)

Microscopic cysts in the stroma derived from the surface epithelium.

These may be precursors of some of the cystic common epithelial tumours. Typically they are lined by epithelium of serous or endometrioid type.

I. Simple cysts

Cysts without an identifiable lining.

Some of these may be cystadenomas of various types and others, follicle cysts, the lining of which has been destroyed.

J. Inflammatory lesions

These include, among others, bacterial infections of the ovary, which are usually associated with salpingitis, echinococcal cysts, and fibroxanthomas.

K. Parovarian cysts

These may be of müllerian or mesonephric derivation. Tumours with the microscopic features of various ovarian tumours are also encountered occasionally in a parovarian location; it is possible that some of these tumours arise in accessory ovarian tissue.
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Unless otherwise stated, all the preparations shown in the photomicrographs reproduced on the following pages were stained with haematoxylin-eosin or haematoxylin-phloxine.
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Primary in colon
Fig. 121. Metastatic adenocarcinoma
Primary in colon. Luteinization of stroma. Associated with endometria hyperplasia.
Patient 78 years old

Fig. 122. Metastatic carcinoid
Primary in ileum. Acinus formation and calcification
Fig. 123. Metastatic carcinoid
Primary in ileum. Abundant stroma

Fig. 124. Malignant lymphoma
Cord-like pattern
Fig. 125. **Pregnancy luteoma**
Two nodules adjacent to corpus luteum

Fig. 126. **Pregnancy luteoma**
Fig. 127. Pregnancy luteoma
Pools of colloid-like material

Fig. 128. Pregnancy luteoma
Degeneration six weeks post partum
Fig. 129. Hyperplasia of ovarian stroma

Fig. 130. Hyperthecosis
Islands of lipid-rich lutein cells in stroma
Fig. 131. Hyperthecosis

Fig. 132. Hyperthecosis
Fig. 133. Massive oedema
Follicles separated by oedematous stroma

Fig. 134. Surface-epithelial inclusion cysts